



# U.S. Department of Health & Human Services

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**Food and Drug Administration**

## SAVE REQUEST

**USER:** (cwf)  
**FOLDER:** K121700 - 388 pages  
**COMPANY:** ULTHERA, INC. (ULTHERA)  
**PRODUCT:** FOCUSED ULTRASOUND FOR TISSUE HEAT OR MECHANICAL CELLULAR DISRUPTION (OHV)  
**SUMMARY:** Product: ULTHERA SYSTEM

**DATE REQUESTED:** Jun 13, 2014

**DATE PRINTED:** Jun 13, 2014

**Note:** Printed



K121700

1/2

OCT 2 2012

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## 510(k) Summary

This 510(k) Summary for the Ulthera® System is submitted in accordance with the requirements of the Safe Medical Device Act (SMDA) of 1990 and follows the Office of Device Evaluation (ODE) guidance concerning the organization and content of a 510(k) summary.

**Applicant:** Ulthera, Inc.

**Address:** 2150 South Country Club Drive, Suite 21  
Mesa, AZ 85210

**Contact Person:** Suzon Lommel, VP of Regulatory & Quality Affairs

**Telephone:** 480-649-4069

**Fax:** 480-619-4071

**Submission Date:** June 7, 2012

**Device Trade Name:** Ulthera® System

**Common Name:** Focused Ultrasound Stimulator Use System for Aesthetic Use

**Classification:** Regulatory Class II

**Classification Name:** Focused Ultrasound Stimulator Use System for Aesthetic Use

**Product Code:** OHV

**Legally Marketed Name:** Ulthera® System

**Predicates:** 510(k): #K072505

**Applicable Guidance:** The *Class II Special Controls Guidance Document: Focused Ultrasound Stimulator System for Aesthetic Use* was developed in response to Ulthera's DeNovo submission and 510(k) clearance K072505 for the Ulthera System.



K121700 2/2

- Device Description:** The Ulthera® System consists of the following components:
- Ulthera® Control Unit
  - Handpiece
  - Transducers
- Indications for Use:** The Ulthera® System is indicated for use as a non-invasive dermatological aesthetic treatment to:
- lift the eyebrow (current cleared indication)
  - lift lax submental (beneath the chin) and neck tissue (requested expanded indication)
- Performance Data:** To support the expanded indication, the Ulthera® System was evaluated in an open-label clinical trial investigating the clinical response following treatment with the Ulthera® System to achieve lifting of lax submental (beneath the chin) and neck tissue. Improvement was evaluated through quantitative assessment, qualitative assessment and patient satisfaction questionnaires. There were 51/70 patients that had an improvement of  $\geq 20$  mm<sup>2</sup> in lift, of these patients 84.3% were identified as showing improvement by masked evaluators. The adverse events resulting from treatment with the Ulthera® System during this study were mild, short-lived in duration, and resolved without incident. There were no serious adverse events (SAEs) or unanticipated adverse device effects (UADEs) related to treatment with the Ulthera® System.
- Conclusion:** Based on the design, materials, principle of operation, and intended use, the Ulthera® System is substantially equivalent to the legally marketed predicate device.





## DEPARTMENT OF HEALTH &amp; HUMAN SERVICES

Public Health Service

Food and Drug Administration  
10903 New Hampshire Avenue  
Document Control Room - WO66-G609  
Silver Spring, MD 20993-0002

Ulthera, Incorporated  
% Ms. Suzon Lommel  
Vice President of Regulatory & Quality Affairs  
2150 South Country Club Drive, Suite 21  
Mesa, Arizona 85210

OCT  
2 2012

Re: K121700  
Trade/Device Name: Ulthera® System  
Regulation Number: 21 CFR 878.4590  
Regulation Name: Focused ultrasound stimulator system for aesthetic use  
Regulatory Class: Class II  
Product Code: OHV  
Dated: August 1, 2012  
Received: August 3, 2012

Dear Ms. Lommel:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical

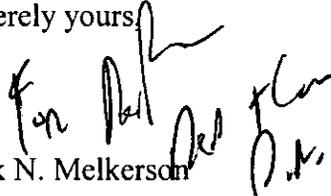
Page 2 - Ms. Suzon Lommel

device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please go to <http://www.fda.gov/AboutFDA/CentersOffices/CDRH/CDRHOffices/ucm115809.htm> for the Center for Devices and Radiological Health's (CDRH's) Office of Compliance. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to <http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm> for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address <http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm>.

Sincerely yours,



Mark N. Melkerson  
Director  
Division of Surgical, Orthopedic  
and Restorative Devices  
Office of Device Evaluation  
Center for Devices and  
Radiological Health

Enclosure

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## Indications for Use Statement

510(k) Number: K121700

Device Name: Ulthera® System

### Indications for Use:

The Ulthera® System is indicated for use as a non-invasive dermatological aesthetic treatment to:

- lift the eyebrow
- lift lax submental (beneath the chin) and neck tissue

Prescription Use  AND/OR Over-The-Counter Use   
(Part 21 CFR 801 Subpart D) (21 CFR 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

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Concurrence of CDRH, Office of Device Evaluation (ODE)

Neil R. Ogden for mxm  
(Division Sign-Off)  
Division of Surgical, Orthopedic,  
and Restorative Devices

510(k) Number K121700



K121700/A1



October 8, 2012

Document Mail Center (HFZ-401)  
Center for Devices and Radiological Health  
Food and Drug Administration  
10903 New Hampshire Avenue  
Silver Spring, MD 20993

FDA CDRH DMC

OCT 09 2012

Received

Re: Ulthera® System - K121700 Add to File

K30

Dear Sir or Madam:

The information provided in this submission is a response to agency request for an updated 510(k) Summary for the Ulthera 510(k) submission, K121700.

The device name is: Ulthera® System.

Sponsor contact information: Ulthera, Inc.  
2150 S. Country Club Drive, Suite 21  
Mesa, AZ 85210-6809  
Contact: Suzon Lommel  
Phone: 480-619-4069  
FAX: 480-619-4071  
Email: [s.lommel@ulthera.com](mailto:s.lommel@ulthera.com)

The indications for use of the device are as follows:

The Ulthera® System is indicated for use as a non-invasive dermatological aesthetic treatment to:

- lift the eyebrow (current cleared indication)
- lift lax submental (beneath the chin) and neck tissue (requested expanded indication)

An exact duplicate of all documentation provide in hard copy is also provided in electronic format in the form of a CD provided with each copy of the response.

Sincerely,

Suzon Lommel  
Vice President Regulatory & Quality Affairs  
Ulthera, Inc.  
Email: [s.lommel@ulthera.com](mailto:s.lommel@ulthera.com)



## DEPARTMENT OF HEALTH &amp; HUMAN SERVICES

Public Health Service

Food and Drug Administration  
 10903 New Hampshire Avenue  
 Document Control Room - WO66-G609  
 Silver Spring, MD 20993-0002

Ulthera, Incorporated  
 % Ms. Suzon Lommel  
 Vice President of Regulatory & Quality Affairs  
 2150 South Country Club Drive, Suite 21  
 Mesa, Arizona 85210

OCT 2 2012

Re: K121700

Trade/Device Name: Ulthera® System  
 Regulation Number: 21 CFR 878.4590  
 Regulation Name: Focused ultrasound stimulator system for aesthetic use  
 Regulatory Class: Class II  
 Product Code: OHV  
 Dated: August 1, 2012  
 Received: August 3, 2012

Dear Ms. Lommel:

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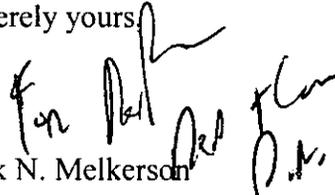
Page 2 - Ms. Suzon Lommel

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Sincerely yours,



Mark N. Melkerson  
Director  
Division of Surgical, Orthopedic  
and Restorative Devices  
Office of Device Evaluation  
Center for Devices and  
Radiological Health

Enclosure

---

## Indications for Use Statement

510(k) Number: K121700

Device Name: Ulthera® System

### Indications for Use:

The Ulthera® System is indicated for use as a non-invasive dermatological aesthetic treatment to:

- lift the eyebrow
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Prescription Use   x   AND/OR Over-The-Counter Use         
(Part 21 CFR 801 Subpart D) (21 CFR 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

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Concurrence of CDRH, Office of Device Evaluation (ODE)

Neil R. Ogden for mxm  
(Division Sign-Off)  
Division of Surgical, Orthopedic,  
and Restorative Devices

510(k) Number   K121700  





## DEPARTMENT OF HEALTH &amp; HUMAN SERVICES

## Public Health Service

U.S. Food and Drug Administration  
 Center for Devices and Radiological Health  
 Document Control Center WO66-G609  
 10903 New Hampshire Avenue  
 Silver Spring, MD 20993-0002

August 03, 2012

ULTHERA, INC.  
 2150 South Country Club Drive  
 Suite 21  
 Mesa, ARIZONA 85210  
 ATTN: SUZON LOMMEL

510k Number: K121700

Product: ULTHERA SYSTEM

The additional information you have submitted has been received.

We will notify you when the processing of this submission has been completed or if any additional information is required. Please remember that all correspondence concerning your submission **MUST** be sent to the Document Mail Center at the above letterhead address. Correspondence sent to any address other than the one above will not be considered as part of your official premarket notification submission. Also, please note the new Blue Book Memorandum regarding Fax and E-mail Policy entitled, "Fax and E-Mail Communication with Industry about Premarket Files Under Review. Please refer to this guidance for information on current fax and e-mail practices at <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089402.htm>. On August 12, 2005 CDRH issued the Guidance for Industry and FDA Staff: Format for Traditional and Abbreviated 510(k)s. This guidance can be found at <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm084365.htm>. Please refer to this guidance for assistance on how to format an original submission for a Traditional or Abbreviated 510(k).

The Safe Medical Devices Act of 1990, signed on November 28, states that you may not place this device into commercial distribution until you receive a letter from FDA allowing you to do so. As in the past, we intend to complete our review as quickly as possible. Generally we do so in 90 days. However, the complexity of a submission or a requirement for additional information may occasionally cause the review to extend beyond 90 days. Thus, if you have not received a written decision or been contacted within 90 days of our receipt date you may want to check with FDA to determine the status of your submission.

**Please ensure that whether you submit a 510(k) Summary as per 21 CFR 807.92, or a 510(k) Statement as per 21 CFR 807.93, it meets the content and format regulatory requirements.**

If you have procedural questions, please contact the Division of Small Manufacturers International and Consumer Assistance (DSMICA) at (301)796-7100 or at their toll-free number (800)638-2041, or contact the 510k staff at (301)796-5640.

Sincerely,

510(k) Staff

**Mcdonald, Lisa \***

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**From:** Microsoft Outlook  
**To:** s.lommel@ulthera.com  
**nt:** Friday, August 03, 2012 2:20 PM  
**ubject:** Relayed: K121700 AI Letter

**Delivery to these recipients or distribution lists is complete, but delivery notification was not sent by the destination:**

s.lommel@ulthera.com

Subject: K121700 AI Letter

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Sent by Microsoft Exchange Server 2007

K121700 V-1



## DEPARTMENT OF HEALTH &amp; HUMAN SERVICES

## Public Health Service

U.S. Food and Drug Administration  
Center for Devices and Radiological Health  
Document Control Center WO66-G609  
10903 New Hampshire Avenue  
Silver Spring, MD 20993-0002

July 09, 2012

ULTHERA, INC.  
2150 South Country Club Drive  
Suite 21  
Mesa, ARIZONA 85210  
ATTN: SUZON LOMMEL

510k Number: K121700

Product: ULTHERA SYSTEM

On Hold As of 7/6/2012

We are holding your above-referenced Premarket Notification (510(k)) for 30 days pending receipt of the additional information that was requested by the Office of Device Evaluation. Please remember that all correspondence concerning your submission MUST cite your 510(k) number and be sent in duplicate to the Document Mail Center at the above letterhead address. Correspondence sent to any address other than the one above will not be considered as part of your official premarket notification submission. Also, please note the new Blue Book Memorandum regarding Fax and E-mail Policy entitled, "Fax and E-Mail Communication with Industry about Premarket Files Under Review. Please refer to this guidance for information on current fax and e-mail practices at

<http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089402.htm>.

The deficiencies identified represent the issues that we believe need to be resolved before our review of your 510(k) submission can be successfully completed. In developing the deficiencies, we carefully considered the statutory criteria as defined in Section 513(i) of the Federal Food, Drug, and Cosmetic Act for determining substantial equivalence of your device. We also considered the burden that may be incurred in your attempt to respond to the deficiencies. We believe that we have considered the least burdensome approach to resolving these issues. If, however, you believe that information is being requested that is not relevant to the regulatory decision or that there is a less burdensome way to resolve the issues, you should follow the procedures outlined in the "A Suggested Approach to Resolving Least Burdensome Issues" document. It is available on our Center web page at: <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overview/MedicalDeviceProvisionsofFDAModer nizationAct/ucm136685.htm>.

If after 30 days the additional information (AI), or a request for an extension of time, is not received, we will *discontinue review of your submission and proceed to delete your file from our review system (21 CFR 807.87(l))*. Please note our guidance document entitled, "Guidance for Industry and FDA Staff, FDA and Industry Actions on Premarket Notification (510(k)) Submissions: Effect on FDA Review Clock and Performance Assessment". If the submitter does submit a written request for an extension, FDA will permit the 510(k) to remain on hold for up to a maximum of 180 days from the date of the AI request. The purpose of this document is to assist agency staff and the device industry in understanding how various FDA and industry actions that may be taken on 510(k)s should affect the review clock for purposes of meeting the Medical Device User Fee and Modernization Act. You may review this document at

<http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089735.htm>. Pursuant to 21 CFR 20.29, a copy of your 510(k) submission will remain in the Office of Device Evaluation. If you then wish to resubmit this 510(k) notification, a new number will be assigned and your submission will be considered a new premarket notification submission.

Please remember that the Safe Medical Devices Act of 1990 states that you may not place this device into commercial distribution until you receive a decision letter from FDA allowing you to do so.

If you have procedural questions, please contact the Division of Small Manufacturers International and Consumer Assistance (DSMICA) at (301)796-7100 or at their toll-free number (800)638-2041, or contact the 510k staff at (301)796-5640.

Sincerely yours,

Marjorie Shulman  
Director, 510(k) Program  
Premarket Notification Section  
Office of Device Evaluation  
Center for Devices and Radiological Health

\* \* \* COMMUNICATION RESULT REPORT ( JUL. 9. 2012 12:24PM ) \* \* \*

FAX HEADER 1:  
FAX HEADER 2:

| TRANSMITTED/STORED :<br>F MODE | JUL. 9. 2012 12:15PM<br>OPTION | ADDRESS      | RESULT  | PAGE |
|--------------------------------|--------------------------------|--------------|---------|------|
| 7377 MEMORY TX                 |                                | 914896194071 | E-3) 3) | 0/2  |

REASON FOR ERROR  
E-1) HANG UP OR LINE FAIL  
E-3) NO ANSWER

E-2) BUSY  
E-4) NO FACSIMILE CONNECTION



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

U.S. Food and Drug Administration  
Center for Devices and Radiological Health  
Document Control Center WO66-G609  
10903 New Hampshire Avenue  
Silver Spring, MD 20993-0002

July 09, 2012

ULTHERA, INC.  
2150 South Country Club Drive  
Suite 21  
Mesa, ARIZONA 85210  
ATTN: SUZON LOMMEL

510k Number: K121700  
Product: ULTHERA SYSTEM  
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\* \* \* COMMUNICATION RESULT REPORT ( JUL. 9. 2012 11:33AM ) \* \* \*

FAX HEADER 1:  
FAX HEADER 2:

| TRANSMITTED/STORED<br>F MODE | JUL. 9. 2012 11:25AM<br>OPTION | ADDRESS      | RESULT  | PAGE |
|------------------------------|--------------------------------|--------------|---------|------|
| 7361 MEMORY TX               |                                | 914896194071 | E-3) 3) | 0/2  |

REASON FOR ERROR  
E-1) HANG UP OR LINE FAIL  
E-3) NO ANSWER

E-2) BUSY  
E-4) NO FACSIMILE CONNECTION



## DEPARTMENT OF HEALTH &amp; HUMAN SERVICES

## Public Health Service

U.S. Food and Drug Administration  
Center for Devices and Radiological Health  
Document Control Center WC66-G609  
10903 New Hampshire Avenue  
Silver Spring, MD 20993-0002

July 09, 2012

ULTHERA, INC.  
2150 South Country Club Drive  
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ATTN: SUZON LOMMEL

510k Number: K121700  
Product: ULTHERA SYSTEM  
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**COVER SHEET MEMORANDUM**

**From:** Reviewer Name Richard P. Feiten  
**Subject:** 510(k) Number K121700  
**To:** The Record

Please list CTS decision code AI

- Refused to accept (Note: this is considered the first review cycle, See Screening Checklist [http://eroom.fda.gov/eRoomReq/Files/CDRH3/CDRHPremarketNotification510kProgram/0\\_5631/Screening%20Checklist%207%202%2007.doc](http://eroom.fda.gov/eRoomReq/Files/CDRH3/CDRHPremarketNotification510kProgram/0_5631/Screening%20Checklist%207%202%2007.doc))
- Hold (Additional Information or Telephone Hold). Electronics Mail 7/9/2012
- Final Decision (SE, SE with Limitations, NSE (select code below), Withdrawn, etc.).

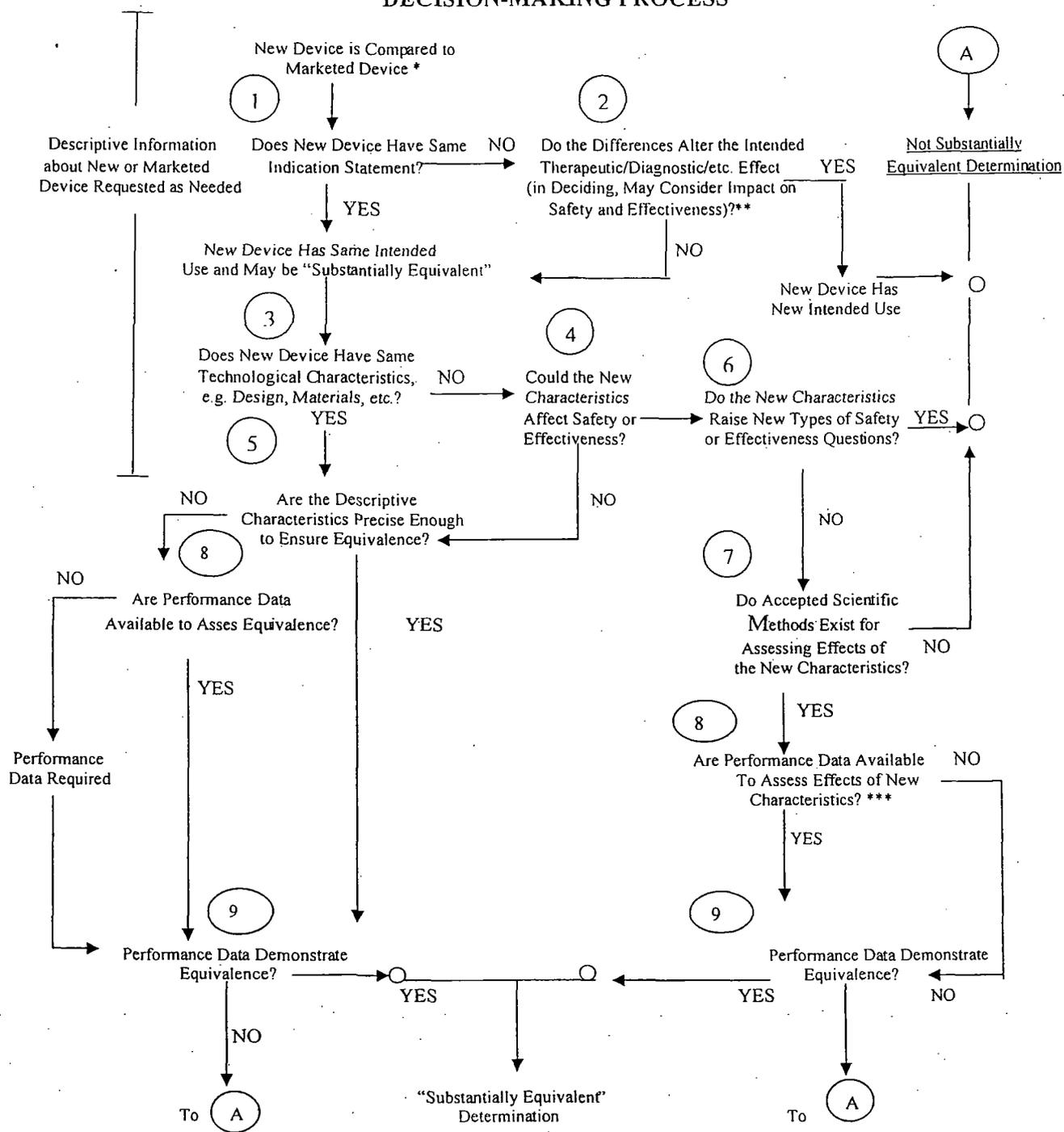
Not Substantially Equivalent (NSE) Codes

- NO NSE for lack of predicate
- NI NSE for new intended use
- NQ NSE for new technology that raises new questions of safety and effectiveness
- NU NSE for new intended use AND new technology raising new questions of safety and effectiveness
- NP NSE for lack of performance data
- NS NSE no response
- NL NSE for lack of performance data AND no response
- NM NSE pre-amendment device call for PMAs (515i)
- NC NSE post-amendment device requires PMAs
- NH NSE for new molecular entity requires PMA
- TR NSE for transitional device

| Please complete the following for a final clearance decision (i.e., SE, SE with Limitations, etc.):  |                                      | YES | NO |
|--|--------------------------------------|-----|----|
| Indications for Use Page   | Attach IFU                           | X   |    |
| 510(k) Summary /510(k) Statement   | Attach Summary                       | X   |    |
| Truthful and Accurate Statement.   | Must be present for a Final Decision | X   |    |
| Is the device Class III?   |                                      |     | X  |
| If yes, does firm include Class III Summary?   | Must be present for a Final Decision |     | X  |
| Does firm reference standards?<br>(If yes, please attach form from <a href="http://www.fda.gov/opacom/morechoices/fdaforms/FDA-3654.pdf">http://www.fda.gov/opacom/morechoices/fdaforms/FDA-3654.pdf</a> )   |                                      |     | NA |
| Is this a combination product?<br>(Please specify category <u>NA</u> , see <a href="http://eroom.fda.gov/eRoomReq/Files/CDRH3/CDRHPremarketNotification510kProgram/0_413b/COMBINATION%20PRODUCT%20ALGORITHM%20(REVISED%203-12-03).DOC">http://eroom.fda.gov/eRoomReq/Files/CDRH3/CDRHPremarketNotification510kProgram/0_413b/COMBINATION%20PRODUCT%20ALGORITHM%20(REVISED%203-12-03).DOC</a> ) |                                      |     |    |
| Is this a reprocessed single use device?<br>(Guidance for Industry and FDA Staff – MDUFMA - Validation Data in 510(k)s for Reprocessed Single-Use Medical Devices, <a href="http://www.fda.gov/cdrh/ode/guidance/1216.html">http://www.fda.gov/cdrh/ode/guidance/1216.html</a> )   |                                      |     | X  |
| Is this device intended for pediatric use only?  |                                      |     | X  |
| Is this a prescription device? (If both prescription & OTC, check both boxes.)   |                                      | X   |    |
| Did the application include a completed FORM FDA 3674, Certification with Requirements of ClinicalTrials.gov Data Bank?  |                                      |     | NA |
| Is clinical data necessary to support the review of this 510(k)?   |                                      |     | X  |
| For United States-based clinical studies <b>only</b> : Did the application include a completed FORM FDA 3674, Certification with Requirements of ClinicalTrials.gov Data Bank? (If study was   |                                      |     | NA |



### 510(k) "SUBSTANTIAL EQUIVALENCE" DECISION-MAKING PROCESS



\* 510(k) Submissions compare new devices to marketed devices. FDA requests additional information if the relationship between marketed and "predicate" (pre-Amendments or reclassified post-Amendments) devices is unclear.

\*\* This decision is normally based on descriptive information alone, but limited testing information is sometimes required.

\*\*\* Data maybe in the 510(k), other 510(k)s, the Center's classification files, or the literature.



## DEPARTMENT OF HEALTH AND HUMAN SERVICES

## MEMORANDUM

Food and Drug Administration  
Office of Device Evaluation  
9200 Corporate Boulevard  
Rockville, MD 20850

**Premarket Notification [510(k)] Review  
Traditional/Abbreviated**

**K121700** \_\_\_\_\_

Date: July 5, 2012

To: The Record

From: Richard P. Felten

Office: ODE

Division: DSORD

510(k) Holder: Ulthera, Inc.

Device Name: Ulthera System

Contact: Suzon Lommel

Phone: 480-649-4069

Fax: 480-619-4071

Email: s.lommel@ulthera.com

**I. Purpose and Submission Summary**

The 510(k) holder would like to introduce add a new indication for use to their already legally marketed focused ultrasound system identified as the Ulthera System.

**II. Administrative Requirements**

|   | Yes | No | N/A |
|---|-----|----|-----|
| Indications for Use page (Indicate if: Prescription or OTC) | X   |    |     |
| Truthful and Accuracy Statement                             | X   |    |     |
| 510(k) Summary or 510(k) Statement                          | X   |    |     |
| Standards Form  |     |    | X   |

**III. Device Description**

|   | Yes | No | N/A |
|---|-----|----|-----|
| Is the device life-supporting or life sustaining?         |     | X  |     |
| Is the device an implant (implanted longer than 30 days)? |     | X  |     |
| Does the device design use software?                      | X   |    |     |
| Is the device sterile?                                    |     | X  |     |
| Is the device reusable (not reprocessed single use)?      | X   |    |     |
| Are "cleaning" instructions included for the end user?    |     |    |     |

The Ulthera System is a focused ultrasound system that is designed to deliver focused ultrasound to a fixed depth to provided localized coagulation for the purpose of production of new collagen that is

intended to result in tissue tightening for the requested indications for use.

**IV. Indications for Use**

The Ulthera System is presently legally marketed for the indication for use of eyebrow lift. The company is now requesting marketing clearance for the indications of "lift lax submental (beneath the chin) and neck tissue" and "lift lax tissue to achieve a desired aesthetic effect for the full face and neck". The "desired aesthetic effect" indication is problematic and it is doubtful at this time whether or not ODE would grant this indication for use.

**V. Predicate Device Comparison**

This is the identical device granted marketing approval through a de Novo reclassification that was approved by letter dated September 11, 2009. Subsequent to this approval the company has expanded the number of transducers via documentation to file. The new transducers include a narrower version of the de Novo approved DS 7-3.0 device and two new transducers DS 10-1.5 and DS 10-1.5N which have a depth of penetration of only 1.5 mm and include the full size and narrow version.

**VI. Labeling**

The User Manual is essentially the same as was originally reviewed in K072505 except for that appears to be an expanded recommended treatment parameter table. This table includes recommendations for infraorbital treatments and includes the new versions of the ultrasound transducers. Also there are two versions of these recommendations, 5.0 and 5.0 Plus. The Plus version has slightly higher number of lines. The company will be asked to provide information to support this difference between the two versions of treatment guidelines.

**VII. Sterilization/Shelf Life/Reuse**

The transducers are sold non-sterile.

**VIII. Biocompatibility**

The devices are the same as described in K072505 and the materials being used have not changed therefore there are no biocompatibility issues.

**IX. Software**

This is unchanged from K072505.

|                                       |  |                      |
|---------------------------------------|--|----------------------|
| Version:                              |  |                      |
| Level of Concern:                     |  |                      |
|                                       |  | <b>Yes</b> <b>No</b> |
| Software description:                 |  |                      |
| Device Hazard Analysis:               |  |                      |
| Software Requirements Specifications: |  |                      |
| Architecture Design Chart:            |  |                      |
| Design Specifications:                |  |                      |
| Traceability Analysis/Matrix:         |  |                      |
| Development:                          |  |                      |
| Verification & Validation Testing:    |  |                      |
| Revision level history:               |  |                      |
| Unresolved anomalies:                 |  |                      |

**X. Electromagnetic Compatibility and Electrical, Mechanical and Thermal Safety**

This is unchanged from K072505.

**XI. Performance Testing – Bench**

N/A

**XII. Performance Testing – Animal**

N/A

**XIII. Performance Testing – Clinical**

The company has provided clinical data to support their request for the expansion of their indication for use to now include lift lax submental and neck tissue. The data was previously presented in K110007 and found not adequate thus this 510(k) was determined to be NSE for lack of performance data. The major problem with the data as presented in K11007 was that the method used to provide quantitative values for submental and neck lift relied on photographs. There was a relatively large loss of data since the photographic system used by the company cropped part of the photographs which prevented quantitative measurement of change. Also the data showed a number of subjects having improvement on one side but not the other. Because of small numbers of apparent success out of a relatively small number of measurable subjects it was determined that the data was not adequate to support the proposed change in indications.

The clinical data provided in this study is the same data set with a new method of measure area of change for submental and neck lift. The new method avoids the issues of photograph cropping and therefore all 70 subjects enrolled into the study can be analyzed.

The clinical data used for support is based on 70 evaluable subjects ranging in age from 35-60 years. Of the subjects enrolled into the study 57 were female and 13 were male. Enrolled patients include Fitzpatrick Skin type I-V with the majority of subjects being type II and III. The company has stated that the treatment targeted the lower face and neck with treatment exposure using up to a 25 mm line of coagulation spots with the distance between spots being 1.5 mm. Follow-ups were at 2, 3, and 6 months with photographic evaluation by blinded evaluators for efficacy being at 3 months and patient satisfaction questionnaires being completed at 3.

The company has stated that the Primary Outcome Measure for the study was improvement in overall lift and tightening of tissue determined by qualitative assessment at three months compared to baseline based on a masked reviewer assessment. The Secondary Outcome Measure was evaluation of improvement in jawline definition and submental skin laxity at three months compared to baseline based on the consensus of the three masked reviewers and patient satisfaction by scores on a patient satisfaction questionnaire at three months post-treatment.

The company has also provided quantitative values for the amount of lift occurring by comparing baseline submental areas at baseline to the same area 3 months after last treatment. The company has stated that if the amount of change between baseline and 3 months is less than 10 mm<sup>2</sup> this would be considered a failure. The company stated that this is a visibly observable change but has not provided any basis for making this statement. The company has not stated whether or not the quantitative measurement values were Primary or Secondary endpoint.

The company has also conducted a patient satisfaction questionnaire at the end of the study. The company claims greater than 60% satisfaction but has not provided the individual patient data for this endpoint.

The company will be requested to provide a table for each individual subject showing the absolute amount of change in submental area; the patient's self satisfaction rating; and the results of the blinded evaluation of photographs for each subject. An Agency decision on whether or not this treatment has improved the definition of the submental area will be based on number of individual subjects showing success for all three of these endpoints. (see attached for a more detailed review of the clinical data)

**XIV. Substantial Equivalence Discussion**

|  | Yes | No |  |
|--|-----|----|--|
| 1. Same Indication Statement?  |     |    | If <b>YES</b> = Go To 3                                  |
| 2. Do Differences Alter The Effect Or Raise New Issues of Safety Or Effectiveness? |     |    | If <b>YES</b> = Stop <b>NSE</b>                          |
| 3. Same Technological Characteristics?   |     |    | If <b>YES</b> = Go To 5                                  |
| 4. Could The New Characteristics Affect Safety Or Effectiveness?                   |     |    | If <b>YES</b> = Go To 6                                  |
| 5. Descriptive Characteristics Precise Enough?                                     |     |    | If <b>NO</b> = Go To 8<br>If <b>YES</b> = Stop <b>SE</b> |
| 6. New Types Of Safety Or Effectiveness Questions?                                 |     |    | If <b>YES</b> = Stop <b>NSE</b>                          |
| 7. Accepted Scientific Methods Exist?  |     |    | If <b>NO</b> = Stop <b>NSE</b>                           |
| 8. Performance Data Available?   |     |    | If <b>NO</b> = Request Data                              |
| 9. Data Demonstrate Equivalence?   |     |    | Final Decision:  |

**XV. Deficiencies**

The following deficiencies have been identified in our review of this application:

1. You have stated that a 10 mm<sup>2</sup> is a visibly observable change and therefore those sites having less than a 10 mm<sup>2</sup> change would be considered a failure. Please provide the basis for this statement since such a small change appears not to be easily observable.
2. Please clarify in the individual data table, Table 20-4, whether or not both sides of the subjects reported as having less than 10 mm<sup>2</sup> change actually had less on both sides or were marked as less based only on a single side failing,
3. You have requested an indication for use of "lift lax tissue to achieve a desired aesthetic effect for full face and neck". It is not clear exactly what this indication for use is measuring or how you would determine "a desired aesthetic effect". Please provide additional discussion of what this indication for use is defining and how you would determine success for this indication for use.
4. Please expand the Performance section of the 510(k) Summary. According to 21 CFR 807.92(b)(2) the 519(k) Summary should include information on patient population tested; discussion of safety and effectiveness data with references to adverse effects and complications observed; and any other information that may be relevant to the substantial equivalence determination.
5. Please describe the process used in selecting the photographs used for the 2 month validation testing.
6. The use of Quantitative analysis is not listed under either the Primary or Secondary Outcome Measure. Please indicate whether or not the Quantitative measurements are a Primary or Secondary endpoint. Please be advised that in reviewing your application the Agency will look at all endpoints as a combined effectiveness result for each individual subject.

- 7. Please provide a copy of the patient satisfaction questionnaire and the individual patients responses to the questionnaire.
- 8. Please provide a table listing the individual subjects with blinded assessment; quantitative lift value; and patient satisfaction values to show if each individual subject is a success across the board.
- 9. The Operator Manual has two tables of suggested Treatment Guidelines identified as 5.0 and 5.0 Plus. It is not clear what is the basis for the guidelines. The Ulthera System is presently cleared for eyebrow lift only and the new requested indication is for submental and neck lift. The charts include infraorbital and orbit treatment which do not appear to be compatible with eyebrow lift or treatment of the submental or neck tissue. Also the 5.0 Plus recommendations contain an increase in number of lines for each of the 5.0 recommendations. Please provide information explaining the basis for the recommended Guidelines including the increase in number of lines for the 5.0 Plus table.
- 10. The narrative on page 77 and 78 under section 20.4.2.1 does not seem to make sense. Page 77 appears to be describing how the unmasked evaluation will be performed but the top of page 78 begins with a statement about each blinded assessor, yet section 20.4.2.2 at the bottom of page 78 is titled Masked Assessment. Please clarify these sections.

**XVI. Contact History**

The above list of deficiencies will be communicated by electronic mail on July 6, 2012 to the contact person for this application Suzon Lommel. Ms. Lommel will also be contacted by telephone to discuss the issues and will be informed that the application is being placed on HOLD.

**XVII. Recommendation HOLD**

Regulation Number: 21 CFR 878.4590  
Regulation Name: Focused Ultrasound Stimulator System for Aesthetic Use  
Regulatory Class: Class II,  
Product Code: OHV

\_\_\_\_\_  
Reviewer

*July 5, 2012*  
\_\_\_\_\_  
Date

\_\_\_\_\_  
Branch Chief

\_\_\_\_\_  
Date

July 2, 2012

Review of K121700

Submitted by Ulthera, Inc.

Reviewed by Richard P. Felten, DSORD, GSDB

This Premarket Notification (510(k)) has been submitted by Ulthera to expand their indications for use for their focused ultrasound system. The device is presently authorized for marketing of their system through an approval granted to their de Novo petition. The order classifying the Ulthera System into Class II was issued by letter dated September 11, 2009 with a corrected letter dated June 9, 2011. The specific indication for use granted in this approval was for eye brow lift.

In the stand alone indication for use submitted with this application the company has provided as the already granted indication "lift the eyebrow". The new indications being requested are:

1. lift lax submental (beneath the chin) and neck tissue
2. lift lax tissue to achieve a desired aesthetic effect for the full face and neck.

The second new indication for use is not acceptable. It appears that the company has taken the term "to achieve a desired aesthetic effect" from the approval order for their de Novo. In constructing this order the wording used for the indication for use for the Ulthera System was "is indicated for use as a non-invasive dermatological aesthetic treatment to lift the eyebrow to achieve a desired aesthetic effect". The desired aesthetic effect language was used in the order to clearly state that this procedure was not a surgical procedure to address a medical condition but was solely a procedure to improve a persons appearance, thus the aesthetic effect statement. The language in the order was not intended to grant a separate indication for use for "achieving a desired aesthetic effect".

The company has provided clinical data to support their request for the expansion of their indication for use to now include lift lax submental and neck tissue. The data was previously presented in K110007 and found not adequate thus this 510(k) was determined to be NSE for lack of performance data. The major problem with the data as presented in K11007 was that the method used to provide quantitative values for submental and neck lift relied on photographs. There was a relatively large loss of data since the photographic system used by the company cropped part of the photographs which prevented quantitative measurement of change. Also the data showed a number of subjects having improvement on one side but not the other. Because of small numbers of apparent success out of a relatively small number of measurable subjects it was determined that the data was not adequate to support the proposed change in indications.

The clinical data provided in this study is the same data set with a new method of measure area of change for submental and neck lift. The new method avoids the issues of photograph cropping and therefore all 70 subjects enrolled into the study can be analyzed.

In addition to the request for a new indication for use, this application also lists 3 new transducers that were not part of the K072505 de Novo application. Two of these are narrower versions of other transducers and one of the narrower transducers and its corresponding larger version or new in terms of output energy and depth of penetration. These latter are less powerful and have a lower penetration depth than the previously cleared transducers. Based on information provided in this application it appears that the company determined they could market these newer transducers through the documentation to file pathway. If this application is ultimately granted SE determination then a specific statement needs to be made adding these new transducers to the list of officially cleared accessories.

Of the six transducers that are now commercially available the clinical study provided as support for the requested indication for use expansion only two were used in the clinical study, the DS 4-4.5 that has output energy of 0.75-1.20 J, a penetration depth of 4.5 mm and operates as 4 MHz and the DS 7-30 that has output energy of 0.25-0.45 J, a penetration depth of 3.0 mm and operates at 7 MHz.

The cleared Ulthera system used in this study is a focused ultrasound delivery system that includes a number of different ultrasound transducers that have factory pre-set energy and depth of penetration. These transducers also function has standard ultrasound imaging systems to allow the user to see underlying structures at the intended treatment site and to also visualize the sites of coagulation produced by the focused ultrasound energy. This system is designed to deliver focused ultrasound at a predetermined depth that generates focused coagulation spots. These spots are delivered in a line pattern within the desired treatment area resulting in tissue coagulation.

The clinical data used for support is based on 70 evaluable subjects ranging in age from 35-60 years. Of the subjects enrolled into the study 57 were female and 13 were male. Enrolled patients include Fitzpatrick Skin type I-V with the majority of subjects being type II and III. The company has stated that the treatment targeted the lower face and neck with treatment exposure using up to a 25 mm line of coagulation spots with the distance between spots being 1.5 mm. Follow-ups were at 2, 3, and 6 months with photographic evaluation by blinded evaluators for efficacy being at 3 months and patient satisfaction questionnaires being completed at 3.

In terms of actual treatment the company has included illustrations showing 4 different treatment patterns, two for neck treatment and two for cheek treatment. The neck treatment patterns have the same total lines performed (50 lines) with the 4.5 mm depth transducer used first followed by the 3.0 mm depth transducer. For the cheek when targeting effects to a depth of 4.5 mm 55 lines per side were used while for the 3.0 mm depth only 40 lines per side were used. The procedure had the 4.5 mm treatment performed first followed by the 3.0 mm pattern.

The company has stated that the Primary Outcome Measure for the study was improvement in overall lift and tightening of tissue determined by qualitative assessment at three months compared to baseline based on a masked reviewer assessment. The Secondary Outcome Measure was evaluation of improvement in jawline definition and submental skin laxity at three months compared to baseline based on the consensus of the three masked reviewers and patient satisfaction by scores on a patient satisfaction questionnaire at three months post-treatment.

It is not clear what the difference is between the Primary outcome and the first Secondary outcome. Also the company has provided a method to quantify the amount of lift experienced and this is not included in either the Primary or Secondary outcome lists. In terms of the quantified amount of lift the company has stated that a site will be considered a failure if the amount of lift is less than 10 mm<sup>2</sup>. The company has stated that if there is less than 10 mm<sup>2</sup> this would be a non-responder but it is not clear if you need to fail on both sides or if you fail on one side you are a non-responder. The company has further stated that a 10 mm<sup>2</sup> is considered a visibly observable tissue lift but did not provide a basis for this statement.

Regarding the blinded qualitative assessment the company has described a validation method in which selected photographs from the 2 month follow-up visit were assessed by two unmasked clinicians who did know the baseline from the post-treatment photographs. After this 3 masked evaluators evaluated the same sets of photographs but did not know which were baseline and which were post-treatment. These individuals did their assessment independently and their scores were then combined to create a final result of improved, all three or two out of three agree; incorrect if two of three are incorrect; and no change if each one was different. The company then created a kappa score for the blinded evaluation compared to the unblinded evaluation and arrived at a score of 74% agreement between masked and non-masked evaluators which they state shows this was a valid method for assessing the change in facial lift.

At this time we have not completed the detail review of the Operator Manual since there are several issues that the company will need to address before we can complete our review of this application. The issues that need to be addressed are:

1. The company needs to provide some additional comments concerning their statement that a 10 mm<sup>2</sup> is a visibly observable change.
2. The company will need to be advised that at this time we do not believe the indication of "lift lax tissue to achieve a desired aesthetic effect for full face and neck is an indication that can be granted based on the data. It is not clear how you evaluate "a desired aesthetic effect".
3. The company will need to expand the performance section of the 510(k) Summary. According to 21 CFR 807.92(b)(2) this summary should include information on patient population tested; discussion of safety and

effectiveness data with references to adverse effects and complications observed; and any other information that may be relevant to the substantial equivalence determination.

4. Need clarification on how the photographs used for the 2 month validation testing were selected.
5. The use of Quantitative analysis is not listed as either a Primary or Secondary Outcome Measure so were is this data to be included in determining study success.
6. Do not have individual satisfaction data nor a copy of the satisfaction questionnaire.
7. Company should provide a table listing the individual subjects with blinded assessment; quantitative lift value; and patient satisfaction values to show if each individual subject is a success across the board.
8. Operator Manual has two tables of suggested Treatment Guidelines identified as 5.0 and 5.0 Plus. It is not clear what are the basis for these guidelines given that the Ulthera System is presently cleared for eyebrow lift only and the new requested indication is for submental and neck lift. The charts include infraorbital and orbit treatment which do not appear to be compatible with eyebrow lift or treatment of the submental or neck tissue.
9. The narrative on page 77 and 78 under section 20.4.2.1 does not seem to make sense. Page 77 appears to be describing how the unmasked evaluation will be performed but the top of page 78 begins with a statement about each blinded assessor, yet section 20.4.2.2 at the bottom of page 78 is titled Masked Assessment.

The above issues need to be communicated to the company. This will be done by electronic mail as well as a telephone call to discuss some of the issues.

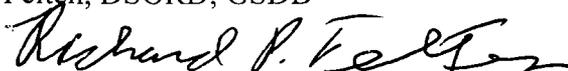
I recommend that this application be placed on HOLD.

July 5, 2012

Deficiencies for K121700

Submitted by Ulthera, Inc.

Reviewed by Richard P. Felten, DSORD, GSDB



The following deficiencies have been identified in our review of this application:

1. You have stated that a 10 mm<sup>2</sup> is a visibly observable change and therefore those sites having less than a 10 mm<sup>2</sup> change would be considered a failure. Please provide the basis for this statement since such a small change appears not to be easily observable.
2. Please clarify in the individual data table, Table 20-4, whether or not both sides of the subjects reported as having less than 10 mm<sup>2</sup> change actually had less on both sides or were marked as less based only on a single side failing.
3. You have requested an indication for use of "lift lax tissue to achieve a desired aesthetic effect for full face and neck". It is not clear exactly what this indication for use is measuring or how you would determine "a desired aesthetic effect". Please provide additional discussion of what this indication for use is defining and how you would determine success for this indication for use.
4. Please expand the Performance section of the 510(k) Summary. According to 21 CFR 807.92(b)(2) the 519(k) Summary should include information on patient population tested; discussion of safety and effectiveness data with references to adverse effects and complications observed; and any other information that may be relevant to the substantial equivalence determination.
5. Please describe the process used in selecting the photographs used for the 2 month validation testing.
6. The use of Quantitative analysis is not listed under either the Primary or Secondary Outcome Measure. Please indicate whether or not the Quantitative measurements are a Primary or Secondary endpoint. Please be advised that in reviewing your application the Agency will look at all endpoints as a combined effectiveness result for each individual subject.
7. Please provide a copy of the patient satisfaction questionnaire and the individual patients responses to the questionnaire.

8. Please provide a table listing the individual subjects with blinded assessment; quantitative lift value; and patient satisfaction values to show if each individual subject is a success across the board.
9. The Operator Manual has two tables of suggested Treatment Guidelines identified as 5.0 and 5.0 Plus. It is not clear what is the basis for the guidelines. The Ulthera System is presently cleared for eyebrow lift only and the new requested indication is for submental and neck lift. The charts include infraorbital and orbit treatment which do not appear to be compatible with eyebrow lift or treatment of the submental or neck tissue. Also the 5.0 Plus recommendations contain an increase in number of lines for each of the 5.0 recommendations. Please provide information explaining the basis for the recommended Guidelines including the increase in number of lines for the 5.0 Plus table.
10. The narrative on page 77 and 78 under section 20.4.2.1 does not seem to make sense. Page 77 appears to be describing how the unmasked evaluation will be performed but the top of page 78 begins with a statement about each blinded assessor, yet section 20.4.2.2 at the bottom of page 78 is titled Masked Assessment. Please clarify these sections.

**Felten, Richard P.**

---

**From:** Felten, Richard P.  
**Sent:** Friday, July 06, 2012 10:18 AM  
**To:** Suzon Lommel (s.lommel@ulthera.com)  
**Subject:** K121700

**Attachments:** Ulthera Cheek and Jaw Lift Deficiencies K121700.doc

Ms. Lommel:

I have finished my review of this application and do have a number of questions that need some clarifications. Also we would like to see the actual patient satisfaction questionnaire and the individual responses. I am also asking the company to put together a table that shows each individual patient, the quantitative change, the qualitative decision, and their satisfaction level so we can see how many subject were successful for all three endpoints.

I will try to call you later this morning to make sure you received the information I have attached as a word document.



Ulthera Cheek and  
Jaw Lift Def...

I am placing the application on HOLD as of today.

Richard P. Felten  
Center for Devices and Radiological Health  
Office of Device Evaluation  
Division of Surgical, Orthopedic, and Restorative Devices  
General Surgery Devices Branch

E-mail: [Richard.Felten@fda.hhs.gov](mailto:Richard.Felten@fda.hhs.gov)  
Phone: (301) 796-6392

**Williams, Michael \***

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**From:** Microsoft Outlook  
**To:** 's.lommel@ulthera.com'  
**Sent:** Monday, June 11, 2012 12:26 PM  
**Subject:** Relayed: Ack Letter for K121700

**Delivery to these recipients or distribution lists is complete, but delivery notification was not sent by the destination:**

's.lommel@ulthera.com'

Subject: Ack Letter for K121700

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Sent by Microsoft Exchange Server 2007



## DEPARTMENT OF HEALTH &amp; HUMAN SERVICES

## Public Health Service

U.S. Food and Drug Administration  
 Center for Devices and Radiological Health  
 Document Control Center WO66-G609  
 10903 New Hampshire Avenue  
 Silver Spring, MD 20993-0002

June 11, 2012

ULTHERA, INC.  
 2150 South Country Club Drive  
 Suite 21  
 Mesa, ARIZONA 85210  
 ATTN: SUZON LOMMEL

510k Number: K121700

Received: 6/7/2012

Product: ULTHERA SYSTEM

The Food and Drug Administration (FDA), Center for Devices and Radiological Health (CDRH), has received the Premarket Notification, (510(k)), you submitted in accordance with Section 510(k) of the Federal Food, Drug, and Cosmetic Act (Act) for the above referenced product and for the above referenced 510(k) submitter. Please note, if the 510(k) submitter is incorrect, please notify the 510(k) Staff immediately. We have assigned your submission a unique 510(k) number that is cited above. Please refer prominently to this 510(k) number in all future correspondence that relates to this submission. We will notify you when the processing of your 510(k) has been completed or if any additional information is required. **YOU MAY NOT PLACE THIS DEVICE INTO COMMERCIAL DISTRIBUTION UNTIL YOU RECEIVE A LETTER FROM FDA ALLOWING YOU TO DO SO.**

Please remember that all correspondence concerning your submission **MUST** be sent to the Document Mail Center (DMC) at the above letterhead address. Correspondence sent to any address other than the one above will not be considered as part of your official 510(k) submission.

On September 27, 2007, the President signed an act reauthorizing medical device user fees for fiscal years 2008 - 2012. The legislation - the Medical Device User Fee Amendments of 2007 is part of a larger bill, the Food and Drug Amendments Act of 2007. Please visit our website at <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overview/MedicalDeviceUserFeeandModernizationActMDUFMA/default.htm> for more information regarding fees and FDA review goals. In addition, effective January 2, 2008, any firm that chooses to use a standard in the review of ANY new 510(k) needs to fill out the new standards form (Form 3654) and submit it with their 510(k). The form may be found at <http://www.fda.gov/AboutFDA/ReportsManualsForms/Forms/default.htm>.

We remind you that Title VIII of the Food and Drug Administration Amendments Act of 2007 (FDAAA) amended the PHS Act by adding new section 402(j) (42 U.S.C. § 282(j)), which expanded the current database known as ClinicalTrials.gov to include mandatory registration and reporting of results for applicable clinical trials of human drugs (including biological products) and devices. Section 402(j) requires that a certification form <http://www.fda.gov/AboutFDA/ReportsManualsForms/Forms/default.htm> accompany 510(k)/HDE/PMA submissions. The agency has issued a draft guidance titled: "Certifications To Accompany Drug, Biological

Product, and Device Applications/Submissions: Compliance with Section 402(j) of The Public Health Service Act, Added By Title VIII of The Food and Drug Administration Amendments Act of 2007”  
<http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/PremarketNotification510k/ucm134034.htm>. According to the draft guidance, 510(k) submissions that do not contain clinical data do not need the certification form.

Please note the following documents as they relate to 510(k) review: 1) Guidance for Industry and FDA Staff entitled, “Interactive Review for Medical Device Submissions: 510(k)s, Original PMAs, PMA Supplements, Original BLAs and BLA Supplements”. This guidance can be found at <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089402.htm>. Please refer to this guidance for information on a formalized interactive review process. 2) Guidance for Industry and FDA Staff entitled, "Format for Traditional and Abbreviated 510(k)s". This guidance can be found at <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm084365.htm>. Please refer to this guidance for assistance on how to format an original submission for a Traditional or Abbreviated 510(k).

In all future premarket submissions, we encourage you to provide an electronic copy of your submission. By doing so, you will save FDA resources and may help reviewers navigate through longer documents more easily. Under CDRH's e-Copy Program, you may replace one paper copy of any premarket submission (e.g., 510(k), IDE, PMA, HDE) with an electronic copy. For more information about the program, including the formatting requirements, please visit our web site at <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/ucm134508.html>. In addition, the 510(k) Program Video is now available for viewing on line at <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/PremarketNotification510k/ucm070201.htm>.

**Please ensure that whether you submit a 510(k) Summary as per 21 CFR 807.92, or a 510(k) Statement as per 21 CFR 807.93, it meets the content and format regulatory requirements.**

Lastly, you should be familiar with the regulatory requirements for medical devices available at Device Advice <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/default.htm>. If you have questions on the status of your submission, please contact DSMICA at (301)796-7100 or the toll-free number (800)638-2041 , or at their internet address <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/default.htm>. If you have procedural questions, please contact the 510(k) Staff at (301)796-5640.

Sincerely,

510(k) Staff



## DEPARTMENT OF HEALTH &amp; HUMAN SERVICES

## Public Health Service

U.S. Food and Drug Administration  
 Center for Devices and Radiological Health  
 Document Control Center WO66-G609  
 10903 New Hampshire Avenue  
 Silver Spring, MD 20993-0002

June 08, 2012

**USER FEE HOLD LETTER - HAVE NOT RECEIVED PAYM**

ULTHERA, INC.  
 2150 South Country Club Drive  
 Suite 21  
 Mesa, ARIZONA 85210  
 ATTN: SUZON LOMMEL

510k Number: K121700

Received: 6/8/2012

User Fee ID Number: 6062174

Product: ULTHERA SYSTEM

The Food and Drug Administration (FDA) Center for Devices and Radiological Health (CDRH), has received the Premarket Notification you submitted in accordance with Section 510(k) of the Federal Food, Drug, and Cosmetic Act (Act) for the above referenced product. We have assigned your submission a unique 510(k) number that is cited above. Please refer prominently to this 510(k) number in all future correspondence that relates to this submission. **YOU MAY NOT PLACE THIS DEVICE INTO COMMERCIAL DISTRIBUTION UNTIL YOU RECEIVE A LETTER FROM FDA ALLOWING YOU TO DO SO.**

The Federal Food, Drug, and Cosmetic Act (the Act), as amended by the Medical Device User Fee and Modernization Act of 2002 (MDUFMA) and the FDA Amendments Act of 2007 (FDAAA) (Public Law 110-85), authorizes FDA to collect user fees for certain types of 510(k) submissions. The submission cannot be accepted for review until the fee is paid in full ; therefore, the file has been placed on hold. When your user fee payment has been received , review of the 510(k) will resume as of that date. Alternatively, you may request withdrawal of your submission. You now have the option to pay online by credit card. We recommend this form of payment. Credit card payments are directly linked to your user fee cover sheet and are processed the next business day. You may also pay by check. If you choose to mail a check, please send a check to one of the addresses listed below:

By Regular Mail  
 Food and Drug Administration  
 P.O. Box 956733  
 St. Louis, MO 63195-6733.

By Private Courier(e.g.,Fed Ex, UPS, etc.)  
 U.S. Bank  
 956733  
 1005 Convention Plaza  
 St. Louis, MO 63101

The check should be made out to the Food and Drug Administration referencing the payment identification number, and a copy of the User Fee Cover sheet should be included with the check. A copy of the Medical Device User Fee Cover Sheet should be faxed to CDRH at (301)847-8120 referencing the 510(k) number if you have not already sent it in with your 510(k) submission. After the FDA has been notified of the receipt of your user fee payment, your 510(k) will be filed and the review will begin. If payment has not been received within 30 days, your 510(k) will be deleted from the system. Additional information on user fees and how to submit your user fee payment may be found at [www.fda.gov/cdrh/mdufma/fy09userfee.html](http://www.fda.gov/cdrh/mdufma/fy09userfee.html). In addition, the 510k Program Video is now available for viewing on line at <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/PremarketNotification510k/ucm070201.htm>.

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Please note that since your 510(k) has not been reviewed, additional information may be required during the review process and the file may be placed on hold once again. If you are unsure as to whether or not you need to file a 510k Submission with FDA or what type of submission to submit, you should first telephone the Division of Small Manufacturers, International and Consumer Assistance (DSMICA), for guidance at (301)796-7100 or its toll-free number (800)638-2041, or contact them at their Internet address <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/default.htm>, or you may submit a 513(g) request for information regarding classification to the Document Mail Center at the address above. If you have any questions concerning receipt of your payment, please contact Edwena Jones at [Edwena.Jones@fda.hhs.gov](mailto:Edwena.Jones@fda.hhs.gov) or directly at (301)796-7200. If you have questions regarding the status of your 510(k) Submission, please contact DSMICA at the numbers or address above.

Sincerely yours,

Edwena Jones  
Consumer Safety Technician  
Premarket Notification Section  
Office of Device Evaluation  
Center for Devices and Radiological Health

**Grayson, Giovanna \***

---

**From:** Microsoft Outlook  
**To:** 's.lommel@ulthera.com'  
**Sent:** Friday, June 08, 2012 11:47 AM  
**Subject:** Relayed: ack letter

**Delivery to these recipients or distribution lists is complete, but delivery notification was not sent by the destination:**

's.lommel@ulthera.com'

Subject: ack letter

---

Sent by Microsoft Exchange Server 2007

**Grayson, Giovanna \***

**From:** Grayson, Giovanna \*  
**Sent:** Friday, June 08, 2012 11:47 AM  
**To:** 's.lommel@ulthera.com'  
**Subject:** ack letter  
**Attachments:** image002.png

**DEPARTMENT OF HEALTH & HUMAN SERVICES****Public Health Service**

U.S. Food and Drug Administration  
 Center for Devices and Radiological Health  
 Document Control Center W-060-G609  
 10903 New Hampshire Avenue  
 Silver Spring, MD 20993-0002

June 08, 2012

SUZON

LOMMEL

**USER FEE HOLD LETTER - HAVE NOT RECEIVED PAYM**

ULTHERA, INC.

2150 South Country Club Drive

Suite 21

Mesa, ARIZONA 85210

ATTN: SUZON LOMMEL

510k Number: K121700

Received: 6/8/2012

Product: ULTHERA SYSTEM

User Fee ID Number: 6062174

The Food and Drug Administration (FDA) Center for Devices and Radiological Health (CDRH), has received the Premarket Notification you submitted in accordance with Section 510(k) of the Federal Food, Drug, and Cosmetic Act (Act) for the above referenced product. We have assigned your submission a unique 510(k) number that is cited above. Please refer prominently to this 510(k) number in all future correspondence that relates to this submission. **YOU MAY NOT PLACE THIS DEVICE INTO COMMERCIAL DISTRIBUTION UNTIL YOU RECEIVE A LETTER FROM FDA ALLOWING YOU TO DO SO.**

The Federal Food, Drug, and Cosmetic Act (the Act), as amended by the Medical Device User Fee and Modernization Act of 2002 (MDUFMA) and the FDA Amendments Act of 2007 (FDAAA) (Public Law 110-85), authorizes FDA to collect user fees for certain types of 510(k) submissions. The submission cannot be accepted for review until the fee is paid in full; therefore, the file has been placed on hold. When your user fee payment has been received, review of the 510(k) will resume as of that date. Alternatively, you may request withdrawal of your submission. You now have the option to pay online by credit card. We recommend this form of payment. Credit card payments are directly linked to your user fee cover sheet and are processed the next business day. You may also pay by check. If you choose to mail a check, please send a check to one of the addresses listed below:

The check should be made out to the Food and Drug Administration referencing the payment identification number, and a copy of the User Fee Cover sheet should be included with the check. A copy of the Medical Device User Fee Cover Sheet should be faxed to CDRH at (301)847-8120 referencing the 510(k) number if you have not already sent it in with your 510(k) submission. After the FDA has been notified of the receipt of your user fee payment, your 510(k) will be filed and the review will begin. If payment has not been received within 30 days, your 510(k) will be deleted from the system. Additional information on user fees and how to submit your user fee payment may be found at [www.fda.gov/cdrh/mdufma/fy09userfee.html](http://www.fda.gov/cdrh/mdufma/fy09userfee.html). In addition, the 510k Program Video is now available for viewing on line at <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/PremarketNotification510k/ucm070201.htm>.

By Private Courier (e.g., Fed Ex, UPS, etc.)

U.S. Bank  
 956733  
 1005 Convention Plaza  
 St. Louis, MO 63101

By Regular Mail

Food and Drug Administration  
 P.O. Box 956733  
 St. Louis, MO 63195-6733.

6/8/2012

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

6/8/2012

Questions? Contact FDA/CDRH/OCE/DID at [CDRH-FOISTATUS@fda.hhs.gov](mailto:CDRH-FOISTATUS@fda.hhs.gov) or 301-796-8118

In all future premarket submissions, we encourage you to provide an electronic copy of your submission. By doing so, you will save FDA resources and may help reviewers navigate through longer documents more easily. Under CDRH's e-Copy Program, you may replace one paper copy of any premarket submission (e.g., 510(k), IDE, PMA, or HDE) with an electronic copy. For more information about the program, including the formatting requirements, please visit our web site at <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/ucm134508.htm>.

Please note that since your 510(k) has not been reviewed, additional information may be required during the review process and the file may be placed on hold once again. If you are unsure as to whether or not you need to file a 510k Submission with FDA or what type of submission to submit, you should first telephone the Division of Small Manufacturers, International and Consumer Assistance (DSMICA), for guidance at (301)796-7100 or its toll-free number (800)638-2041, or contact them at their Internet address <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/default.htm>, or you may submit a 513(g) request for information regarding classification to the Document Mail Center at the address above. If you have any questions concerning receipt of your payment, please contact Edwena Jones at [Edwena.Jones@fda.hhs.gov](mailto:Edwena.Jones@fda.hhs.gov) or directly at (301)796-7200. If you have questions regarding the status of your 510(k) Submission, please contact DSMICA at the numbers or address above.

Sincerely yours,

Edwena Jones  
Consumer Safety Technician  
Premarket Notification Section  
Office of Device Evaluation  
Center for Devices and Radiological Health

6/8/2012

Questions? Contact FDA/CDRH/OCE/DID at [CDRH-FOISTATUS@fda.hhs.gov](mailto:CDRH-FOISTATUS@fda.hhs.gov) or 301-796-8118

## Traditional 510(k) - Ulthera® System



June 7, 2012

Ulthera, Inc.  
2150 South Country Club Drive Suite 21  
Mesa, AZ 85210 USA  
Phone: (480) 619-4069  
Website: [www.ulthera.com](http://www.ulthera.com)



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# 1. MDUFMA

Site: null

Page 1 of 1

Form Approved: OMB No. 0910-511. See Instructions for OMB Statements

|  |   |
|--|---|
| DEPARTMENT OF HEALTH AND HUMAN SERVICES<br>FOOD AND DRUG ADMINISTRATION<br><b>MEDICAL DEVICE USER FEE COVER SHEET</b>  | PAYMENT IDENTIFICATION NUMBER: <b>MD6053423-956733</b><br>Write the Payment Identification number on your check.  |
| A completed cover sheet must accompany each original application or supplement subject to fees. If payment is sent by U.S. mail or courier, please include a copy of this completed form with payment. Payment and mailing instructions can be found at: <a href="http://www.fda.gov/oc/mdufma/cover-sheet.html">http://www.fda.gov/oc/mdufma/cover-sheet.html</a>   |   |
| 1. COMPANY NAME AND ADDRESS (include name, street address, city state, country, and post office code)<br><br>ULTHERA, INC.<br>2150 S Country Club Dr<br>Suite 21<br>Mesa AZ 85210<br>US<br>1.1 EMPLOYER IDENTIFICATION NUMBER (EIN)<br>*****6233   | 2. CONTACT NAME<br>Patrick Meier<br>2.1 E-MAIL ADDRESS<br>p.meier@ulthera.com<br>2.2 TELEPHONE NUMBER (include Area code)<br>480-819-4069<br>2.3 FACSIMILE (FAX) NUMBER (include Area code)<br>480-819-4071 |
| 3. TYPE OF PREMARKET APPLICATION (Select one of the following in each column; if you are unsure, please refer to the application descriptions at the following web site: <a href="http://www.fda.gov/oc/mdufma">http://www.fda.gov/oc/mdufma</a> )<br>Select an application type:<br><input checked="" type="checkbox"/> Premarket notification (510(k)); except for third party<br><input type="checkbox"/> 513(g) Request for Information<br><input type="checkbox"/> Biologics License Application (BLA)<br><input type="checkbox"/> Premarket Approval Application (PMA)<br><input type="checkbox"/> Modular PMA<br><input type="checkbox"/> Product Development Protocol (PDP)<br><input type="checkbox"/> Premarket Report (PMR)<br><input type="checkbox"/> Annual Fee for Periodic Reporting (APR)<br><input type="checkbox"/> 30-Day Notice |   |
| 3.1 Select a center<br><input checked="" type="checkbox"/> CDRH<br><input type="checkbox"/> CBER<br>3.2 Select one of the types below<br><input checked="" type="checkbox"/> Original Application<br>Supplement Types:<br><input type="checkbox"/> Efficacy (BLA)<br><input type="checkbox"/> Panel Track (PMA, PMR, PDP)<br><input type="checkbox"/> Real-Time (PMA, PMR, PDP)<br><input type="checkbox"/> 180-day (PMA, PMR, PDP)  |   |
| 4. ARE YOU A SMALL BUSINESS? (See the instructions for more information on determining this status)<br><input checked="" type="checkbox"/> YES, I meet the small business criteria and have submitted the required qualifying documents to FDA<br><input type="checkbox"/> NO, I am not a small business<br>4.1 If Yes, please enter your Small Business Decision Number: SBD110158  |   |
| 5. FDA WILL NOT ACCEPT YOUR SUBMISSION IF YOUR COMPANY HAS NOT PAID AN ESTABLISHMENT REGISTRATION FEE THAT IS DUE TO FDA. HAS YOUR COMPANY PAID ALL ESTABLISHMENT REGISTRATION FEES THAT ARE DUE TO FDA?<br><input checked="" type="checkbox"/> YES (All of our establishments have registered and paid the fee, or this is our first device, and we will register and pay the fee within 30 days of FDA's approval/clearance of this device.)<br><input type="checkbox"/> NO (If "NO," FDA will not accept your submission until you have paid all fees due to FDA. This submission will not be processed; see <a href="http://www.fda.gov/oc/dm/ndufma">http://www.fda.gov/oc/dm/ndufma</a> for additional information)  |   |
| 6. IS THIS PREMARKET APPLICATION COVERED BY ANY OF THE FOLLOWING USER FEE EXCEPTIONS? IF SO, CHECK THE APPLICABLE EXCEPTION.<br><input type="checkbox"/> This application is the first PMA submitted by a qualified small business, including any affiliates<br><input type="checkbox"/> The sole purpose of the application is to support conditions of use for a pediatric population<br><input type="checkbox"/> This biologics application is submitted under section 351 of the Public Health Service Act for a product licensed for further manufacturing use only<br><input type="checkbox"/> The application is submitted by a state or federal government entity for a device that is not to be distributed commercially  |   |
| 7. IS THIS A SUPPLEMENT TO A PREMARKET APPLICATION FOR WHICH FEES WERE WAIVED DUE TO SOLE USE IN A PEDIATRIC POPULATION THAT NOW PROPOSES CONDITION OF USE FOR ANY ADULT POPULATION? (If so, the application is subject to the fee that applies for an original premarket approval application (PMA)).<br><input type="checkbox"/> YES<br><input checked="" type="checkbox"/> NO   |   |
| PAPERWORK REDUCTION ACT STATEMENT<br>Public reporting burden for this collection of information is estimated to average 18 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to the address below.<br><br>Department of Health and Human Services, Food and Drug Administration, Office of Chief Information Officer, 1350 Piccard Drive, 4th Floor Rockville, MD 20850<br>[Please do NOT return this form to the above address, except as it pertains to comments on the burden estimate.]   |   |
| 8. USER FEE PAYMENT AMOUNT SUBMITTED FOR THIS PREMARKET APPLICATION<br>\$2,174.00 <span style="float: right;">20-Dec-2010</span>   |   |

Form FDA 3601 (01/2007)

"Close Window" Print Cover sheet

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Online Payment

Online Payment

Step 3: Confirm Payment

1 | 2 | 3

Thank you.

Your transaction has been successfully completed.

Pay.gov Tracking Information

Application Name: FDA User Fees

Pay.gov Tracking ID: 256TUIJF

Agency Tracking ID: 6062174

Transaction Date and Time: 06/06/2012 16:46 EDT

Payment Summary

Account Holder Name: ULTHERA, INC.

Payment Amount: \$2,024.00

Account Type: Business Checking

Routing Number: 121140399

Account Number: \*\*\*\*\*6841

Payment Date: 06/07/2012

<https://www.pay.gov/paygov/payments/authorizeACHPayment.html>

6/6/2012





## DEPARTMENT OF HEALTH &amp; HUMAN SERVICES

Food and Drug Administration  
10903 New Hampshire Avenue  
Room 4606, Building 66  
Silver Spring, MD 20993-0002

January 5, 2012

ULTHERA INCORPORATED  
2150 S. Country Club Dr., Suite 21  
Mesa, AZ 85210

To: Randall E. Miller, Vice President of Clinical & Regulatory Affairs, Ulthera Incorporated  
Subject: Request for Qualification as a Small Business

Small Business Decision Number: **SBD126132**  
Expires: **September 30, 2012**

This responds to your request for eligibility for Small Business Qualification on Form FDA 3602.

After review of your submission, I am pleased to inform you that your firm does qualify under MDUFMA as a small business for reduced or waived fees for medical device submissions made during the fiscal year 2012.

Please include your Small Business Decision Number (see above) whenever you submit a Medical Device User Fee Coversheet (Form FDA 3601). This form is available at <http://www.fda.gov/oc/mdufma/coversheet/html>. In completing the form, the **Business EIN Number** and the **user fee organization number 227178** must correspond to the **Business Name** in the top line of the mailing address above.

If you are registering as a new user to the User Fee System, please use this organization number to register as an existing organization. If you currently have a User Fee account and the organization number in your profile does not match this organization number, please contact the **User Fees Help Desk** for further assistance at **301-796-7200** or at [userfees@fda.gov](mailto:userfees@fda.gov).

Your Small Business status expires at the close of business September 30, 2012. FDA will provide information on how to qualify as a Small Business for FY 2013 in a Federal Register Notice to be published on or around August 1, 2012. We will also provide this information on our MDUFMA website at <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overview/MedicalDeviceUserFeeandModernizationActMDUFMA/default.htm>

Sincerely,

Bonnie J. Alderton  
Small Business Reviewer  
Division of Small Manufacturers, International  
and Consumer Assistance  
Center for Devices and Radiological Health  
U.S. Food and Drug Administration  
[Bonnie.alderon@fda.hhs.gov](mailto:Bonnie.alderon@fda.hhs.gov)

---

## 2. CDRH

| DEPARTMENT OF HEALTH AND HUMAN SERVICES<br>FOOD AND DRUG ADMINISTRATION  |  | Form Approval<br>OMB No. 0910-0120<br>Expiration Date: August 31, 2010.<br>See OMB Statement on page 5.   |  |  |
|--|--|---|--|--|
| <b>CDRH PREMARKET REVIEW SUBMISSION COVER SHEET</b>  |  |   |  |  |
| Date of Submission<br>June 7, 2012   | User Fee Payment ID Number<br>MD6062174-956733   | FDA Submission Document Number (if known)<br>Not Known  |  |  |
| <b>SECTION A TYPE OF SUBMISSION</b>  |  |   |  |  |
| <b>PMA</b><br><input type="checkbox"/> Original Submission<br><input type="checkbox"/> Premarket Report<br><input type="checkbox"/> Modular Submission<br><input type="checkbox"/> Amendment<br><input type="checkbox"/> Report<br><input type="checkbox"/> Report Amendment<br><input type="checkbox"/> Licensing Agreement | <b>PMA &amp; HDE Supplement</b><br><input type="checkbox"/> Regular (180 day)<br><input type="checkbox"/> Special<br><input type="checkbox"/> Panel Track (PMA Only)<br><input type="checkbox"/> 30-day Supplement<br><input type="checkbox"/> 30-day Notice<br><input type="checkbox"/> 135-day Supplement<br><input type="checkbox"/> Real-time Review<br><input type="checkbox"/> Amendment to PMA & HDE Supplement<br><input type="checkbox"/> Other | <b>PDP</b><br><input type="checkbox"/> Original PDP<br><input type="checkbox"/> Notice of Completion<br><input type="checkbox"/> Amendment to PDP | <b>510(k)</b><br><input checked="" type="checkbox"/> Original Submission:<br><input checked="" type="checkbox"/> Traditional<br><input type="checkbox"/> Special<br><input type="checkbox"/> Abbreviated (Complete section I, Page 5)<br><input type="checkbox"/> Additional Information<br><input type="checkbox"/> Third Party | <b>Meeting</b><br><input type="checkbox"/> Pre-510(K) Meeting<br><input type="checkbox"/> Pre-IDE Meeting<br><input type="checkbox"/> Pre-PMA Meeting<br><input type="checkbox"/> Pre-PDP Meeting<br><input type="checkbox"/> Day 100 Meeting<br><input type="checkbox"/> Agreement Meeting<br><input type="checkbox"/> Determination Meeting<br><input type="checkbox"/> Other (specify): |
| <b>IDE</b><br><input type="checkbox"/> Original Submission<br><input type="checkbox"/> Amendment<br><input type="checkbox"/> Supplement  | <b>Humanitarian Device Exemption (HDE)</b><br><input type="checkbox"/> Original Submission<br><input type="checkbox"/> Amendment<br><input type="checkbox"/> Supplement<br><input type="checkbox"/> Report<br><input type="checkbox"/> Report Amendment  | <b>Class II Exemption Petition</b><br><input type="checkbox"/> Original Submission<br><input type="checkbox"/> Additional Information             | <b>Evaluation of Automatic Class III Designation (De Novo)</b><br><input type="checkbox"/> Original Submission<br><input type="checkbox"/> Additional Information  | <b>Other Submission</b><br><input type="checkbox"/> 513(g)<br><input type="checkbox"/> Other (describe submission):  |
| Have you used or cited Standards in your submission? <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No (if Yes, please complete Section I, Page 5)   |  |   |  |  |
| <b>SECTION B SUBMITTER, APPLICANT OR SPONSOR</b>   |  |   |  |  |
| Company / Institution Name<br>Ulthera, Incorporated  |  | Establishment Registration Number (if known)  |  |  |
| Division Name (if applicable)  |  | Phone Number (including area code)<br>480-619-4069  |  |  |
| Street Address<br>2150 South Country Club Drive, Suite 21  |  | FAX Number (including area code)<br>480-619-4071  |  |  |
| City<br>Mesa   | State / Province<br>Arizona  | ZIP/Postal Code<br>85210  | Country<br>USA   |  |
| Contact Name<br>Suzon Lommel   |  |   |  |  |
| Contact Title<br>Vice President of Regulatory & Quality Affairs  |  | Contact E-mail Address<br>s.lommel@ulthera.com  |  |  |
| <b>SECTION C APPLICATION CORRESPONDENT (e.g., consultant, if different from above)</b>   |  |   |  |  |
| Company / Institution Name   |  |   |  |  |
| Division Name (if applicable)  |  | Phone Number (including area code)  |  |  |
| Street Address   |  | FAX Number (including area code)  |  |  |
| City   | State / Province   | ZIP Code  | Country  |  |
| Contact Name   |  |   |  |  |
| Contact Title  |  | Contact E-mail Address  |  |  |

| SECTION D1  |   |   | REASON FOR APPLICATION - PMA, PDP, OR HDE |  |  |
|---|---|---|---|--|--|
| <input type="checkbox"/> New Device<br><input type="checkbox"/> Withdrawal<br><input type="checkbox"/> Additional or Expanded Indications<br><input type="checkbox"/> Request for Extension<br><input type="checkbox"/> Post-approval Study Protocol<br><input type="checkbox"/> Request for Applicant Hold<br><input type="checkbox"/> Request for Removal of Applicant Hold<br><input type="checkbox"/> Request to Remove or Add Manufacturing Site | <input type="checkbox"/> Change in design, component, or specification:<br><input type="checkbox"/> Software / Hardware<br><input type="checkbox"/> Color Additive<br><input type="checkbox"/> Material<br><input type="checkbox"/> Specifications<br><input type="checkbox"/> Other ( <i>specify below</i> )               | <input type="checkbox"/> Location change:<br><input type="checkbox"/> Manufacturer<br><input type="checkbox"/> Sterilizer<br><input type="checkbox"/> Packager  |   |  |  |
| <input type="checkbox"/> Process change:<br><input type="checkbox"/> Manufacturing <input type="checkbox"/> Packaging<br><input type="checkbox"/> Sterilization<br><input type="checkbox"/> Other ( <i>specify below</i> )  | <input type="checkbox"/> Labeling change:<br><input type="checkbox"/> Indications<br><input type="checkbox"/> Instructions<br><input type="checkbox"/> Performance Characteristics<br><input type="checkbox"/> Shelf Life<br><input type="checkbox"/> Trade Name<br><input type="checkbox"/> Other ( <i>specify below</i> ) | <input type="checkbox"/> Report Submission:<br><input type="checkbox"/> Annual or Periodic<br><input type="checkbox"/> Post-approval Study<br><input type="checkbox"/> Adverse Reaction<br><input type="checkbox"/> Device Defect<br><input type="checkbox"/> Amendment |   |  |  |
| <input type="checkbox"/> Response to FDA correspondence:  |   | <input type="checkbox"/> Change in Ownership<br><input type="checkbox"/> Change in Correspondent<br><input type="checkbox"/> Change of Applicant Address  |   |  |  |
| <input type="checkbox"/> Other Reason ( <i>specify</i> ):   |   |   |   |  |  |

| SECTION D2   |   |   | REASON FOR APPLICATION - IDE |  |  |
|--|---|---|------------------------------|--|--|
| <input type="checkbox"/> New Device<br><input type="checkbox"/> New Indication<br><input type="checkbox"/> Addition of Institution<br><input type="checkbox"/> Expansion / Extension of Study<br><input type="checkbox"/> IRB Certification<br><input type="checkbox"/> Termination of Study<br><input type="checkbox"/> Withdrawal of Application<br><input type="checkbox"/> Unanticipated Adverse Effect<br><input type="checkbox"/> Notification of Emergency Use<br><input type="checkbox"/> Compassionate Use Request<br><input type="checkbox"/> Treatment IDE<br><input type="checkbox"/> Continued Access | <input type="checkbox"/> Change in:<br><input type="checkbox"/> Correspondent / Applicant<br><input type="checkbox"/> Design / Device<br><input type="checkbox"/> Informed Consent<br><input type="checkbox"/> Manufacturer<br><input type="checkbox"/> Manufacturing Process<br><input type="checkbox"/> Protocol - Feasibility<br><input type="checkbox"/> Protocol - Other<br><input type="checkbox"/> Sponsor | <input type="checkbox"/> Response to FDA Letter Concerning:<br><input type="checkbox"/> Conditional Approval<br><input type="checkbox"/> Deemed Approved<br><input type="checkbox"/> Deficient Final Report<br><input type="checkbox"/> Deficient Progress Report<br><input type="checkbox"/> Deficient Investigator Report<br><input type="checkbox"/> Disapproval<br><input type="checkbox"/> Request Extension of Time to Respond to FDA<br><input type="checkbox"/> Request Meeting<br><input type="checkbox"/> Request Hearing |                              |  |  |
| <input type="checkbox"/> Report submission:<br><input type="checkbox"/> Current Investigator<br><input type="checkbox"/> Annual Progress Report<br><input type="checkbox"/> Site Waiver Report<br><input type="checkbox"/> Final   |   |   |                              |  |  |
| <input type="checkbox"/> Other Reason ( <i>specify</i> ):  |   |   |                              |  |  |

| SECTION D3  |  |   | REASON FOR SUBMISSION - 510(k) |  |  |
|---|--|---|--------------------------------|--|--|
| <input type="checkbox"/> New Device                       | <input checked="" type="checkbox"/> Additional or Expanded Indications | <input type="checkbox"/> Change in Technology |                                |  |  |
| <input type="checkbox"/> Other Reason ( <i>specify</i> ): |  |   |                                |  |  |

| SECTION E  |     |   |  |   |  |   |  | ADDITIONAL INFORMATION ON 510(K) SUBMISSIONS  |  |  |  |
|--|-----|---|--|---|--|---|--|---|--|--|--|
| Product codes of devices to which substantial equivalence is claimed |     |   |  |   |  |   |  | Summary of, or statement concerning, safety and effectiveness information<br><input checked="" type="checkbox"/> 510 (k) summary attached<br><input type="checkbox"/> 510 (k) statement |  |  |  |
| 1  | OHV | 2 |  | 3 |  | 4 |  |   |  |  |  |
| 5  |     | 6 |  | 7 |  | 8 |  |   |  |  |  |

| Information on devices to which substantial equivalence is claimed (if known) |   |                                    |                         |
|---|---|------------------------------------|-------------------------|
|   | 510(k) Number                                     | Trade or Proprietary or Model Name | Manufacturer            |
| 1   | K072505<br>DeNovo 510k cleared September 11, 2009 | 1 Ulthera System                   | 1 Ulthera, Incorporated |
| 2   |   | 2                                  | 2                       |
| 3   |   | 3                                  | 3                       |
| 4   |   | 4                                  | 4                       |
| 5   |   | 5                                  | 5                       |
| 6   |   | 6                                  | 6                       |

**SECTION F PRODUCT INFORMATION - APPLICATION TO ALL APPLICATIONS**

Common or usual name or classification name  
 Focused Ultrasound Stimulator for Aesthetic Use - Class II 21 CFR 878.4590

|   | Trade or Proprietary or Model Name for This Device | Model Number |
|---|--|--------------|
| 1 | Ulthera System                                     | 1 8850-0001  |
| 2 |  | 2            |
| 3 |  | 3            |
| 4 |  | 4            |
| 5 |  | 5            |

| FDA document numbers of all prior related submissions (regardless of outcome) |         |    |             |    |            |
|---|---------|----|-------------|----|------------|
| 1   | K072505 | 2  | IDE G060261 | 3  | DeNovo510k |
| 4   | K110007 | 5  |             | 6  |            |
| 7   |         | 8  |             | 9  |            |
| 10  |         | 11 |             | 12 |            |

Data Included in Submission  
 Laboratory Testing       Animal Trials       Human Trials

**SECTION G PRODUCT CLASSIFICATION - APPLICATION TO ALL APPLICATIONS**

|   |   |   |
|---|---|---|
| Product Code<br>OHV   | C.F.R. Section (if applicable)<br>21 CFR 878.4590 | Device Class<br><input type="checkbox"/> Class I <input checked="" type="checkbox"/> Class II<br><input type="checkbox"/> Class III <input type="checkbox"/> Unclassified |
| Classification Panel<br>General & Plastic Surgery Devices Panel |   |   |

Indications (from labeling)  
 The Ulthera System is indicated for use as a non-invasive dermatological aesthetic treatment to:  
 - lift the eyebrow  
 - lift lax submental (beneath the chin) and neck tissue  
 - lift lax tissue to achieve a desired aesthetic effect for the full face and neck

|  |  |   |  |
|--|--|---|--|
| <b>Note:</b> Submission of this information does not affect the need to submit a 2891 or 2891a Device Establishment Registration form. |  | FDA Document Number (if known)<br>N/A   |  |
| <b>SECTION H MANUFACTURING / PACKAGING / STERILIZATION SITES RELATING TO A SUBMISSION</b>  |  |   |  |
| <input checked="" type="checkbox"/> Original<br><input type="checkbox"/> Add <input type="checkbox"/> Delete                           |  | Facility Establishment Identifier (FEI) Number  |  |
|  |  | <input checked="" type="checkbox"/> Manufacturer <input type="checkbox"/> Contract Sterilizer<br><input type="checkbox"/> Contract Manufacturer <input type="checkbox"/> Repackager / Relabeler |  |
| Company / Institution Name<br>Ulthera, Inc.  |  | Establishment Registration Number<br>3006560326   |  |
| Division Name (if applicable)  |  | Phone Number (including area code)<br>480-619-4069  |  |
| Street Address<br>2150 South Country Club Drive, Suite 21  |  | FAX Number (including area code)<br>489-619-4071  |  |
| City<br>Mesa   |  | State / Province<br>AZ  | ZIP Code<br>85210                              |
|  |  | Country<br>USA  |  |
| Contact Name<br>Suzon Lommel   |  | Contact Title<br>Vice President of Regulatory and Quality Affairs   | Contact E-mail Address<br>s.lommel@ulthera.com |
| <input checked="" type="checkbox"/> Original<br><input type="checkbox"/> Add <input type="checkbox"/> Delete                           |  | Facility Establishment Identifier (FEI) Number  |  |
|  |  | <input type="checkbox"/> Manufacturer <input type="checkbox"/> Contract Sterilizer<br><input checked="" type="checkbox"/> Contract Manufacturer <input type="checkbox"/> Repackager / Relabeler |  |
| Company / Institution Name<br>Ardent Sound, Inc  |  | Establishment Registration Number<br>3005461986   |  |
| Division Name (if applicable)  |  | Phone Number (including area code)<br>480-649-4399  |  |
| Street Address<br>33 South Sycamore Street   |  | FAX Number (including area code)<br>480-649-1605  |  |
| City<br>Mesa   |  | State / Province<br>AZ  | ZIP Code<br>85202                              |
|  |  | Country<br>USA  |  |
| Contact Name<br>Suzon Lommel   |  | Contact Title<br>Vice President of Regulatory and Quality Affairs   | Contact E-mail Address<br>s.lommel@ulthera.com |
| <input type="checkbox"/> Original<br><input checked="" type="checkbox"/> Add <input type="checkbox"/> Delete                           |  | Facility Establishment Identifier (FEI) Number  |  |
|  |  | <input type="checkbox"/> Manufacturer <input type="checkbox"/> Contract Sterilizer<br><input checked="" type="checkbox"/> Contract Manufacturer <input type="checkbox"/> Repackager / Relabeler |  |
| Company / Institution Name<br>BIT MedTech  |  | Establishment Registration Number<br>2032077  |  |
| Division Name (if applicable)  |  | Phone Number (including area code)<br>858-613-1200  |  |
| Street Address<br>15870 Bernardo Center Drive  |  | FAX Number (including area code)<br>858-613-1201  |  |
| City<br>San Diego  |  | State / Province<br>CA  | ZIP Code<br>92127                              |
|  |  | Country<br>USA  |  |
| Contact Name<br>Suzon Lommel   |  | Contact Title<br>Vice President of Regulatory and Quality Affairs   | Contact E-mail Address<br>s.lommel@ulthera.com |

|  |  |   |  |
|--|--|---|--|
| <b>Note:</b> Submission of this information does not affect the need to submit a 2891 or 2891a Device Establishment Registration form. |  | FDA Document Number (if known)  |  |
| <b>SECTION H (Continued)</b>   |  |   |  |
| <input type="checkbox"/> Original<br><input checked="" type="checkbox"/> Add <input type="checkbox"/> Delete                           |  | Facility Establishment Identifier (FEI) Number  |  |
|  |  | <input type="checkbox"/> Manufacturer <input type="checkbox"/> Contract Sterilizer<br><input checked="" type="checkbox"/> Contract Manufacturer <input type="checkbox"/> Repackager / Relabeler |  |
| Company / Institution Name<br>Sound Technologies, Inc  |  | Establishment Registration Number   |  |
| Division Name (if applicable)  |  | Phone Number (including area code)<br>814-235-3760  |  |
| Street Address<br>1363 South Atherton Street   |  | FAX Number (including area code)<br>814-234-5033  |  |
| City<br>State College  |  | State / Province<br>Pennsylvania  | ZIP Code<br>16801                              |
| Country  |  |   |  |
| Contact Name<br>Suzon Lommel   |  | Contact Title<br>Vice President of Regulatory and Quality Affairs   | Contact E-mail Address<br>s.lommel@ulthera.com |
| <b>SECTION H (Continued)</b>   |  |   |  |
| <input type="checkbox"/> Original<br><input checked="" type="checkbox"/> Add <input type="checkbox"/> Delete                           |  | Facility Establishment Identifier (FEI) Number  |  |
|  |  | <input type="checkbox"/> Manufacturer <input type="checkbox"/> Contract Sterilizer<br><input checked="" type="checkbox"/> Contract Manufacturer <input type="checkbox"/> Repackager / Relabeler |  |
| Company / Institution Name<br>Jabil Circuit, Inc.  |  | Establishment Registration Number   |  |
| Division Name (if applicable)  |  | Phone Number (including area code)<br>480-968-6790  |  |
| Street Address<br>615 South River Drive  |  | FAX Number (including area code)<br>480-829-4000  |  |
| City<br>Tempe  |  | State / Province<br>AZ  | ZIP Code<br>85281                              |
| Country<br>USA   |  |   |  |
| Contact Name<br>Suzon Lommel   |  | Contact Title<br>Vice President of Regulatory and Quality Affairs   | Contact E-mail Address<br>s.lommel@ulthera.com |
| <b>SECTION H (Continued)</b>   |  |   |  |
| <input type="checkbox"/> Original<br><input type="checkbox"/> Add <input type="checkbox"/> Delete                                      |  | Facility Establishment Identifier (FEI) Number  |  |
|  |  | <input type="checkbox"/> Manufacturer <input type="checkbox"/> Contract Sterilizer<br><input type="checkbox"/> Contract Manufacturer <input type="checkbox"/> Repackager / Relabeler            |  |
| Company / Institution Name   |  | Establishment Registration Number   |  |
| Division Name (if applicable)  |  | Phone Number (including area code)  |  |
| Street Address   |  | FAX Number (including area code)  |  |
| City   |  | State / Province  | ZIP Code                                       |
| Country  |  |   |  |
| Contact Name   |  | Contact Title   | Contact E-mail Address                         |

| <b>SECTION I UTILIZATION OF STANDARDS</b>  |  |                                  |   |                           |                        |
|--|--|----------------------------------|---|---------------------------|------------------------|
| <b>Note:</b> Complete this section if your application or submission cites standards or includes a "Declaration of Conformity to a Recognized Standard" statement.   |  |                                  |   |                           |                        |
| 1  | Standards No.<br>EN 6060 1-1/<br>IEC 60601-1 | Standards Organization<br>EN/IEC | Standards Title<br>Medical Electrical Equipment,<br>Part 1: General requirements for basic safety and essential performance   | Version<br>Third Edition  | Date<br>2005-December  |
| 2  | Standards No.<br>EN 60601-2                  | Standards Organization<br>EN     | Standards Title<br>Medical Electrical Equipment<br>Part 1-2: General requirements for safety collateral standard:<br>Electromagnetic Compatibility -- requirements and tests. | Version<br>Second Edition | Date<br>2001-September |
| 3  | Standards No.<br>EN 60601-1-4                | Standards Organization<br>EN     | Standards Title<br>Medical Electrical Equipment,<br>Part 1-4: General requirements for safety --<br>Collateral standard: Programmable electrical medical systems.             | Version<br>Third Edition  | Date<br>2005-December  |
| 4  | Standards No.<br>EN 60601-2-37               | Standards Organization<br>EN     | Standards Title<br>Particular requirements for the safety of ultrasonic medical<br>diagnostic and monitoring equipment  | Version<br>Second Edition | Date<br>2004-August    |
| 5  | Standards No.<br>ISO 10993-1                 | Standards Organization<br>ISO    | Standards Title<br>Biological Evaluation of Medical Devices   | Version<br>Third Edition  | Date<br>2003-August    |
| 6  | Standards No.                                | Standards Organization           | Standards Title   | Version                   | Date                   |
| 7  | Standards No.                                | Standards Organization           | Standards Title   | Version                   | Date                   |
| <b>Please include any additional standards to be cited on a separate page.</b>   |  |                                  |   |                           |                        |
| <p><b>Public reporting burden for this collection of information</b> is estimated to average 0.5 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:</p> <p style="text-align: center;">Department of Health and Human Services<br/>Food and Drug Administration<br/>Office of the Chief Information Officer (HFA-710)<br/>5600 Fishers Lane<br/>Rockville, Maryland 20857</p> <p><i>An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.</i></p> |  |                                  |   |                           |                        |

### 3. 510(k) Cover Letter

June 7, 2012

Document Mail Center (HFZ-401)  
Center for Devices and Radiological Health  
Food and Drug Administration  
10903 New Hampshire Avenue  
Silver Spring, MD 20993

K121700  
FDA CDRH DMC  
JUN - 8 2012  
Received K18

Re: Ulthera® System - 510(k) Notification - Traditional

Dear Sir or Madam:

In accordance with Section 510(k) of the Food, Drug, and Cosmetic Act, as amended, Ulthera, Inc. hereby notifies FDA of our intent to market the Ulthera® System for an expanded indication for use. Clinical data to support the expanded indication are provided. The proposed labels and revised Instructions for Use reflecting the expanded indication for use are provided in this submission. No changes have been made to the Ulthera® System either for the expanded indication or for the method of device operation. The requested expanded indication for use is as follows:

The Ulthera® System is indicated for use as a non-invasive dermatological aesthetic treatment to:

- lift the eyebrow (current cleared indication)
- lift lax submental (beneath the chin) and neck tissue (requested expanded indication)
- lift lax tissue to achieve a desired aesthetic effect for the full face and neck (current cleared indication + requested expanded indication)

The practitioner would select from one of six Ulthera® System transducers, based on the area to be treated. Thus, the device under review is already cleared, and review is requested only for the expanded indication for use.

To support this request for the expanded indication for use, Ulthera is providing human clinical data as evidence of safety and efficacy of the expanded indication (see Section 20).

In 21 CFR 878.4590, Product Code OHV, FDA defines this type of device:

*Focused Ultrasound Stimulator System for Aesthetic Use is a device using focused ultrasound to produce localized, mechanical motion within tissues and cells for the purpose of producing either localized heating for tissue coagulation or for mechanical cellular membrane disruption intended for non-invasive aesthetic use.*

On September 11, 2009, FDA classified the Ulthera® System as a Class II device through the De Novo 510k process. The petition for classification was filed under Section 513(f)(2) of the Act. In accordance with Section 513(f)(1) of the Act, FDA issued an order on March 14, 2008 automatically classifying the Ulthera® System in Class III because it was not a type of device, which was introduced or delivered for introduction into interstate commerce for commercial distribution before May 28, 1976, nor subsequently reclassified

CONFIDENTIAL—Proprietary Information

06/07/2012

as Class I or II. After review of the information submitted in the petition, FDA determined that the Ulthera® System was indicated for use as a non-invasive treatment to lift the eyebrow to achieve a desired aesthetic effect and would be classified as Class II with establishment of special controls. FDA agreed that Class II special controls provide reasonable assurance of device safety and efficacy.

FDA concluded on September 11, 2009 that the Ulthera® System and substantially equivalent devices should be classified as Class II. The order therefore classified the Ulthera® System and substantially equivalent devices as Class II under the generic name, Focused Ultrasound Stimulator System for Aesthetic Use.

The term “substantially equivalent” is used only as it is defined in the Medical Device Amendment of 1976, as amended by the Safe Medical Device Act of 1990. In accordance with Section 510(k) of the Food, Drug, and Cosmetic Act, Ulthera, Inc. hereby notifies FDA of our intent to market the Ulthera® System. Clinical data to support the expanded indication is included in this submission. No changes have been made to the device or to the device’s performance parameters. The Instructions for Use does not change, with the exception of the requested expanded indication for use.

Ulthera, Inc. considers the information in this submission to be confidential pending substantial equivalency determination and official 510(k) clearance. Please feel free to contact me at Ulthera, Inc. (480) 649-4069.

Sincerely,



Suzon Lommel  
Vice President Regulatory & Quality Affairs  
Ulthera, Inc.  
Email: s.lommel@ulthera.com

## 4. Indications for Use Statement

**510(k) Number:** Unknown

**Device Name:** Ulthera® System

**Indications for Use:**

The Ulthera® System is indicated for use as a non-invasive dermatological aesthetic treatment to:

- lift the eyebrow
- lift lax submental (beneath the chin) and neck tissue
- lift lax tissue to achieve a desired aesthetic effect for the full face and neck

Prescription Use  AND/OR Over-The-Counter Use   
 (Part 21 CFR 801 Subpart D) (21 CFR 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)



## 5. 510(k) Summary

This 510(k) Summary for the Ulthera<sup>®</sup> System is submitted in accordance with the requirements of the Safe Medical Device Act (SMDA) of 1990 and follows the Office of Device Evaluation (ODE) guidance concerning the organization and content of a 510(k) summary.

**Applicant:** Ulthera, Inc.

**Address:** 2150 South Country Club Drive, Suite 21  
Mesa, AZ 85210

**Contact Person:** Suzon Lommel, VP of Regulatory & Quality Affairs

**Telephone:** 480-649-4069

**Fax:** 480-619-4071

**Submission Date:** June 7, 2012

**Device Trade Name:** Ulthera<sup>®</sup> System

**Common Name:** Focused Ultrasound Stimulator Use System for Aesthetic Use

**Classification:** Regulatory Class II

**Classification Name:** Focused Ultrasound Stimulator Use System for Aesthetic Use

**Product Code:** OHV

**Legally Marketed Name:** Ulthera<sup>®</sup> System

**Predicates:** 510(k): #K072505

**Applicable Guidance:** The *Class II Special Controls Guidance Document: Focused Ultrasound Stimulator System for Aesthetic Use* was developed in response to Ulthera's DeNovo submission and 510(k) clearance K0272505 for the Ulthera System.

**Device Description:** The Ulthera<sup>®</sup> System consists of the following components:

- Ulthera<sup>®</sup> Control Unit
- Handpiece
- Transducers

06/07/2012

**Indications for Use:**

The Ulthera® System is indicated for use as a non-invasive dermatological aesthetic treatment to:

- lift the eyebrow (current cleared indication)
- lift lax submental (beneath the chin) and neck tissue (requested expanded indication)
- lift lax tissue to achieve a desired aesthetic effect for the full face and neck (current cleared indication + requested expanded indication)

**Performance Data:**

Clinical analysis was conducted in clinical trials to support the clinical performance of the Ulthera® System. Sufficient safety data has been gathered to determine that the Ulthera® System performs as clinically intended.

**Conclusion:**

Based on the design, materials, principle of operation, and intended use, the Ulthera® System is substantially equivalent to the legally marketed predicate device.

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## 6. Truthful and Accuracy Statement

Pursuant to 21 CFR 807.87(k), I certify that, in my capacity as Vice President Regulatory & Quality Affairs, I believe to the best of my knowledge, that all data and information submitted in this pre-market notification are truthful and accurate and that no material fact has been omitted.

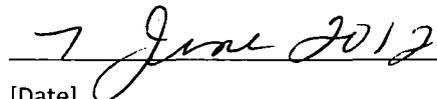


---

[Signature]

Suzon Lommel

Vice President, Regulatory & Quality Affairs



---

[Date]

---

## 7. Class III Summary and Certification

N/A

---

## 8. Financial Certification

DEPARTMENT OF HEALTH AND HUMAN SERVICES  
Food and Drug Administration

Form Approved: OMB No. 0910-0396  
Expiration Date: August 31, 2012

**CERTIFICATION: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS**

TO BE COMPLETED BY APPLICANT

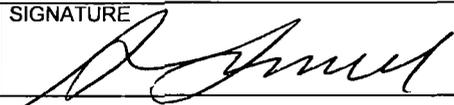
With respect to all covered clinical studies (or specific clinical studies listed below (if appropriate)) submitted in support of this application, I certify to one of the statements below as appropriate. I understand that this certification is made in compliance with 21 CFR part 54 and that for the purposes of this statement, a clinical investigator includes the spouse and each dependent child of the investigator as defined in 21 CFR 54.2(d).

Please mark the applicable checkbox.

- (1) As the sponsor of the submitted studies, I certify that I have not entered into any financial arrangement with the listed clinical investigators (enter names of clinical investigators below or attach list of names to this form) whereby the value of compensation to the investigator could be affected by the outcome of the study as defined in 21 CFR 54.2(a). I also certify that each listed clinical investigator required to disclose to the sponsor whether the investigator had a proprietary interest in this product or a significant equity in the sponsor as defined in 21 CFR 54.2(b) did not disclose any such interests. I further certify that no listed investigator was the recipient of significant payments of other sorts as defined in 21 CFR 54.2(f).

|                        |                                   |  |
|------------------------|-----------------------------------|--|
| Clinical Investigators | Jeffrey M. Kenkel, M.D., F.A.C.S. |  |
|                        | Ronald E. Hoxworth, M.D.          |  |
|                        | Sumeet S. Testia, M.D.            |  |

- (2) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that based on information obtained from the sponsor or from participating clinical investigators, the listed clinical investigators (attach list of names to this form) did not participate in any financial arrangement with the sponsor of a covered study whereby the value of compensation to the investigator for conducting the study could be affected by the outcome of the study (as defined in 21 CFR 54.2(a)); had no proprietary interest in this product or significant equity interest in the sponsor of the covered study (as defined in 21 CFR 54.2(b)); and was not the recipient of significant payments of other sorts (as defined in 21 CFR 54.2(f)).
- (3) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that I have acted with due diligence to obtain from the listed clinical investigators (attach list of names) or from the sponsor the information required under 54.4 and it was not possible to do so. The reason why this information could not be obtained is attached.

|  |  |
|--|--|
| NAME<br>Suzon Lommel   | TITLE<br>Vice President Regulatory & Quality Affairs |
| FIRM/ORGANIZATION<br>Ulthera, Inc.   |  |
| SIGNATURE<br> | DATE (mm/dd/yyyy)<br>7 June 2012                     |

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Department of Health and Human Services  
Food and Drug Administration  
Office of Chief Information Officer  
1350 Piccard Drive, 420A  
Rockville, MD 20850

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## 9. Declaration of Conformity

## Declaration of Conformity



Ulthera®, Inc.  
 2150 South Country Club Drive  
 Suite 21  
 Mesa, AZ 85210  
[info@ulthera.com](mailto:info@ulthera.com)  
 Phone: (480) 619-4069

We, Ulthera® Inc., declare under our sole responsibility that the following

| Description                           | Product Code |
|---------------------------------------|--------------|
| Ulthera Control Unit                  | UC-1         |
| Ulthera DeepSEE Handpiece             | UH-2         |
| Ulthera DeepSEE Transducer DS 7-3.0   | UT-1         |
| Ulthera DeepSEE Transducer DS 7-3.0N  | UT-1N        |
| Ulthera DeepSEE Transducer DS 4-4.5   | UT-2         |
| Ulthera DeepSEE Transducer DS 7-4.5   | UT-3         |
| Ulthera DeepSEE Transducer DS 10-1.5  | UT-4         |
| Ulthera DeepSEE Transducer DS 10-1.5N | UT-4N        |

Is in conformity with the following standards:

- a) IEC 60601-1, Medical Electrical Equipment, Part 1: General requirements for safety
- b) IEC 60601-1-2, Medical Electrical Equipment, Part 1-2: General requirements for safety-Collateral standard: Electromagnetic compatibility – Requirements and tests
- c) IEC 60601-1-4, Medical Electrical Equipment, Part 1-4: General requirements for safety-Collateral standard: Programmable electrical medical systems,
- d) IEC 60601-2-37: 2004-08 Particular requirements for the safety of ultrasonic medical diagnostic and monitoring equipment.

Testing was performed at the following two certified test facilities:

|            |        |   |
|------------|--------|---|
| Electrical | (a-c): | Nemko USA, Inc.<br>11696 Sorrento Valley Road, Suite F<br>San Diego, CA 92121-1024, USA                                       |
| Acoustic   | (d):   | Sonic Technologies Laboratory Services<br>(Sonora Medical Systems)<br>1751 S. Fordham Street, Suite 100<br>Longmont, CO 80503 |

Documents are maintained on file in the Device History File.

Signed:

  
 Suzon Lommel  
 Ulthera®, Inc.

Date:



Document Number 1000608FRM Rev. A



## Declaration of Conformity



Ulthera®, Inc.  
 2150 South Country Club Drive  
 Suite 21  
 Mesa, AZ 85210  
[info@ulthera.com](mailto:info@ulthera.com)  
 Phone: (480) 619-4069

We, Ulthera® Inc., declare under our sole responsibility that the

| Description                           | Product Code |
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| Ulthera Control Unit                  | UC-1         |
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| Ulthera DeepSEE Transducer DS 7-3.0   | UT-1         |
| Ulthera DeepSEE Transducer DS 7-3.0N  | UT-1N        |
| Ulthera DeepSEE Transducer DS 4-4.5   | UT-2         |
| Ulthera DeepSEE Transducer DS 7-4.5   | UT-3         |
| Ulthera DeepSEE Transducer DS 10-1.5  | UT-4         |
| Ulthera DeepSEE Transducer DS 10-1.5N | UT-4N        |

has an acoustic imaging output power that is in conformity with the following standards:

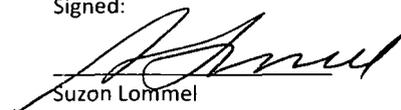
- a) "Acoustic Output Measurement Standard for Diagnostic Ultrasound Equipment" (AIUM, NEMA UD2-2004)
- b) "Standard for Real-Time Display of Thermal and Mechanical Acoustic Output indices on Diagnostic Ultrasound Equipment" (AIUM, NEMA 1998).

Testing was performed at the following certified facility:

Certified Lab (a-b): Sonic Technologies Laboratory Services  
 (Sonora Medical Systems)  
 1751 S. Fordham Street, Suite 100  
 Longmont, CO 80503

Documents are maintained on file in the Device Master Record.

Signed:

  
 Suzon Lohmell  
 Ulthera®, Inc.

Date:



Document Number 1000973FRM Rev. A



**Declaration of Conformity**



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We, Ulthera® Inc., declare under our sole responsibility that the following

| Description                           | Product Code |
|---------------------------------------|--------------|
| Ulthera Control Unit                  | UC-1         |
| Ulthera DeepSEE Handpiece             | UH-2         |
| Ulthera DeepSEE Transducer DS 7-3.0   | UT-1         |
| Ulthera DeepSEE Transducer DS 7-3.0N  | UT-1N        |
| Ulthera DeepSEE Transducer DS 4-4.5   | UT-2         |
| Ulthera DeepSEE Transducer DS 7-4.5   | UT-3         |
| Ulthera DeepSEE Transducer DS 10-1.5  | UT-4         |
| Ulthera DeepSEE Transducer DS 10-1.5N | UT-4N        |

are in conformity with ISO-10993-1 and USP Class VI, for patient contact materials following standards:

| Trade Name                              | Generic Material            | Biocompatibility Data   |
|---|-----------------------------|---|
| PEEK Classix, BC2-WH<br>Invibio, Ltd.   | Polyetheretherketone (PEEK) | ISO 10993-1, -5, and -10<br>Compliant,<br>USP Class VI Certification,<br>Records maintained in Device<br>History File |
| Lexan HPSI-1H1124,<br>GE Plastics, Inc. | Polycarbonate               | ISO 10993-1 -7 Compliant,<br>USP Class VI Certification,<br>Records maintained in Device<br>History File.             |

Signed:

Suzon Lommel  
 Ulthera®, Inc.

Date:

Document Number 1000974FRM Rev. A



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## 10. Executive Summary

### 10.1. Device Description

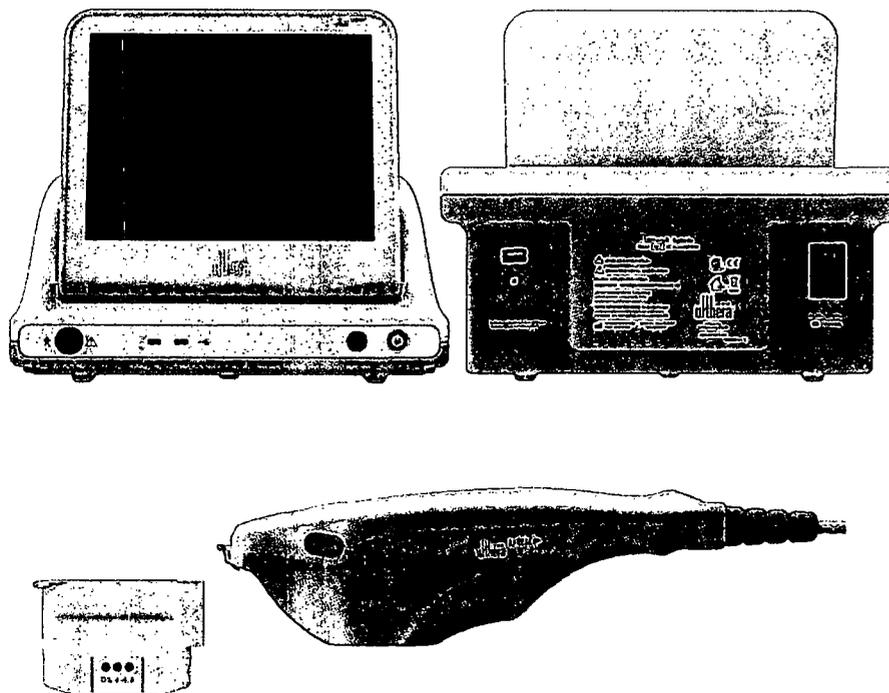
The Ulthera® System integrates the capabilities of ultrasound imaging with those of ultrasound therapy.

The imaging feature allows the user to assure proper skin contact in order to deliver the energy safely at desired depths.

The therapy feature directs micro-focused acoustic waves to the treatment area. This acoustic energy heats tissue as a result of frictional losses during energy absorption, producing discrete points of tissue coagulation.

The Ulthera® System consists of three primary components: the control unit with integrated touchscreen, the handpiece with cable, and interchangeable transducers (see Figure 10-1).

**Figure 10-1: Main Components of the Ulthera® System**



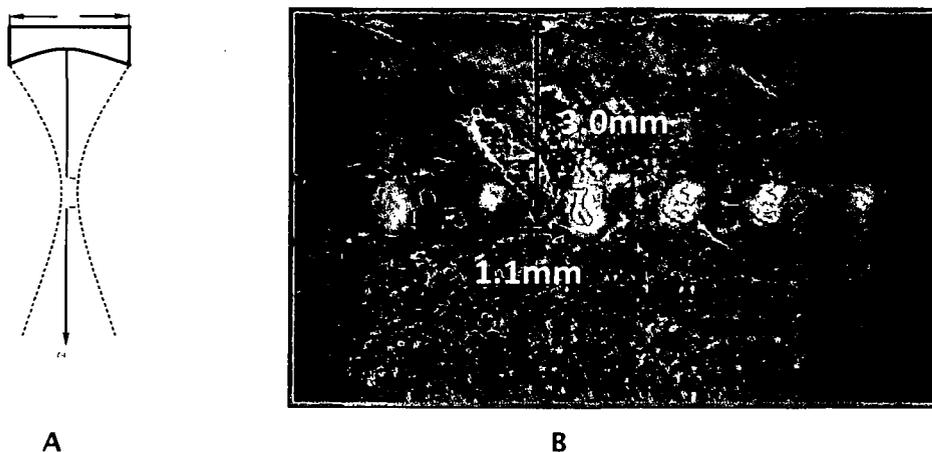
The Ulthera® System is indicated for use as a non-invasive dermatological aesthetic treatment to:

- lift the eyebrow (current cleared indication)
- lift submental (lower chin) and neck tissue (requested expanded indication)
- lift lax tissue to achieve a desired aesthetic effect for the full face and neck (current cleared indication + requested expanded indication)

The Ulthera® System is designed to focus acoustic energy within skin tissue to achieve well defined regions of tissue coagulation in a non-invasive manner. In the case of aesthetic applications with the Ulthera® System, a spatially confined zone of thermal coagulation (on the order of  $1 \text{ mm}^3$ ) results from a short ( $< 100\text{ms}$  long), low energy ( $< 2 \text{ J}$ ), ultrasound controlled energy delivery. The focusing of the ultrasound beam for the Ulthera® System is shown in the schematic below, as well as results from a representative porcine skin experiment (Figure 10-2).

In order to achieve the confined, shallow zone of coagulation in skin tissue (surface – 5 mm), the Ulthera® System transducers are designed to geometrically focus ultrasound energy only at these depth zones and not deeper. Further, this precise focusing at selected depths is achieved by using highly focused ultrasound transducers (Figure 10-2).

**Figure 10-2: Focus Beam (A) and Coagulated Zone (B)**



- (A) Schematic of a focused beam for skin coagulation. The target zone is at the focus and is on the order of  $< 1 \text{ mm}^3$ .
- (B) Example of coagulated zones in porcine skin tissue.

## 10.2. Predicate Comparison

Please note that no changes have been made to the Ulthera® System since it was reviewed and cleared by FDA under the original 510(k), K072505 that would result in a new 510(k).

The Ulthera® System images and delivers focused ultrasound (US) energy to a specific soft tissue layer under the superficial layers of epidermis. Treatment with the Ulthera System creates a focal coagulation point below the skin surface, causing thermally induced contraction of tissue

and a "natural inflammatory process" to stimulate the formation of new collagen which produces a tissue-tightening and lifting effect.

Extensive safety studies with the Ulthera® System were provided in the original 510(k), K072505. Previous studies have demonstrated that the Ulthera® System has a significant safety profile and is safe for the device's expanded use indication.

The difference in labeling relates only to the indication for use and does not differ from the intended effect or mechanism of action of the Ulthera® System. The expanded indication for use does not bear materially on the safe and effective use of the device. There are no other changes in technology, design, materials, sterilization, shelf life, or performance characteristics from the predicate device; and therefore no new safety or effectiveness questions are relevant. Table 10-1 provides a comparison of the predicate and the subject device.

**Table 10-1: Predicate and Subject Device Comparison**

|                                      | <b>Predicate Device</b>  | <b>Subject Device</b>   |
|--------------------------------------|--|---|
|                                      | <b>Ulthera® System;<br/>cleared under K072505</b>  | <b>Ulthera® System; same as the<br/>cleared system K072505;<br/>Expanded indication for use</b>   |
| Classification/<br>Product Code      | 878.4590<br>OHV  | 878.4590<br>OHV<br><br>Same   |
| Intended Use/<br>Indications for Use | Non-invasive dermatological<br>aesthetic treatment to:<br><br>· lift the eyebrow (current cleared<br>indication) | Non-invasive dermatological<br>aesthetic treatment to:<br><br>· lift the eyebrow (current cleared<br>indication)<br>· lift lax submental (beneath the<br>chin) and neck tissue<br>(requested expanded<br>indication)<br>· lift lax tissue to achieve a<br>desired aesthetic effect for the<br>full face and neck (current<br>cleared indication + requested<br>expanded indication) |
| Where Used                           | Clinic/doctor's office   | Clinic/doctor's office<br><br>Same  |
| Anatomical Site                      | Skin   | Skin<br><br>Same  |
| Type of Energy                       | Thermal<br>< 2 J   | Thermal<br>< 2 J<br><br>Same  |

|  | <b>Predicate Device</b><br><b>Ulthera® System;</b><br><b>cleared under K072505</b>   | <b>Subject Device</b><br><b>Ulthera® System; same as the</b><br><b>cleared system K072505;</b><br><b>Expanded indication for use</b>   |
|--|--|--|
| Biological Effect                                | Lifting of tissue via High Intensity Focused Ultrasound (HIFU) directed beneath the outer dermis in localized points at a specified depth and distance between points. | Lifting of tissue via High Intensity Focused Ultrasound (HIFU) directed beneath the outer dermis in localized points at a specified depth and distance between points.<br><br>Same |
| Lifting of Lax Tissue                            | Eyebrow  | Submental (beneath the chin) and neck  |
| Demonstrated Safety and Efficacy in treated area | Provided in K072505 cleared September 11, 2009   | Performance Testing - Clinical<br><br>Provided in Section 20   |
| Patient Contact Material                         | Biocompatible  | Biocompatible<br><br>Same  |
| Electromagnetic Compatibility Standards          | Compliant  | Compliant<br><br>Same  |
| Medical Electrical Equipment Safety Standards    | Compliant  | Compliant<br><br>Same  |
| Thermal Coagulation Point                        | Confined to focal zone; shallow (< 5 mm); no thermal coagulation below focal zone  | Confined to focal zone; shallow (< 5 mm); no thermal coagulation below focal zone<br><br>Same  |
| Epidermal Impact                                 | Non-invasive; no cooling required  | Non-invasive; no cooling required<br><br>Same  |
| Pigmentation Effect                              | Chromophore insensitive  | Chromophore insensitive<br><br>Same  |
| Packaging  | Nylon / Aluminum foil laminate bag with very low water vapor transmission rate. The bag is enclosed within a cardboard box for storage.                                | Nylon / Aluminum foil laminate bag with very low water vapor transmission rate. The bag is enclosed within a cardboard box for storage.<br><br>Same                                |
| Sterilization                                    | Provided non-sterile   | Provided non-sterile<br><br>Same   |

|            | <b>Predicate Device</b>                           | <b>Subject Device</b>   |
|------------|---|---|
|            | <b>Ulthera® System;<br/>cleared under K072505</b> | <b>Ulthera® System; same as the<br/>cleared system K072505;<br/>Expanded indication for use</b> |
| Shelf Life | 6 months  | 6 months<br><br>Same  |

### 10.3. Clinical Study (Basis for Expanded Indication)

This open-label clinical trial was conducted to establish the safety and efficacy of the Ulthera® System, an investigational device designed to image and deliver focused ultrasound energy to a specific soft tissue layer. The clinical trial was a prospective safety and efficacy study to evaluate the Ulthera® System for achieving lifting of the lax submental (beneath the chin) and neck tissue.

A goal of this study was to investigate the clinical response of Ulthera® ultrasound exposures to achieve a lift of submental (lower chin) and neck tissue and improvement of skin laxity through tissue coagulation and skin tightening in an aesthetically relevant manner. Improvement in the above stated areas was confirmed by assessment and comparison of pre- and post-treatment photographs by three masked clinician reviewers. Ulthera executed the masked assessment for both the validation process and the 90-day efficacy assessment according to the specific guidelines discussed and agreed upon with FDA for Ulthera's predicate device De-Novo premarket submission (K072505) and approval.

Detailed assessments of pre- and post-treatment photographs by masked clinicians, patient satisfaction questionnaires, and quantitative analysis have shown successful lift of lax submental (beneath the chin) and neck tissue after Ulthera® System treatments.

This safety and efficacy study successfully achieved all the goals stated in the protocol. The study demonstrated that Ulthera® System procedures can be safely performed on the face and neck in a professional setting. Delivery of ultrasound energy using the Ulthera® System produces a favorable aesthetic result based on comparative review of the pre- and post-treatment photographs, measurement of tissue lift and patient satisfaction. The results of the qualitative masked clinician assessment, quantitative analysis and patient assessment indicated there was lifting of the lax submental (beneath the chin) and neck tissue.

Improvement in lax tissue in the lower face combined with the current indication for eyebrow lift creates a lift in lax tissue to achieve a desired aesthetic effect for the full face and neck after the Ulthera® procedure.

---

## 11. Device Description

### 11.1. Introduction

Please note that no changes have been made to the Ulthera® System since it was reviewed and cleared by FDA under the original 510(k), K072505.

The Ulthera® System produces controlled tissue coagulation below the skin surface (epidermis) within the first few millimeters of tissue (dermis) using highly focused, low energy (< 2 joules) ultrasound deposition. Acoustic energy heats tissue as a result of frictional losses during energy absorption, inducing a micro-coagulated zone of skin tissue. Other medical devices, which utilize different types of energy, rely upon a similar principle of thermal response. The Ulthera System differs from these other device in that energy is delivered below the epidermis in an extremely controlled fashion (micro-focused vs. radiofrequency bulk heating) without affecting the skin surface or requiring a secondary action to protect the skin surface.

In addition to its micro-coagulation capability, the Ulthera® System has a supplemental imaging mode of operation. The operator may use the supplemental imaging capability to visualize the treatment area and aid in assuring full skin contact of the Ulthera® System transducer to the skin in the treatment area.

The Ulthera® System is indicated for use as a non-invasive dermatological aesthetic treatment to:

- lift the eyebrow (current cleared indication)
- lift lax submental (beneath the chin) and neck tissue (requested expanded indication)
- lift lax tissue to achieve a desired aesthetic effect for the full face and neck (current cleared indication + requested expanded indication)

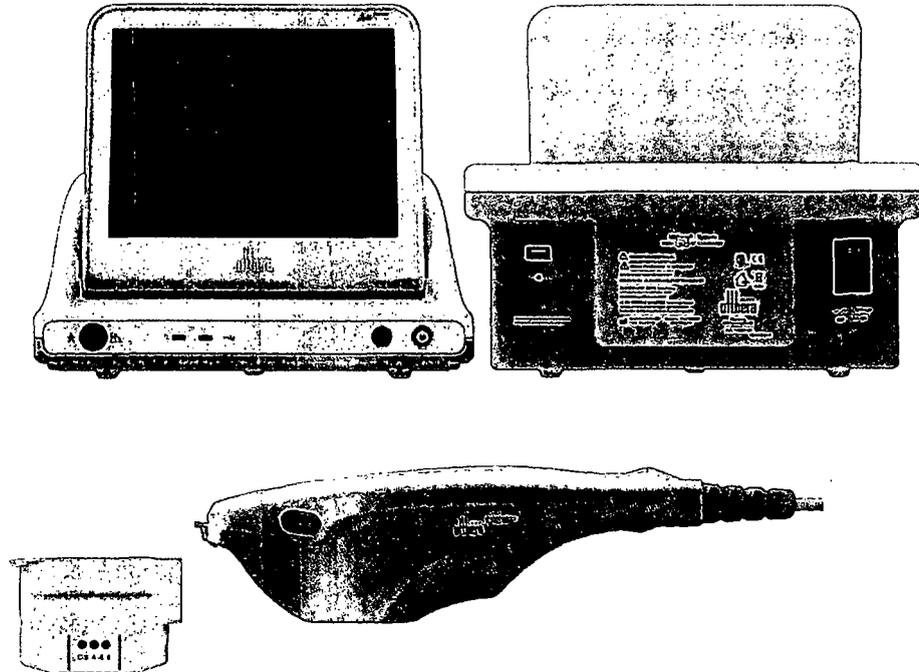
### 11.2. System Description

The Ulthera® System integrates the capabilities of ultrasound imaging with those of ultrasound therapy. It allows the user to confirm proper skin contact in order to deliver the energy at desired depths.

The therapy feature directs micro-focused acoustic waves to the treatment area. This acoustic energy heats tissue as a result of frictional losses during energy absorption, producing discrete points of thermal coagulation.

### 11.3. System Components and Features

The Ulthera® System consists of three primary components: the control unit with integrated touchscreen, the handpiece with cable, and interchangeable transducers (see Figure 11-1).

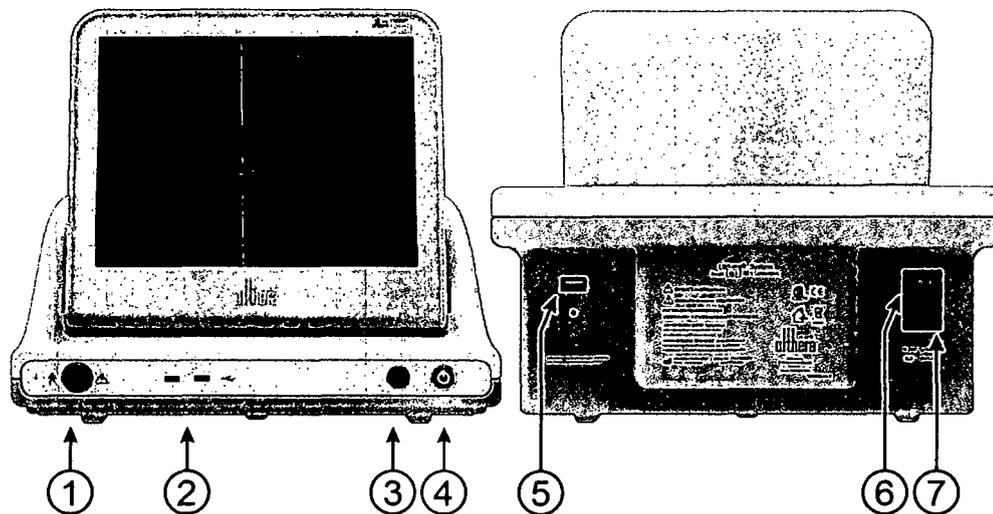
**Figure 11-1: Main Components of the Ulthera® System**

### 11.3.1. Control Unit

The control unit is the tabletop information center for the Ulthera System. It houses the touchscreen monitor and Graphical User Interface (GUI) that allows the user to interact with the device. This screen sets and displays the operating conditions, including equipment activation status, treatment parameters, system messages and prompts, and ultrasound images.

Figure 11-2 illustrates the physical features of the control unit, such as the various connector ports and power controls. Table 11-1 identifies the individual components.

**Figure 11-2: Control Unit, Front View (Left) and Rear View (Right)**



**Table 11-1: Control Unit Connector Ports and Controls Shown Figure 11-2**

| Item | Description   |
|------|---|
| 1    | Handpiece Connector Receptacle<br>Socket for plugging in handpiece cable  |
| 2    | Front USB Ports (two)<br>For optional USB removable storage device  |
| 3    | Emergency Stop<br>Halts system operation if pressed   |
| 4    | On/Off Switch<br><ul style="list-style-type: none"> <li>• Momentarily press to turn system ON</li> <li>• Momentarily press to turn system OFF</li> <li>• Press and hold to force system shutdown</li> </ul> |
| 5    | Rear Panel USB port<br>For Ulthera System User Access key   |
| 6    | Main Power Switch<br>Supplies power to system. Leave ON (1 symbol pressed in)   |
| 7    | Power Cord Receptacle<br>Socket for attachment of power cord  |

Below the monitor, on the front panel of the control unit is a handpiece connector receptacle that interfaces with the handpiece cable. On the front right of the panel is an On/Off button and an emergency Stop button. When turned OFF via the On/Off button the system goes into a very low power standby mode unless the Main Power Switch is also turned to the OFF position by pressing the 'O' symbol. The front of the control unit also has two Universal Serial Bus (USB) ports: both ports may be used for the Ulthera System User Access Key or for an optional removable storage device ("thumb drive").

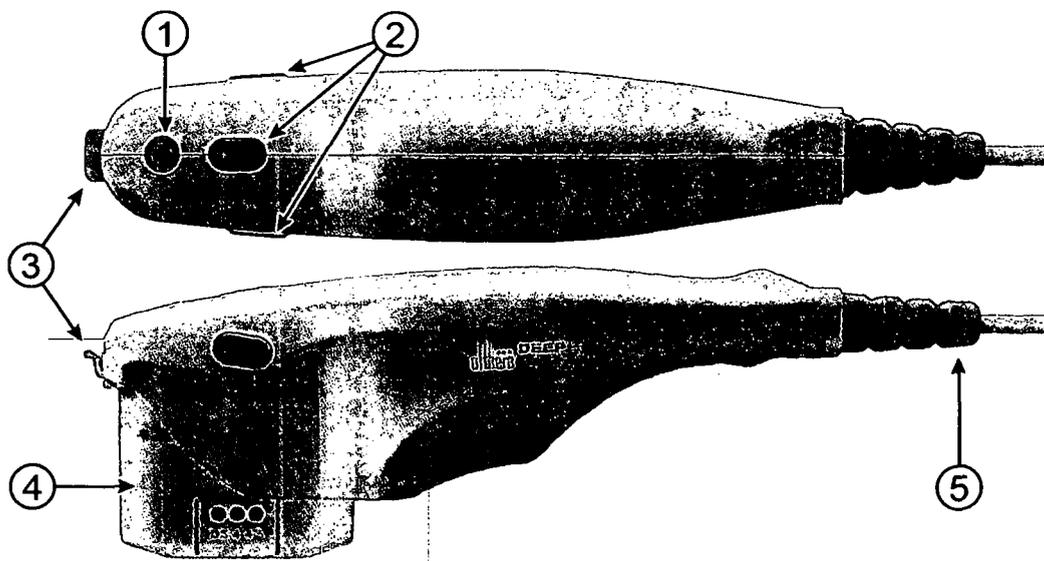
The Ulthera System User Access Key is a safety feature and must be inserted in the USB port in order for the Ulthera System to function. When not in use by trained personnel, the Ulthera System User Access Key should be removed from the system to help prevent unauthorized use

### 11.3.2. Handpiece

The handpiece is a handle with an integrated receptacle for insertion of a transducer on one end and an electrical cable for attachment to the control system on the other end. The handpiece has two types of buttons: one to image (SEE) and the other to deliver therapy (TREAT). Figure 11 4 provides two views of the handpiece, including one showing it connected to an Image/Treat transducer.

Table 11-2 is a description of the various components and features illustrated in Figure 11-3.

**Figure 11-3: Handpiece with Transducer Inserted, top and side views**



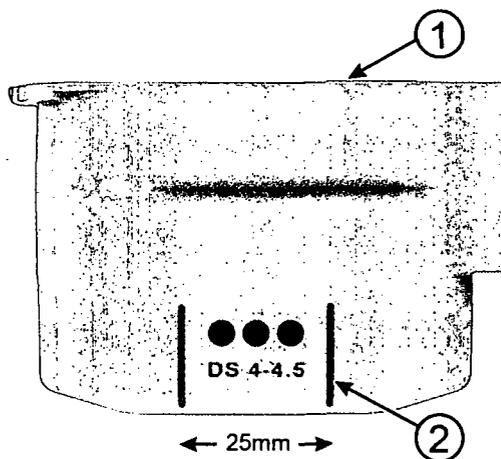
**Table 11-2: Handpiece and Transducer**

| Item                      | Description  |
|---------------------------|--|
| 1 SEE Pushbutton          | <ul style="list-style-type: none"> <li>Engages IMAGING state (if not already imaging)</li> <li>Places system in READY state (times out in 40 seconds)</li> <li>Stops TREATING if treatment is in progress</li> </ul> |
| 2 TREAT Pushbutton        | <ul style="list-style-type: none"> <li>Engages TREATING state</li> </ul>   |
| 3 Latch                   | Locks transducer into handpiece  |
| 4 Transducer              | Image/treat transducer   |
| 5 Strain Relief and Cable | Connects handpiece to Control Unit   |

### 11.3.3. Transducers

Figure 11-4 is an illustration of a transducer. The transducer can treat a region of tissue up to 25 mm long and can image contact with skin surface. Treatment occurs along a line less than or equal to the transducer's active length, which is indicated by guides on the sides of the transducer, as described in Table 11-3 an additional guide at the front tip of the transducer represents the center of the treatment line. In therapy mode, controlled delivery of ultrasound energy creates a linear sequence of individual, discrete, thermal coagulation zones. A label atop the transducer provides the transducer type, expiration date, and other information.

**Figure 11-4: Transducer, Separated from Handpiece**



**Table 11-3: Labeling on the Transducer**

| Item |              | Description                                    |
|------|--------------|--|
| 1    | Labeling     | Transducer type and other information          |
| 2    | Treat guides | Markers denoting maximum treatment line length |

The available transducers provide the frequencies and depth of treatment zone shown in Table 11-4. The imaging center frequency is 18MHz.

Table 11-4: Transducer Types

| Product Code | Transducer Model | Treatment Frequency (MHz) | Energy Allowed (J) | Depth of Treatment Zone (mm) | Treatment Length (mm) | *Footprint | *Profile |
|--------------|------------------|---------------------------|--------------------|------------------------------|-----------------------|------------|----------|
| UT-2         | DS 4 - 4.5       | 4                         | 0.75 - 1.20        | 4.5                          | 25                    | Standard   | Straight |
| UT-1         | DS 7 - 3.0       | 7                         | 0.25 - 0.45        | 3.0                          | 25                    | Standard   | Straight |
| UT-1N        | DS 7 - 3.0N      | 7                         | 0.25 - 0.45        | 3.0                          | 14                    | Narrow     | Tapered  |
| UT-3         | DS 7 - 4.5       | 7                         | 0.66 - 1.05        | 4.5                          | 25                    | Standard   | Straight |
| UT-4         | DS 10 - 1.5      | 10                        | 0.15 - 0.25        | 1.5                          | 25                    | Standard   | Straight |
| UT-4N        | DS 10 - 1.5N     | 10                        | 0.15 - 0.25        | 1.5                          | 14                    | Narrow     | Tapered  |

\*See Figure 11-5 and Figure 11-6 for more information

Each transducer has a maximum allowable energy at a specific treatment depth to ensure safety. Higher energies are excluded by way of software limitations. A physician may lower energy within the predetermined range, but may not increase it above the maximum allowable energy. A deeper treatment depth requires a higher energy setting in order to achieve the required tissue coagulation to produce the aesthetic effect. The Ulthera System is very safe, because tissue coagulation occurs only at the focal zone with micro-focused ultrasound. The treatment energies outlined above have been shown to be safe during clinical and commercial evaluation. These treatment ranges have been used safely in over 90,000 commercial treatments worldwide.

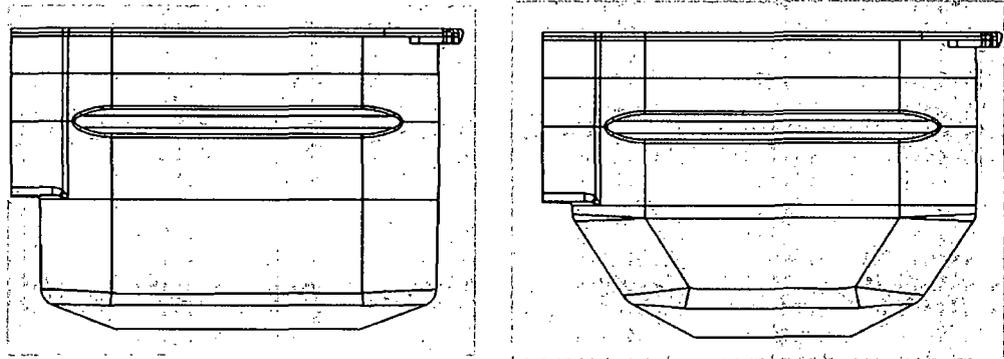
The DS 7-3.0N, DS 10-1.5 and DS 10-1.5N transducers are marketed through *FDA guidance document: Guidance for Industry and FDA Staff: Deciding When to Submit a 510(k) for a Change to an Existing Device.*

It is important to note that the function and performance of the DS 7-3.0N transducer is identical to the DS 7-3.0 transducer, which was cleared in the original K072705. The only parameter that has changed is the outer shell of the transducer, which is more ergonomic for operation due to anatomical variability (e.g. shape of frontal bone may prevent good skin contact at 25mm, patients with small faces) that makes it difficult to use the shape of the standard transducer safely.

The DS 10-1.5 and DS 10-1.5N transducers deliver the lowest amount of energy in the transducer family. The DS 10-1.5N transducer is identical to the DS 10-1.5 transducer with regard to allowable treatment energy and depth of treatment zone. The DS 10-1.5N is equivalent to the narrow transducer (DS 7-3.0N) in outer shell dimensions, treatment length and footprint. The DS 10-1.5 is equivalent to the other standard transducers (DS 7-3.0, DS 4 - 4.5 and DS 7 - 4.5) in outer shell dimensions, treatment length and footprint.

Figure 11-5 and Figure 11-6 include side by side comparisons of the standard and narrow transducer.

**Figure 11-5: Comparison of Standard (left) and Narrow (right) Transducer Shells**



**Figure 11-6: Comparison of Standard (left) and Narrow (right) Transducer Profiles**

|                  |              |            |
|------------------|--------------|------------|
|                  | <br>Standard | <br>Narrow |
| Footprint        |              |            |
| Profile          | Straight     | Tapered    |
| Treatment Length | 25mm         | 14mm       |

### 11.3.4. Essential Accessories

Other essential components provided for operation of the Ulthera System are the power cord that connects the Ulthera System to an AC power outlet, and the proprietary Ulthera System User Access Key which must be inserted into the system to deliver energy as an additional safety feature to prevent use by unauthorized personnel. USB removable drives are optional for patient data storage.

Ultrasound gel to facilitate transmission of the acoustic energy is also required but is not provided as part of the system.

## 11.4. Patient Contacting Materials

There have been no changes to the patient contacting materials in the original 510(k), K072705. Patient Contact Materials are shown in Table 11-5. They consist of the transducer housing material (polycarbonate), which may incidentally contact the patient, and the acoustic window material (PEEK). Both materials are ISO-10933-1 and USP Class VI compliant.

**Table 11-5: Patient Contact Materials**

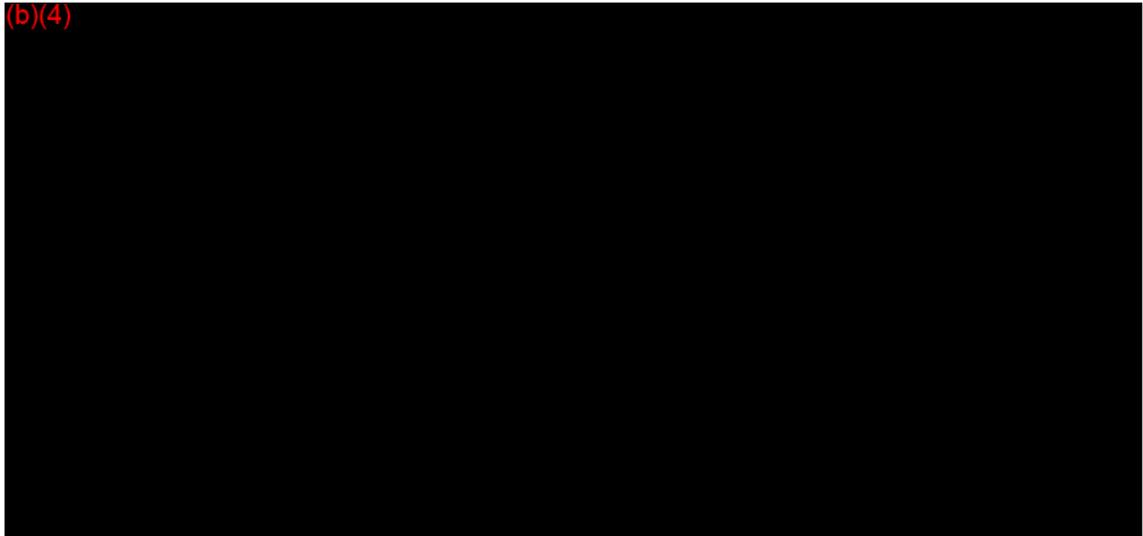
| Trade Name  | Generic Material | Biocompatibility Data |
|---|------------------|-----------------------|
| <b>Function:</b> Acoustic Window (Short term patient contact):    |                  |                       |
| (b)(4)  |                  |                       |
| <b>Function:</b> Transducer Housing (Incidental patient contact): |                  |                       |
| (b)(4)  |                  |                       |

## 11.5. Diagrams and Specifications

The simple block diagram of the Ulthera<sup>®</sup> System in

Figure 11-7 illustrates how the touch screen, embedded host, imaging subsystem, therapy subsystem, and control-subsystem of the control unit interface with the handpiece and transducer. The Ulthera<sup>®</sup> System limits therapy acoustic energy to preset levels that cannot be increased by the user.

**Figure 11-7: Interfacing of Ulthera<sup>®</sup> System Components**



The therapy subsystem contains an RF driver circuit, which delivers and monitors electric power going to the transducer.

The imaging subsystem contains pulse-echo imaging electronics and is controlled by the microcontroller software on the controller board.

The control subsystem consists of controller hardware, which mechanically which contains microcontroller software that directs the transducer to move from one treatment to the next for therapy, controls therapy hardware settings, and provides all other control functions, including interfacing with the embedded host.

### 11.5.1. Control Unit Description

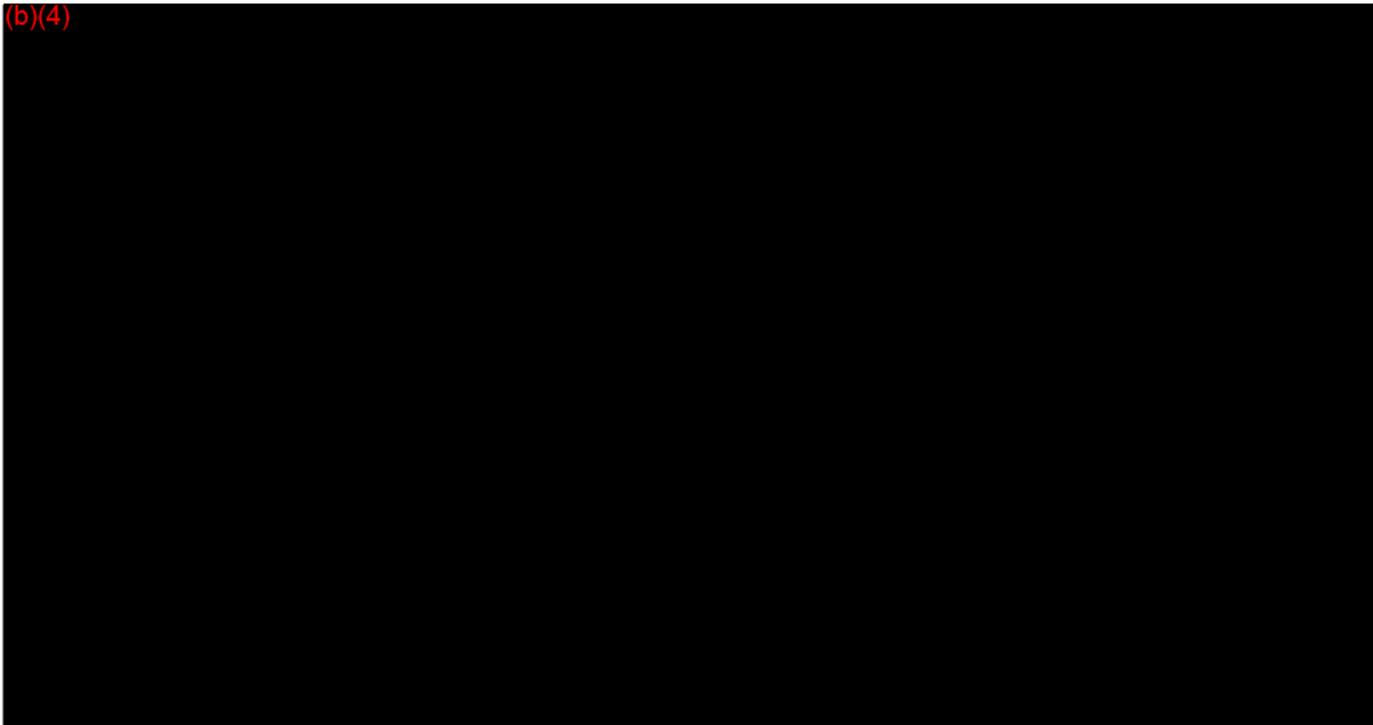
The Control Unit contains the six major electronic components shown in the leftmost panel of Figure 11-8:

1. An international, medical grade power supply;
2. An embedded host computer for collecting user input, transferring it to the system controller, and displaying images and system status;

3. An LCD touch screen;
4. A custom RF driver for providing power to the therapy transducer; and
5. A custom digital system controller with imaging engine and hardware-based therapy control for setting frequency, treatment timing, and voltage (power) levels to the driver; and for monitoring system status.
6. The Control Unit's front panel connector and flexible printed circuit cable interconnect.

The end of the handpiece cable has a quick connect/release multi-pin connector plug which connects the Control Unit to the handpiece and transducer.

**Figure 11-8: Ulthera® System Hardware Layout Block Diagram**

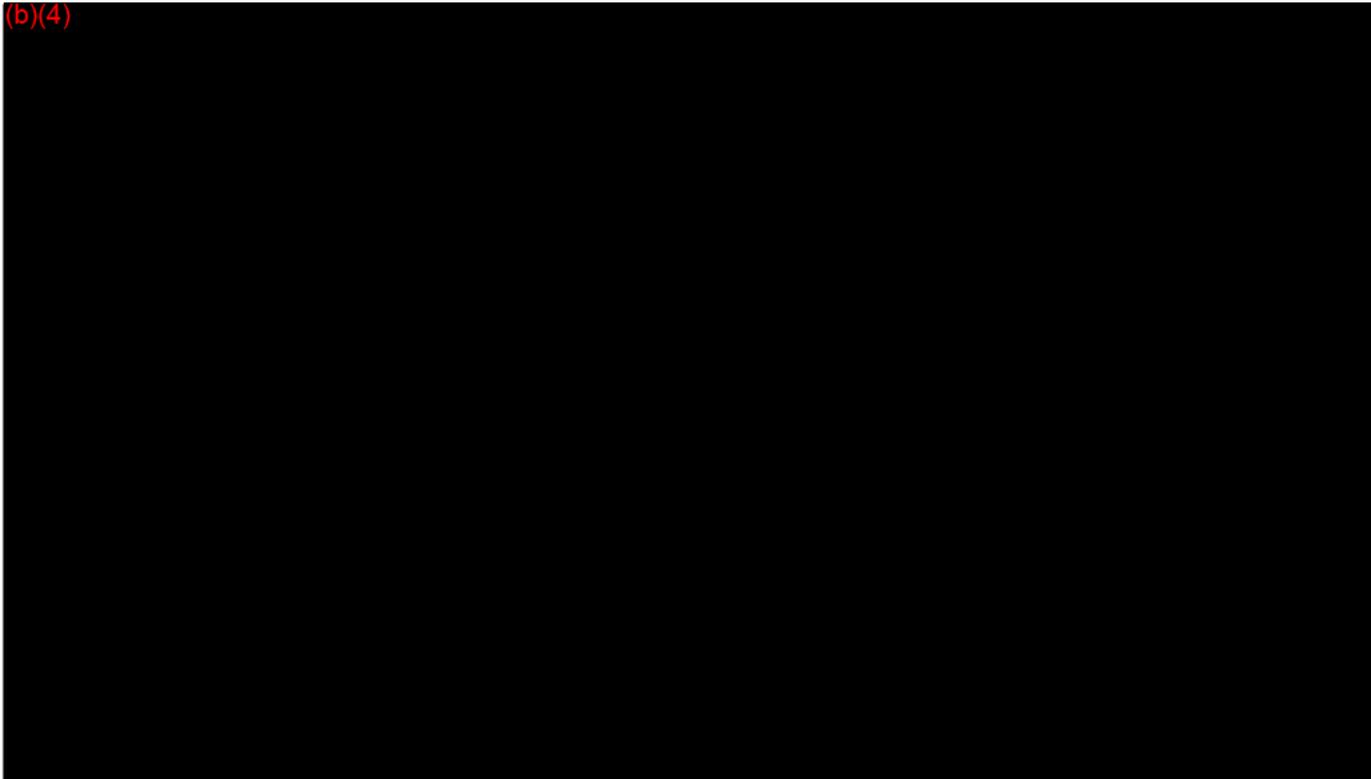


## 11.5.2. Handpiece and Transducer Description

The handpiece and transducer have a number of components to accomplish their functions. Figure 11-9 is a block diagram illustrating these functions.

**Figure 11-9: Handpiece and Transducer**

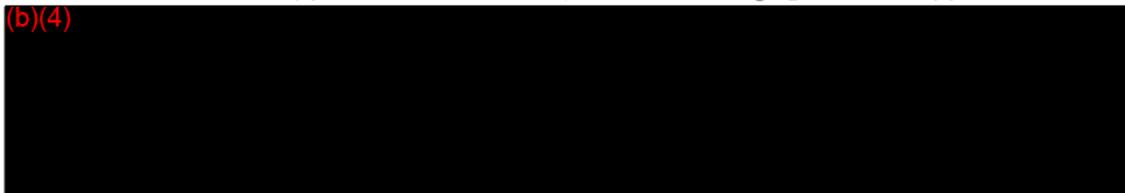
(b)(4)



Handpiece components are enclosed within a plastic clamshell holding a high-speed linear motion mechanism and 0.1mm accuracy optical position encoder mounted on an aluminum frame. Also mounted on the frame is a printed circuit board interfacing to the handpiece cable and the handpiece electronics including switches, temperature sensor, EEPROM, and electric contactor pins. The contactor pins are configured to mate to pads on the transducer's printed circuit board when a transducer is inserted into the transducer receptacle in the handpiece.

The transducer PCB also contains a calibration and information-storage secure EEPROM, a sensor which measures the fluid-filled transducer's water temperature, an electric matching network for the therapy transducer element, and both imaging and therapy transducer

(b)(4)



## 11.6. Description of Safety Features

Many safety features have been designed into the Ulthera<sup>®</sup> System, some of which are described in the following sections. In addition, the system has been designed for compliance with the international safety standards and classifications listed in the “General Specifications and Standards” section.

### 11.6.1. Calibration Data

Characteristics for each transducer reside on a secure EEPROM, including uniquely traceable serial number, transducer ID, frequency setting, acoustic power versus voltage look-up-table, electric power versus voltage look-up-table, maximum power levels, date codes, usage, and other information.

### 11.6.2. Safe Operating Area

For all transducers, energy output is limited to a safe maximum setting which cannot be altered or exceeded by the user. For a given acoustic power level (power supply voltage) the duration that the system is turned on is limited in hardware (via digital control logic) and software (via transducer file finite limits).

### 11.6.3. High Mismatch Detect

If a fault occurs in which the reflected power from the load (transducer) is large compared to forward power (such as a transducer failure, open circuit, or high reflected energy), a system STOP state is automatically and immediately invoked via a comparator circuit, latched in hardware, and the user is notified.

### 11.6.4. High Current Detect

If a driver fault or load fault (e.g., a short circuit or electronic component failure) occurs, a STOP state is automatically and immediately invoked, hardware is latched, and the user is notified.

### 11.6.5. RF Driver Supply Voltage Monitoring

The system measures the driver’s power supply voltage setting before, during, and after therapy to ensure the correct level. If the voltage exceeds pre-defined parameters, a system STOP state is invoked and the user is notified.

### 11.6.6. Forward and Reverse Electric Power Monitoring

Forward and reverse electric power are monitored during therapy and verified to be in an acceptable (expected) range. The net electric power is also calculated.

### 11.6.7. Acoustic Coupling

Real-time B-Mode imaging indicates to the user if the treatment probe is acoustically coupled to tissue before and after treatment.

### 11.6.8. General Specifications and Standards

#### 11.6.8.1. Treatment Position Sensing

An optical sensor indicates the position of the linear motion mechanism. The B-mode image confirms that the transducer is scanning the treatment area.

#### 11.6.8.2. Thermal Monitoring

The transducer, handpiece, Control Unit, controller, and RF driver temperatures are monitored to ensure an acceptable range.

#### 11.6.8.3. Transducer Sensor

A Transducer Sensor immediately stops therapy and/or imaging if the transducer is disconnected while in use.

#### 11.6.8.4. System Diagnostics

Software checks for errors and unexpected events, and monitors normal usage events. Diagnostics are logged for corrective and preventative purposes or product usage analysis.

#### 11.6.8.5. Fuses

Fuses will shut down the system if currents exceed safe limits.

#### 11.6.8.6. System Power Supply Over-Voltage and Over-Current Limiting

Built into power supply hardware limit voltage.

#### 11.6.8.7. EMC Susceptibility and ESD Discharge Protection

Extensive filtering, shielding, and clamping mechanisms have been tested to ISO/EN 60601-1-2.

#### 11.6.8.8. Fire Safety

94V0 rated PCBs are contained in metal enclosures, flame-rated plastic housing, flame-rated, and flame barrier in probe handle, thermostat in control unit enclosure in case of fan failure.

#### 11.6.8.9. Electrical Safety

ISO/EN 60601-1 compliant medical grade system power supply; Class B tested patient applied part; no leakage current from touchable contacts.

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## 12. Substantial Equivalency Discussion

### 12.1. Device Description

The Ulthera® System delivers focused ultrasound (US) energy to a specific soft tissue layer under the superficial layers of epidermis. Treatment with the Ulthera System creates a focal coagulation point in the dermis with no effect on the epidermal layer, causing thermally induced contraction of tissue and a "natural inflammatory process" to stimulate the formation of new collagen which produces a tissue-tightening and lifting effect.

The Ulthera® System produces controlled tissue coagulation below the skin surface (epidermis) within the first few millimeters of tissue (dermis) using highly focused, low energy (< 2 joules) ultrasound deposition. Acoustic energy heats tissue as a result of frictional losses during energy absorption, inducing a micro-coagulated zone of skin tissue. Other medical devices using other types of energy (laser, radio frequency, etc.) rely upon a similar principle of thermal response. The Ulthera System differs from these other device in that energy is delivered below the epidermis in an extremely controlled fashion (micro-focused vs. radiofrequency bulk heating) without affecting the skin surface or requiring a secondary action to protect the skin surface.

In addition to the treatment capability, the Ulthera® System has a supplemental imaging capability to assure full skin contact of the transducer to the skin surface to enable the safe delivery of energy.

### 12.2. Predicate and Subject Device Comparison

Ulthera has demonstrated that the expanded indication does not introduce questions about safety or effectiveness different from those that were posed by the predicate device's intended use.

The difference in labeling relates only to the indication for use and does not differ from the intended effect or mechanism of action of the Ulthera System. The expanded indication for use does not bear materially on the safe and effective use of the device. There are no other changes in technology, design, materials, sterilization, shelf life, or performance characteristics from the predicate device; and therefore do not pose new safety or effectiveness questions.

Table 12-1 provides a comparison of the predicate and the subject device.

Table 12-1: Predicate and Subject Device Comparison

|   | Predicate Device<br>Ulthera® System;<br>cleared under K072505   | Subject Device<br>Ulthera® System; same as the<br>cleared system K072505;<br>Expanded indication for use   |
|---|---|--|
| <b>Classification/<br/>Product Code</b>                         | 878.4590<br>OHV   | 878.4590<br>OHV<br><br>Same  |
| <b>Intended Use/<br/>Indications for Use</b>                    | Non-invasive dermatological<br>aesthetic treatment to:<br><br>· lift the eyebrow (current cleared<br>indication)  | Non-invasive dermatological<br>aesthetic treatment to:<br><br>· lift the eyebrow (current cleared<br>indication)<br>· lift lax submental (beneath the<br>chin) and neck tissue (requested<br>expanded indication)<br>· lift lax tissue to achieve a<br>desired aesthetic effect for the full<br>face and neck (current cleared<br>indication + requested expanded<br>indication) |
| <b>Where Used</b>   | Clinic/doctor's office  | Clinic/doctor's office<br><br>Same   |
| <b>Anatomical Site</b>  | Skin  | Skin<br><br>Same   |
| <b>Type of Energy</b>   | Thermal<br>< 2 J  | Thermal<br>< 2 J<br><br>Same   |
| <b>Biological Effect</b>  | Lifting of tissue via High Intensity<br>Focused Ultrasound (HIFU)<br>directed beneath the outer dermis<br>in localized points at a specified<br>depth and distance between<br>points. | Lifting of tissue via High Intensity<br>Focused Ultrasound (HIFU)<br>directed beneath the outer dermis<br>in localized points at a specified<br>depth and distance between<br>points.<br><br>Same  |
| <b>Lifting of Lax Tissue</b>                                    | Eyebrow   | Submental (beneath the chin) and<br>neck   |
| <b>Demonstrated Safety<br/>and Efficacy in<br/>treated area</b> | Provided in K072505 cleared<br>September 11, 2009   | Performance Testing - Clinical<br><br>Provided in Section 20   |
| <b>Patient Contact<br/>Material</b>                             | Biocompatible   | Biocompatible<br><br>Same  |

|  | <b>Predicate Device</b><br><b>Ulthera® System</b><br><b>cleared under K072505</b>   | <b>Subject Device</b><br><b>Ulthera® System; same as the</b><br><b>cleared system K072505;</b><br><b>Expanded indication for use</b>                |
|--|---|---|
| <b>Electromagnetic Compatibility Standards</b>       | Compliant   | Compliant<br><br>Same   |
| <b>Medical Electrical Equipment Safety Standards</b> | Compliant   | Compliant<br><br>Same   |
| <b>Thermal Coagulation Point</b>                     | Confined to focal zone; shallow (< 5 mm); no thermal coagulation below focal zone   | Confined to focal zone; shallow (< 5 mm); no thermal coagulation below focal zone<br><br>Same   |
| <b>Epidermal Impact</b>                              | Non-invasive; no cooling required   | Non-invasive; no cooling required<br><br>Same   |
| <b>Pigmentation Effect</b>                           | Chromophore insensitive   | Chromophore insensitive<br><br>Same   |
| <b>Packaging</b>                                     | Nylon / Aluminum foil laminate bag with very low water vapor transmission rate. The bag is enclosed within a cardboard box for storage. | Nylon / Aluminum foil laminate bag with very low water vapor transmission rate. The bag is enclosed within a cardboard box for storage.<br><br>Same |
| <b>Sterilization</b>                                 | Provided non-sterile  | Provided non-sterile<br><br>Same  |
| <b>Shelf Life</b>                                    | 6 months  | 6 months<br><br>Same  |

### 12.3. Conclusion of Substantial Equivalence

As indicated by the table above, there have been no changes to the technology, design, materials, sterilization, shelf life or performance that would result in a new 510(k) since clearance of K072505. Updates to the labeling only relate only to the proposed Indications for Use. The proposed expanded indication for use does not pose new questions of safety or effectiveness.

Performance testing (see clinical trial in Section 20) demonstrated safety and effectiveness of the Ulthera System to achieve lift of submental (beneath the chin) and neck tissue (proposed expanded indication). The studies for the predicate and subject device utilized the same methodologies. The

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06/07/2012

results from this trial demonstrate safety and effectiveness of the subject device are comparable to the predicate. Therefore, the predicate device is substantially equivalent to the subject device.

The predicate device's indication for the upper face and the subject device's indication for lower face support the indication for lifting lax tissue to achieve a desired aesthetic effect for the full face and neck after the Ulthera® procedure.

Based on the design, materials, principle of operation, and intended use, the Ulthera® System is substantially equivalent to the legally marketed predicate device.

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## 13. Proposed Labeling

The Ulthera System Instructions for Use has been updated to reflect the new indications (see Appendix 1.)

In addition, the treatment guidelines (see Appendix A of the IFU) have been updated for the lower face indication and additional transducers. It should be noted that treatment guidelines are set forth for the levels of energy, available transducer and the number of treatment lines to be delivered for each treatable region. Treatment guidelines are provided only to ensure safe use of the Ulthera® System based on clinical usage.

The remainder of the labeling has not changed from the previously cleared in the original 510(k), K072505

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## 14. Sterilization and Shelf Life

There have been no changes to sterilization or shelf life previously reviewed and cleared in the predicate device 510(k) (K072505).

Transducers are supplied non-sterile within a re-sealable 6.0 mil nylon / aluminum foil laminate bag with very low water vapor transmission rate (WVTR < 0.0003 g / 100 in<sup>2</sup> / 24 hours). In addition, the approximately 5.5 x 4 inch bag is enclosed within a cardboard box for storage. Packaging was validated based on ASTM F 1980 – 07 Standard Guide For Accelerated Aging of Sterile Barrier Systems for Medical Devices.

Measurements revealed that packaging can safely store the transducer for at least one year. However, at this time, the shelf-life for the Ulthera® System transducer is set at six months and may be extended at a later date based on additional testing and validation.

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## 15. Biocompatibility

There have been no changes to the patient contacting materials reviewed and cleared in the predicate device 510(k) (K072505). Identical materials and identical material processing are used in the predicate device and the subject device.

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## 16. Software

There have been no changes to the software previously reviewed and cleared in the predicate device 510(k) (K072505) that would result in a new 510(k). As previously stated in the predicate device 510(k) (K072505), the software level of concern is moderate.

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## 17. Electromagnetic Compatibility and Electrical Safety

There have been no changes to the electromagnetic compatibility or electrical safety previously reviewed and cleared in the predicate device 510(k) (K072505) that would result in a new 510(k). Ulthera has continued to maintain compliance to the most current revision of IEC 60601-1 (3<sup>rd</sup> Edition).

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## 18. Performance Testing – Bench

There have been no changes to the bench performance testing previously reviewed and cleared in the predicate device 510(k) (K072505) that would result in a new 510(k).

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## 19. Performance Testing - Animal

There have been no changes to the animal performance testing previously reviewed and cleared in the predicate device 510(k) (K072505).

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## 20. Performance Testing - Clinical

### 20.1. Introduction

#### 20.1.1. Name and Current Indications for Use

Name: The Ulthera® System

Indication for Use:

The Ulthera® System is indicated for use as a non-invasive dermatological aesthetic treatment to:

- lift the eyebrow (current cleared indication)
- lift lax submental (beneath the chin) and neck tissue (requested expanded indication)
- lift lax tissue to achieve a desired aesthetic effect for the full face and neck (current cleared indication + requested expanded indication)

#### 20.1.2. Device Overview

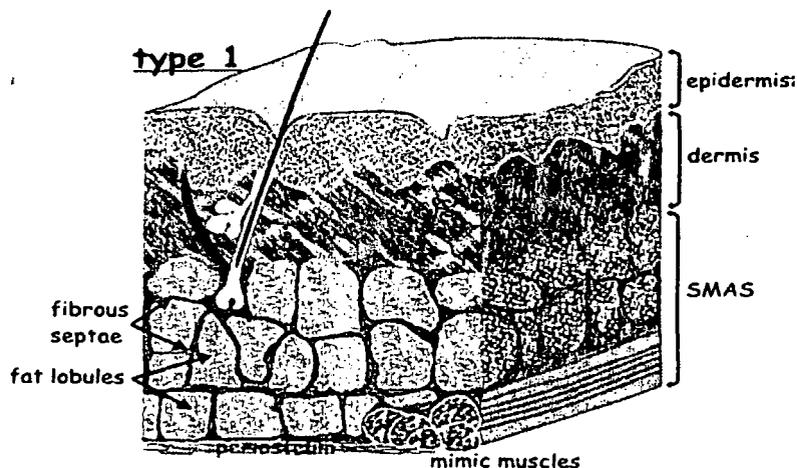
The Ulthera® System integrates high-resolution ultrasound imaging with micro-focused ultrasound therapy. The Ulthera® System has been demonstrated to be safe and effective in previous clinical trials as a non-invasive treatment to produce improvement in the areas of treatment (i.e., eyebrow lift) through sub-dermal tissue coagulation and tightening.

Previous clinical trials reviewed by the Food and Drug Administration (FDA) for clearance of K072505 through the De Novo process, evaluated clinical outcomes associated with the non-invasive dermatological aesthetic treatment for eyebrow lift and to achieve a desired aesthetic effect. Patient satisfaction was measured at protocol-specified visits using a questionnaire.

#### 20.1.3. Disease Background

The normal aging process results in characteristic changes in the skin and underlying connective tissue of the face, termed the "Aging Face Syndrome."<sup>1</sup> These biologic changes result from cutaneous photo damage after repeated sun exposure and other factors, such as genetic predisposition. Knowledge of facial anatomy is essential to evaluate each subject (Figure 20-1), and to develop a treatment plan for the aging face based on an individual's clinical presentation.  
1,2,3,4,5,6

Figure 20-1: Skin Anatomy



#### 20.1.4. Mechanism of Action

Ultrasound is an energy modality that can be focused to penetrate deeper in the tissue and cause targeted thermal coagulation, while avoiding the intermediary tissues.<sup>7,8</sup> Ultrasound can also be used to image the region of interest.<sup>7,8</sup> The Ulthera® System delivers ultrasound energy to cutaneous layers in the skin, such as the reticular dermis.<sup>7,8,9</sup> Treatment with the Ulthera System creates a focal coagulation point in the dermis, causing thermally induced contraction of tissue and a "natural inflammatory process" to stimulate the formation of new collagen which produces a tissue-tightening and lifting effect. Focused ultrasound energy is able to confine heating to small focal regions with a combination of precision and depth. Depending on transducer selection, the system can create micro-focal points of tissue coagulation up to approximately 5mm deep.<sup>9</sup>

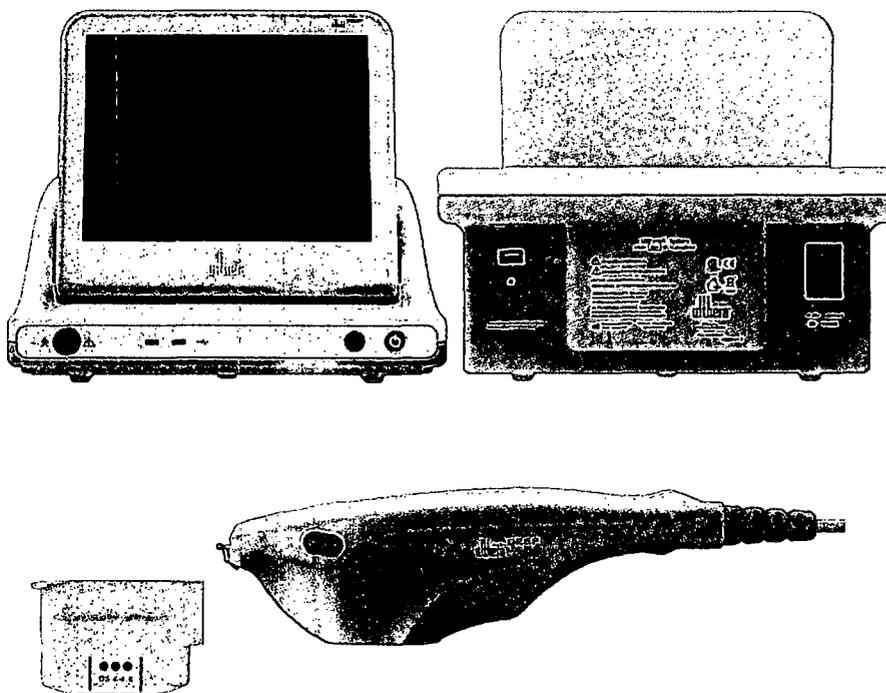
The Ulthera® System produces controlled tissue coagulation below the skin surface (epidermis) within the first few millimeters of tissue (dermis) using highly focused, low energy (< 2 joules) ultrasound deposition. Acoustic energy heats tissue as a result of frictional losses during energy absorption, inducing a micro-coagulated zone of skin tissue. Other medical devices (such as lasers and radio frequency devices) rely upon a similar principle of thermal response. The Ulthera System differs from these other device in that energy is delivered below the surface of the skin in a controlled fashion (micro-focused vs. radiofrequency bulk heating) without affecting the skin surface or requiring a secondary action such as skin cooling to protect the skin surface.

In addition to the treatment capability, the Ulthera® System has a supplemental imaging capability to assure full skin contact of the transducer to the skin surface to enable the safe delivery of energy.

## 20.1.5. Device Overview

The Ulthera® System consists of three primary components: the control unit with integrated touchscreen, the handpiece with cable, and interchangeable transducers (see Figure 20-2).

**Figure 20-2: Main Components of the Ulthera® System**



Control Unit (top), Transducer (left bottom) and Handpiece (right bottom)

The components and use of the Ulthera® System and its operation are fully described in the Instructions for Use (see Appendix 1).

Use of the Ulthera® System is an automatic, computer-driven process that includes a planning stage prior to the treatment stage. The transducer can be used to image the treatment area prior to and during the treatment stage. The face and neck are divided into the following regions: upper third of face (hairline to cheekbone), lower two thirds of face (cheekbone to jawline), and neck (submental and submandibular). During the planning phase, a treatment guideline is initiated by selecting the desired treatment region and the appropriate transducer is displayed.

There are six transducers currently available. The transducers differ in the frequency of ultrasound energy emitted: either 4 MHz (a higher level of energy) at 4.5mm treatment depth, 7 MHz (an intermediate and low level of energy) at 3.0 and 4.5mm treatment depth and 10 MHz (low level of energy) at 1.5mm treatment depth. Transducer capabilities are shown in Table 20-1.

Table 20-1: Transducer Types

| Transducer Type | Treatment Frequency | Energy Allowed (J) | Depth of Treatment Zone (mm) |
|-----------------|---------------------|--------------------|------------------------------|
| DS 4 - 4.5      | 4 MHz               | 0.75 - 1.20        | 4.5                          |
| DS 7 - 4.5      | 7 MHz               | 0.66 - 1.05        | 4.5                          |
| DS 7 - 3.0      | 7 MHz               | 0.25 - 0.45        | 3.0                          |
| DS 7 - 3.0N     | 7 MHz               | 0.25 - 0.45        | 3.0                          |
| DS 10 - 1.5     | 10 MHz              | 0.15 - 0.25        | 1.5                          |
| DS 10 - 1.5     | 10 MHz              | 0.15 - 0.25        | 1.5                          |

### 20.1.6. Pre-Clinical Studies

The Ulthera® System has been evaluated in a series of pre-clinical studies to demonstrate that the device performs as intended, meets its specifications, and is safe and suitable for clinical use. These studies verified and validated electrical safety, electromagnetic compatibility, mechanical properties, and software performance. In addition, functional preclinical studies were conducted to verify and validate device performance.

Pre-clinical studies were conducted at Massachusetts Eye and Ear Infirmary-Harvard Medical School (MEEI) and Ulthera® laboratories using a porcine skin model, which has a similar structure to human skin. These studies demonstrated that the Ulthera® System reliably creates small, well-confined thermal coagulation points in the reticular dermis layer.

Similar findings have been confirmed in human cadaver studies at the University of California at San Diego (UCSD), MEEI, and Wellman Lab—Harvard Medical School.<sup>9,10,11</sup> Cadaver skin tissue was treated using the Ulthera® System at frequencies of 4 to 7 MHz. The focal depths of the 4 MHz transducer were 4.5 mm and 6 mm. The focal depths of the 7 MHz transducer were 3 mm and 4.5 mm. These studies further demonstrated that the Ulthera® System reliably creates small, well-confined thermal coagulation points.

### 20.1.7. Previous Clinical Studies

Two previous clinical studies have been conducted using the Ulthera® System: 1) a clinical safety study at MEEI (Protocol Number 05-06-032); 2) a pivotal study at Northwestern University in Chicago (Protocol Number 1253-014, IDE G060261). During these studies, in which the Ulthera® System was extensively used, safe and efficacious energy delivery protocols were established.

Appendix 2 of the 510(k) submission provides a brief overview of the previous clinical testing of the Ulthera® System because Ulthera provided this information in detail in its previous cleared premarket notification (K072505). Previous studies have demonstrated that the Ulthera® System has a significant safety profile and is safe for the device's expanded use indication. This information is available via cross-reference to K072505.

## 20.2. Clinical Study University of Texas Southwestern (Basis for Expanded Indication)

### 20.2.1. Executive Summary

This open-label clinical trial was conducted to establish the safety and efficacy of the Ulthera® System, device currently marked device cleared under K072505. Designed to deliver focused ultrasound energy to a specific soft tissue layer. The clinical trial was entitled, *"Evaluation of the Ulthera® System for Obtaining Lift and Tightening of the Cheek Tissue and Improvement in Jawline Definition and Submental Skin Laxity"*. The study was approved and conducted by the University of Texas, Southwest, Human Studies Committee on June 30, 2010 and conducted by Principal Investigator Jeffrey M. Kenkel, M.D., F.A.C.S., M.D., and co-investigators, Ronald E. Hoxworth, M.D., and Sumeet S. Teotia, M.D.<sup>12</sup>

A goal of this study was to investigate the clinical response of treatment with the Ulthera® System to achieve lifting of lax submental (beneath the chin) and neck tissue through tissue coagulation and subsequent neocollagenesis in an aesthetically relevant manner which was assessed through a reduction in the overall area of the submental region. Improvement was determined based on the following:

- Quantitative analysis by calculating the amount of tissue lift based on pre- and post-treatment photographs.
- Qualitative assessment by evaluating pre- and post-treatment photographs by three masked clinician reviewers.
- Safety data and patient satisfaction questionnaire results.

Detailed assessments of pre- and post-treatment photographs by masked clinicians (qualitative assessment), patient satisfaction questionnaires, and quantitative analysis have shown lax submental (beneath the chin) and neck tissue lift as a result of Ulthera® System treatments in the lower face (cheek, submental and neck regions).

Clinical and commercial evaluations (over 90,000 commercial treatments worldwide) have demonstrated that the Ulthera® System has a significant safety profile and is safe for the device's expanded use indication.

## 20.2.2. Clinical Protocol Summary

Study Population: Adults between 35 and 60 years of age who chose an Ulthera® treatment, who provided informed consent, and who met inclusion/exclusion criteria.

Inclusion Criteria:

- Male or female, aged 35 to 60 years;
- Subject in good health;
- Desire lifted and tightened cheek tissue, improved jawline definition and/or submental skin laxity; and
- Willing and able to provide informed consent and attend follow-up visits.

Exclusion Criteria:

- Pregnant or lactating;
- Presence of an active systemic or local skin disease that may alter wound healing;
- Severe solar elastosis;
- Excessive subcutaneous fat on the cheeks;
- Excessive skin laxity on the lower face and neck;
- Significant scarring in areas to be treated;
- Significant open facial wounds or lesions;
- Severe or cystic facial acne;
- Presence of a metal stent or implant in the facial area;
- History of smoking in last 10 years;
- Inability to understand the protocol or to give informed consent;
- Mental illness;
- History of cosmetic treatments in the facial area to be treated including: facial skin tightening procedure within the past year, injectable filler of any type within the past year; BOTOX® on the lower face within the past six months, ablative resurfacing laser treatment, nonablative, rejuvenative laser or light treatment within the past six months, dermabrasion or deep facial peels, facelift, blepharoplasty or browlift including contour threads; or
- Taking Accutane or other retinoids within the past two weeks, taking psychiatric drugs, Coumadin, or Heparin.

Treatment Outline:

- Screening visit for inclusion/exclusion criteria and informed consent. If the subject met criteria, the treatment could be performed. Baseline photography of face, and treatment visit.
- Follow-up visits for efficacy: two and three months after the treatment visit (photography at three months; patient satisfaction scoring).

Follow-up visits for safety:

- Immediately post-treatment;
- Two months (subset of patients);
- Three months after treatment
- Six months after treatment

Efficacy Outcome Measures:

Primary:

- Improvement in overall lifting and tightening of tissue determined by qualitative assessment at three months compared to baseline, based on a masked reviewer assessment.

Secondary

- Evaluation of improvement in jawline definition and submental skin laxity at three months compared to baseline, based on the consensus of the three masked reviewers.
- Patient satisfaction was determined by scores on a patient satisfaction questionnaire at three months post-treatment.

Safety Variables:

- Subject assessment of pain using a 10-point scale; and
- Adverse events.

Study Duration: After treatment, subjects were assessed immediately post-treatment, and at two months (subset of patients) and three months for efficacy and safety. In addition, 180-day follow-up data was gathered for safety data was gathered for a subset of patients. With two months for recruitment, the duration of the study was eight months.

## 20.2.3. Clinical Protocol

The first subject entered the study on July 6, 2010 and the last subject entered the study on August 31, 2010.

Standardized photographs of the subjects, using a fixed camera and lighting conditions, were taken prior to the Ulthera® procedure.

Patients in some cases were given pre-treatment medications. Pre-medication was administered at the discretion of the physician and patient. Comfort is very subjective, and there is a broad range of sensory responses to an Ulthera® treatment. For instance, if the patient has had prior cosmetic treatments, he or she may have a higher threshold.

If physicians chose to prescribe pre-meds, the patients took oral medication at least 30 minutes prior to their treatment or intra-muscular medication 60 minutes prior.

60 minutes before treatment:

- Toradol 60 mg IM

OR

30 minutes before treatment:

- Valium 5-10mg
- Hydrocodone 5/325mg (1-2 tablets)

The subjects underwent a clinical assessment by the investigator prior to receiving the Ulthera treatment on the lower face, and neck region. Clinicians used the same transducer types and energy settings. All subjects received the same treatment as shown on the treatment guideline provided within the protocol shown in Figure 20-4.

Three different transducers for the ultrasound exposure studies were available for use:

**Table 20-2: Available Transducers for Study**

| Transducer Type | Treatment Frequency | Energy Allowed (J) | Depth of Treatment Zone (mm) |
|-----------------|---------------------|--------------------|------------------------------|
| DS 4 - 4.5      | 4 MHz               | 0.75 - 1.20        | 4.5                          |
| DS 7 - 4.5      | 7 MHz               | 0.66 - 1.05        | 4.5                          |
| DS 7 - 3.0      | 7 MHz               | 0.25 - 0.45        | 3.0                          |

\*Please note that all physicians chose to use the DS 4-4.5 and the DS 7-3.0 transducers. The DS 4-4.5 transducer was chosen over the DS 7-4.5 transducer due to physician preference to utilize higher treatment energies.

Each exposure line of ultrasound energy represents either 21 or 17 individual ultrasound pulses per 25 mm (using a spacing of 1.1mm or 1.5 mm, respectively between each pulse) to produce a series of thermal coagulative zones in the dermal tissue while sparing the epidermis. Ultrasound exposure lines using the Ulthera® System were placed on the subject's face and neck. In each

case, ultrasound imaging was performed of the treatment area in order to ensure appropriate acoustic coupling of the transducer to the skin surface. The depth of the thermal coagulative zone in the tissue is determined by the focal depth in tissue of a particular transducer.

The treatment guidelines in Figure 20-4 were utilized for all of the patients in the study. The treatment guidelines provided in all four illustrations were applied to each patient in the study as a single treatment for tightening of the cheek tissue, improvement in jawline definition and submental skin laxity utilizing both the 3.0 and 4.5 mm depth transducers.

1. The neck (submental and submandibular areas) was first treated with the DS 4-4.5 or DS 7-4.5 transducer, which penetrates to a depth of 4.5mm (illustrated in quadrant 1).
2. The DS 7-3.0 transducer was used for the second neck treatment, which penetrates to a depth of 3.0 mm (illustrated in quadrant 3).
3. The cheeks (right and left) were first treated with the DS 4-4.5 or DS 7-4.5 transducer at a depth of 4.5 mm (illustrated in quadrant 2).
4. Then cheeks (right and left) were treated with the DS 7-3.0 transducer at a depth of 3.0 mm (illustrated in quadrant 4).

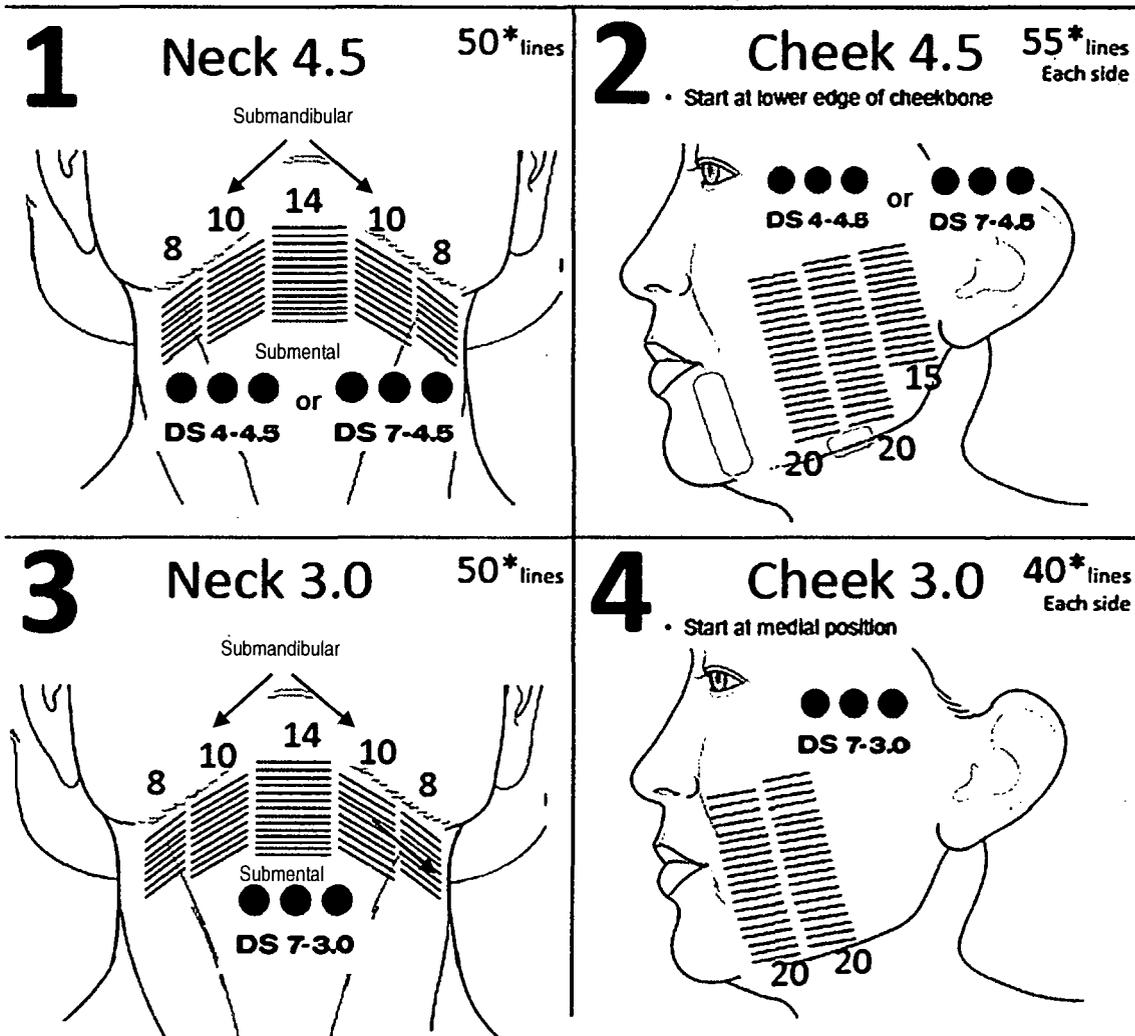
\*Please note that all physicians chose to use the DS 4-4.5 and the DS 7-3.0 transducers. The DS 4-4.5 transducer was chosen over the DS 7-4.5 transducer due to physician preference to utilize higher treatment energies.

The treatment guidelines and the anatomical regions treated are shown in Figure 20-3.

Figure 20-3: Patterns in Targeted Anatomical Regions



○ Facial nerve locations – Do not treat



\*Please note that all physicians chose to use the DS 4-4.5 and the DS 7-3.0 transducers. The DS 4-4.5 transducer was chosen over the DS 7-4.5 transducer due to physician preference to utilize higher treatment energies (see Table 20-2).

## 20.2.4. Study Subject Demographics

The Ulthera<sup>®</sup> procedure was performed on 70 evaluable subjects ranging in age from 35 to 58 years. Table 20-3 shows subject demographics.

**Table 20-3: Subject Demographics**

(n = 70)

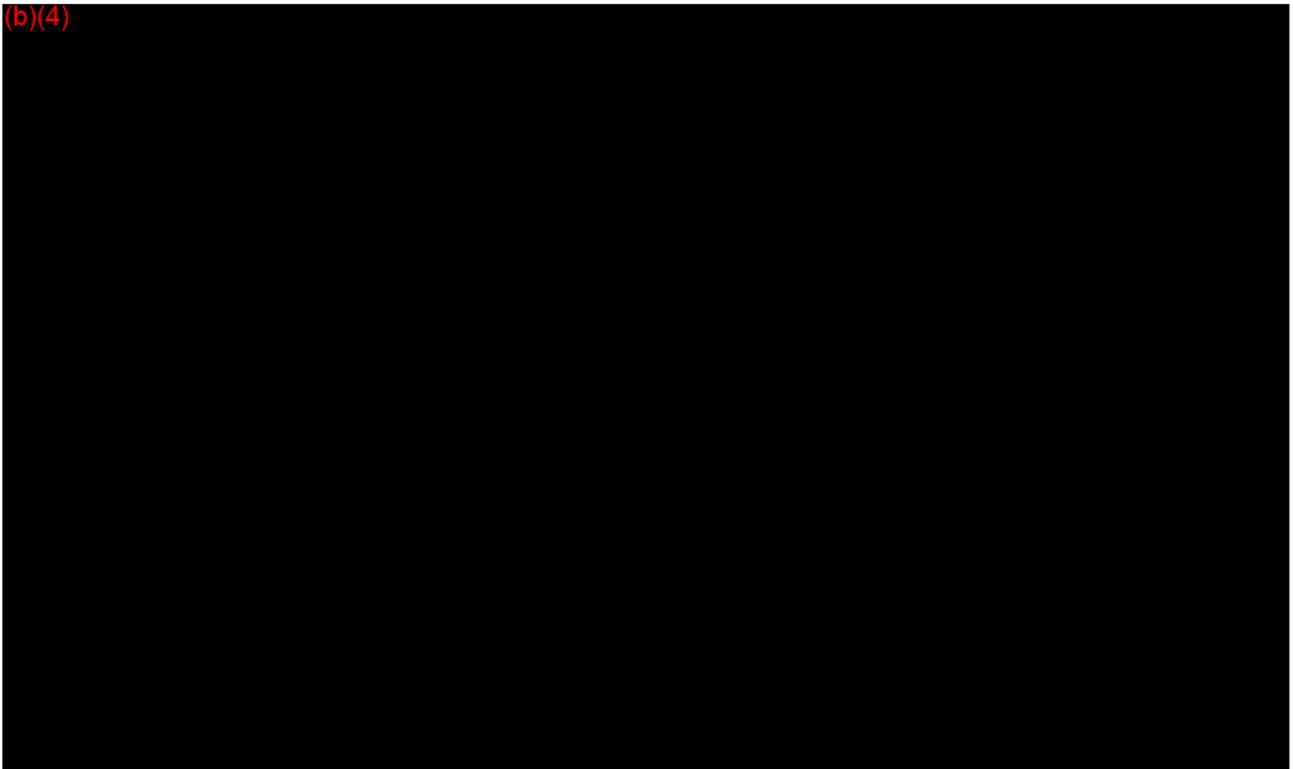
|                      | Gender |      | Sun-Reactive Skin Type |       |       |      |      |
|----------------------|--------|------|------------------------|-------|-------|------|------|
|                      | Female | Male | I                      | II    | III   | IV   | V    |
| # Subjects           | 57     | 13   | 9                      | 46    | 12    | 2    | 1    |
| % Subjects Evaluated | 80%    | 20%  | 12.9%                  | 67.1% | 15.7% | 2.9% | 1.4% |

\*See Section 20.7 Safety

The inclusion criteria for the study specified the age range of 35-60 because individuals in this age range are more likely to have Aging Face Syndrome and more likely to seek cosmetic treatment for lifting lax submental (beneath the chin) and neck tissue.

## 20.3. Quantitative Methodologies and Results

### 20.3.1. Quantitative Methodology



(b)(4)

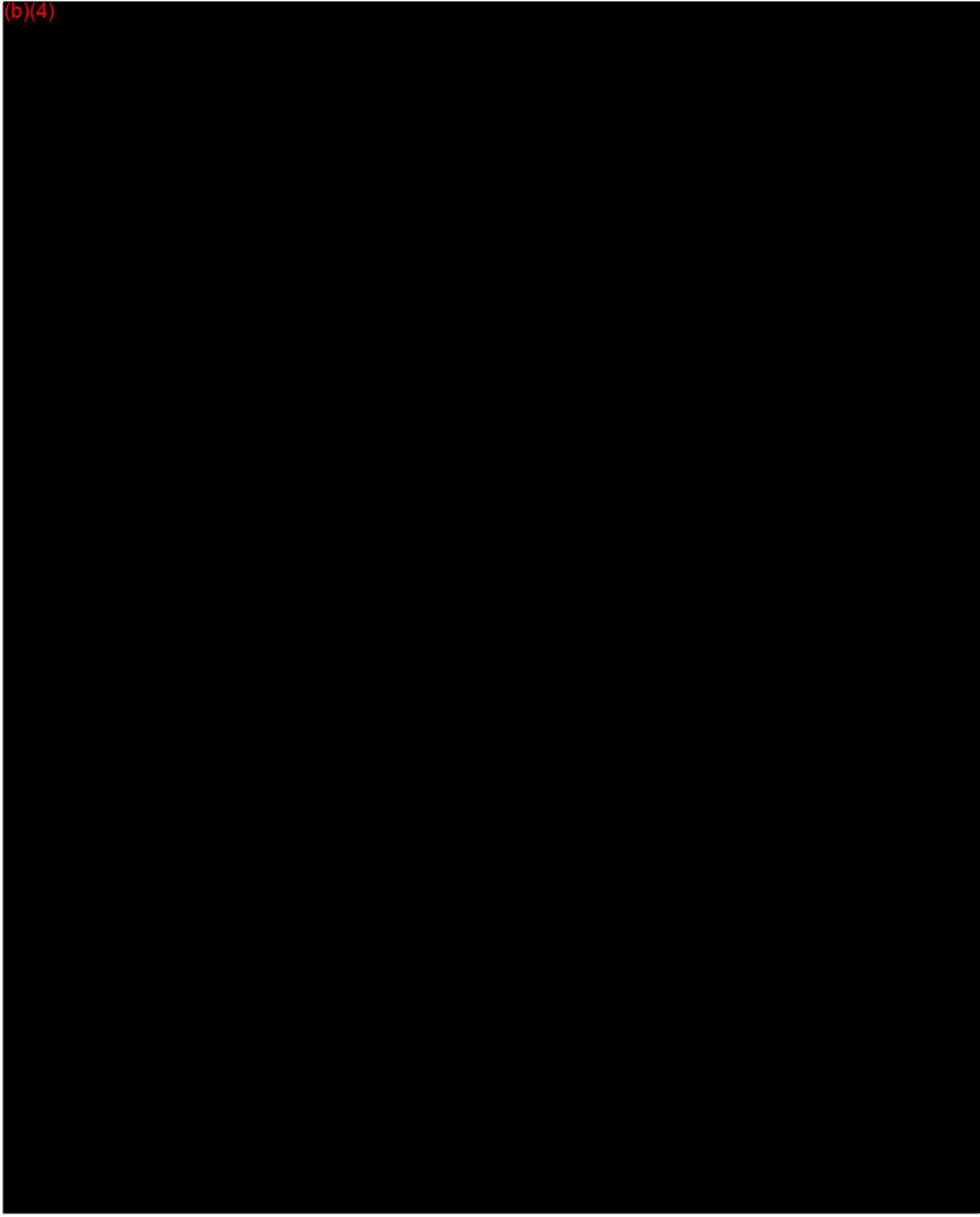
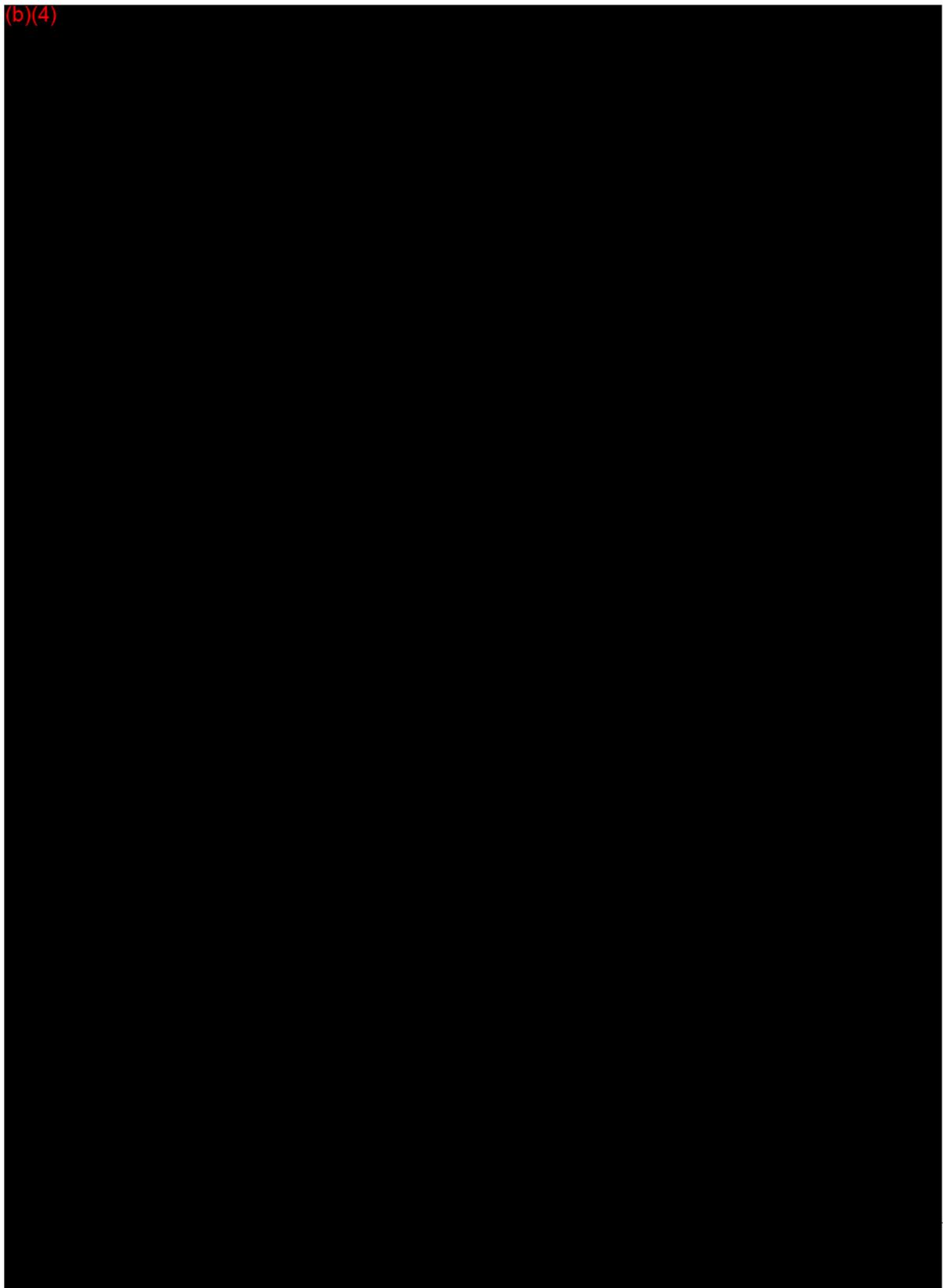


Figure 20-5 identifies the “region of interest” evaluated for lifting of lax tissue in the submental (beneath the chin) and neck.

**Figure 20-5: “Region of Interest” (Area with Hatch Marks)**



(b)(4)

### 20.3.2. Quantitative Results

Based on the quantitative methodology, a measurement of chin and neck tissue lift will be performed on the lateral-profile view of Pre- and Day 90 Post treatment photos for each subject. The delta area between the pre and post treatment area of the chin and neck will determine the amount of tissue lift in the area. A tissue lift  $\geq 10.0 \text{ mm}^2$  is considered to be visibly observable tissue lift. Non-responders are identified as having  $< 10.0 \text{ mm}^2$  tissue lift. The quantitative results by patients are in Table 20-4.

**Table 20-4: Quantitative Results - Area**

| Subject ID | Masked Review Number (MRN) | Amount of Tissue Lift - Left ( $\text{mm}^2$ ) | Amount of Tissue Lift - Right ( $\text{mm}^2$ ) |
|------------|----------------------------|--|---|
| 002Y       | 364664                     | 71.13  | 70.79   |
| 005Y       | 506851                     | 60.89  | 60.16   |
| 006Y       | 143594                     | 58.87  | 61.13   |
| 007Y       | 281786                     | 39.34  | 34.69   |
| 009Y       | 810511                     | 30.06  | 30.17   |

| Subject ID | Masked Review Number (MRN) | Amount of Tissue Lift - Left (mm <sup>2</sup> ) | Amount of Tissue Lift - Right (mm <sup>2</sup> ) |
|------------|----------------------------|---|--|
| 011Y       | 990881                     | 77.82   | 81.54  |
| 013Y       | 710936                     | 106.78  | 96.33  |
| 016Y       | 734634                     | 25.84   | 23.56  |
| 017Y       | 309406                     | 30.06   | 30.23  |
| 018Y       | 554757                     | 64.03   | 66.32  |
| 019Y       | 465683                     | 164.88  | 161.6  |
| 021Y       | 435811                     | 98.27   | 96.11  |
| 023Y       | 629222                     | 79.92   | 77.48  |
| 024Y       | 840899                     | 51.1  | 51.33  |
| 027Y       | 775550                     | <10.00  | <10.00   |
| 029Y       | 199312                     | 33.78   | 34.02  |
| 030Y       | 854016                     | 43.67   | 45.12  |
| 035Y       | 931529                     | 17.36   | 18.92  |
| 037Y       | 418900                     | 182.44  | 180.89   |
| 039Y       | 937724                     | <10.00  | <10.00   |
| 040Y       | 923432                     | 120.87  | 119.06   |
| 041Y       | 576805                     | 92.01   | 91.59  |
| 044Y       | 946834                     | 28.64   | 28.8   |
| 045Y       | 616379                     | 40.61   | 42.36  |
| 046Y       | 917439                     | 29.65   | 29.04  |
| 048Y       | 461179                     | <10.00  | <10.00   |
| 049Y       | 141661                     | <10.00  | <10.00   |
| 050Y       | 125105                     | 19.56   | 18.42  |
| 051Y       | 511912                     | 69.05   | 69.66  |
| 052Y       | 750601                     | <10.00  | <10.00   |
| 055Y       | 276689                     | <10.00  | <10.00   |
| 057Y       | 359113                     | <10.00  | <10.00   |
| 060Y       | 572794                     | 53.99   | 51.66  |
| 062Y       | 709208                     | 78.57   | 78.35  |
| 064Y       | 811646                     | <10.00  | <10.00   |
| 065Y       | 252891                     | 217.66  | 218.5  |
| 066Y       | 463369                     | <10.00  | <10.00   |
| 067Y       | 549999                     | <10.00  | <10.00   |
| 068Y       | 487259                     | 39.06   | 38.46  |
| 069Y       | 567449                     | 181.4   | 178.47   |
| 070Y       | 686205                     | 43.98   | 43.76  |
| 071Y       | 968722                     | 106.75  | 107.4  |
| 072Y       | 567089                     | 56.37   | 57.53  |
| 074Y       | 923407                     | 38.88   | 37.58  |
| 075Y       | 902310                     | 79.30   | 80.34  |

| Subject ID   | Masked Review Number (MRN) | Amount of Tissue Lift - Left (mm <sup>2</sup> ) | Amount of Tissue Lift - Right (mm <sup>2</sup> ) |
|--|----------------------------|---|--|
| 077Y   | 843156                     | 74.92   | 74.81  |
| 079Y   | 116974                     | 94.69   | 109.46   |
| 080Y   | 963641                     | 131.73  | 136.76   |
| 081Y   | 707506                     | 28.76   | 30.01  |
| 083Y   | 360239                     | <10.00  | <10.00   |
| 084Y   | 518293                     | 36.84   | 35.85  |
| 085Y   | 626898                     | 131.37  | 131.08   |
| 087Y   | 733357                     | <10.00  | <10.00   |
| 091Y   | 340008                     | <10.00  | <10.00   |
| 093Y   | 640436                     | 31.87   | 28.14  |
| 095Y   | 707299                     | <10.00  | <10.00   |
| 097Y   | 340338                     | 38.74   | 38.36  |
| 098Y   | 307430                     | 28.12   | 26.91  |
| 099Y   | 345839                     | <10.00  | <10.00   |
| 100Y   | 854790                     | 65.61   | 64.07  |
| 105Y   | 880701                     | 46.51   | 46.43  |
| 106Y   | 931610                     | <10.00  | <10.00   |
| 107Y   | 932611                     | 135.77  | 130.2  |
| 108Y   | 698638                     | 45.4  | 42.68  |
| 109Y   | 126224                     | 73.36   | 76.43  |
| 110Y   | 758248                     | 50.01   | 48.46  |
| 111Y   | 899886                     | <10.00  | <10.00   |
| 112Y   | 122021                     | 93.37   | 95.21  |
| 115Y   | 691534                     | 22.41   | 21.78  |
| 116Y   | 272788                     | 45.21   | 45.67  |
| <b>Response Rate %<br/>(tissue lift ≥ 10.0 mm<sup>2</sup>)</b> |                            | <b>75.7%</b>                                    | <b>75.7%</b>                                     |
| <b>Average Tissue Lift (mm<sup>2</sup>) of Responders</b>      |                            | <b>71.97</b>                                    | <b>71.69</b>                                     |

There was a 75.7% response rate [53/70] (for both the left and right side of the face) of subjects that had a tissue lift  $\geq 10.0$  mm<sup>2</sup>. There was a 71.97 mm<sup>2</sup> and 71.69 mm<sup>2</sup> average area of tissue lift on the left and right side, respectively in responding patients. The data for the area of tissue lift and the response rate yielded consistent results for both the right and left side of the face.

## 20.4. Qualitative Methodology and Results

The masked clinician assessment of pre- and post-treatment photographs for lower facial tissue changes was validated according to guidelines set forth in the FDA approval of the IDE for the Northwestern study of eyebrow position changes. (Ref.: G060261/S2, June 13, 2007) This masked assessment method was suggested by FDA for the validation process in earlier clinical trials and served as the basis for product clearance for K072505 by FDA.

### 20.4.1. Qualitative Methodology

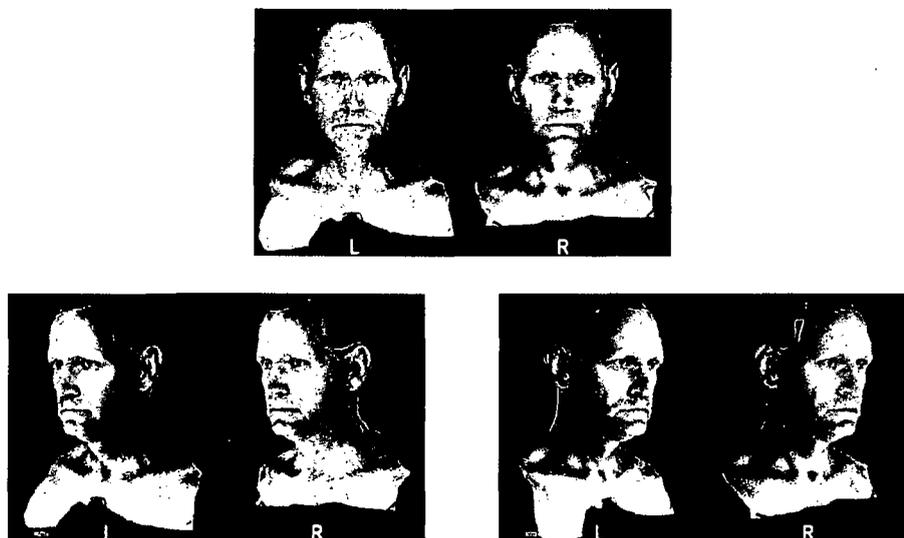
Three experienced clinicians evaluated paired pre- and post-treatment (day-90) photographs (five views) of 70 evaluable subjects in a masked fashion (did not know which image was pre- or post-treatment).

The analyzed photographs included five views: one frontal, two 45-degree (left and right), and two lateral (left and right). See Figure 20-5 for a complete representative photo set.

For each subject, the placement of pre- and post-treatment (day 90) images was random (on either the right or left side of the photograph), however the placement of the pre- and post-treatment images were consistent throughout all five views.

The pre- and post- treatment photos will be comparable in lighting, subject positioning and focus. There is no identification information on the photo that would identify pre- or post-treatment as demonstrated by the example below.

**Figure 20-7: Complete Photo Set**





Each blinded assessor conducted their assessment independently. Each blinded assessor reviewed the set of images for improvement in the submental (lower chin) and neck tissue. The following definitions were used:

- **Improvement:** Visibly observable tissue lift
- **No Change:** No visibly observable tissue lift

After comparing each set of pre- and post-treatment (day 90) photographs:

- If the assessor sees a visibly observable tissue lift, the assessor will mark “Improvement” on the data sheet and then mark “L” or “R” based on the image they believe to be the post-treatment photo (i.e., Left (L) image or Right (R) image based on image location).
- If the assessor sees no visibly observable tissue lift, the assessor will mark “No change” on the data sheet and will not choose which image is the post-treatment photo.

**Table 20-5: Example of Masked Reviewer Assessment Data Sheet**

| Masked ID Number | Improvement | Post-Treatment Screen Location (L or R) | No Change |
|------------------|-------------|---|-----------|
| #####            | X           | R                                       |           |
| #####            | X           | R                                       |           |
| #####            | X           | L                                       |           |
| #####            |             |   | X         |

Since the position of the pre- and post-treatment photos on the right or left side of the screen for a given patient was randomly determined by Ulthera and study personnel, the positions were recorded on a list (“reference key”).

Table 20-6 provides an example of the reference key.

**Table 20-6: Example of Reference Key**

| Masked ID Number | Pre -Treatment Screen Location (L or R) | Post-Treatment Screen Location (L or R) |
|------------------|---|---|
| #####            | L                                       | R                                       |
| #####            | L                                       | R                                       |
| #####            | L                                       | R                                       |
| #####            | R                                       | L                                       |

The three masked reviewers' assessments were recorded on a data sheet for all 70 evaluable subjects. The results of the image assessments for each masked clinician were analyzed by comparing the clinician's results with the reference key.

If the reviewer identified the correct image as the post-treatment image, based on the reference key, the result was recorded as be "improved".

- If the reviewer observed no change, the result was recorded as "no change".
- If the reviewer identified the wrong image as the post-treatment image, based on the reference key, the result was recorded as "incorrect".

Table 20-7 provides an example of how each masked reviewers results were recorded.

**Table 20-7: Example of One Masked Assessor Results**

| Masked ID Number | Reference Key Post-Treatment Photos | Masked Reviewer 1 Assessment | Results   |
|------------------|-------------------------------------|------------------------------|-----------|
| #####            | R                                   | R                            | Improved  |
| #####            | R                                   | R                            | Improved  |
| #####            | R                                   | L                            | Incorrect |
| #####            | L                                   | No Change                    | No Change |

After the three masked reviewers completed their assessment independently, the majority opinion was determined based on the following criteria:

- If the masked reviewers had different assessments, the majority opinion was recorded.
- If the masked reviewers had three different responses (improved, no change, and incorrect) were recorded as the middle response (no change).

**Table 20-8: Example of Three Masked Assessment Results**

| Masked ID | Masked Reviewer 1 Result | Masked Reviewer 2 | Masked Reviewer 3 | Final Result     |
|-----------|--------------------------|-------------------|-------------------|------------------|
| #####     | Improved                 | Improved          | Improved          | <b>Improved</b>  |
| #####     | Improved                 | Incorrect         | Improved          | <b>Improved</b>  |
| #####     | Incorrect                | Incorrect         | No Change         | <b>Incorrect</b> |
| #####     | No Change                | Incorrect         | Improved          | <b>No Change</b> |

During the course of the study, the results from the reference key and the outcome (percentage of success) of the masked reviewers' assessments were not shared with the reviewers

## 20.4.2. Validation of Qualitative Methodology

Validation of the qualitative assessment (masked clinician assessment of pre- and post-treatment photographs) included:

- **Unmasked Qualitative Assessment:** consensus assessment of day 60 pre- and post-treatment photographs by two experienced clinicians
- **Masked Qualitative Assessment:** independent assessment of day 60 pre- and post-treatment photographs by three experienced clinicians

The unmasked qualitative assessment results were compared to the majority masked qualitative assessment results to validate the method using the kappa statistic.

### 20.4.2.1. Unmasked Qualitative Assessment

Two experienced clinicians collectively evaluated pairs of pre- and post-treatment (day 60) images of 23 evaluable study subjects in an unmasked fashion (the assessor knew which image was the pre- and post-treatment image).

The pre- and post- treatment photos will be comparable in lighting, subject positioning and focus. The analyzed photographs included five views: one frontal, two 45-degree (left and right), and two lateral (left and right). See Figure 20-7 for a complete representative photo set.

The clinicians were presented paired pre- and post-treatment images, with five pre-treatment views and five post-treatment views per subject: one frontal, two 45-degree (left and right), and two lateral (left and right). The post-treatment images were on the right and the pre-treatment images were on the left. The pre- and post- treatment photos will be comparable in lighting, subject positioning and focus.

Each blinded assessor conducted their assessment independently. Each blinded assessor reviewed the set of images for improvement in the submental (lower chin) and neck tissue. The following definitions were used:

- **Improvement:** Visibly observable tissue lift
- **No Change:** No visibly observable tissue lift

After comparing each set of pre- and post-treatment (day 60) photographs:

- If the assessor sees a visibly observable tissue lift, the assessor will mark "Improvement" on the data sheet.
- If the assessor sees no visibly observable tissue lift, the assessor will mark "No change" on the data sheet.

**Figure 20-8: Example of Unmasked Reviewer Assessment Data Sheet**

| Masked ID Number | Improvement | No Change |
|------------------|-------------|-----------|
| #####            | X           |           |
| #####            | X           |           |
| #####            | X           |           |
| #####            |             | X         |

The unmasked reviewers had two possible responses: "improved" or "no change". The unmasked reviewers had to come to a consensus on their response.

#### 20.4.2.2. Masked Qualitative Assessment

Three experienced clinicians evaluated paired pre- and post-treatment (day-60) photographs (five views) of 23 evaluable subjects in a masked fashion (did not know which image was pre- or post-treatment).

The analyzed photographs included five views: one frontal, two 45-degree (left and right), and two lateral (left and right). See Figure 20-7 for a complete representative photo set.

For each subject, the placement of pre- and post-treatment (day 60) images was random (on either the right or left side of the photograph), however the placement of the pre- and post-treatment images were consistent throughout all five views.

The pre- and post- treatment photos will be comparable in lighting, subject positioning and focus. There is no identification information on the photo that would identify pre- or post-treatment as demonstrated by the example in Figure 20-7.

Each blinded assessor conducted their assessment independently. Each blinded assessor reviewed the set of images for improvement in the submental (lower chin) and neck tissue. The following definitions were used:

- **Improvement:** Visibly observable tissue lift
- **No Change:** No visibly observable tissue lift

After comparing each set of pre- and post-treatment (day 60) photographs:

- If the assessor sees a visibly observable tissue lift, the assessor will mark "Improvement" on the data sheet and then mark "L" or "R" based on the image they believe to be the post-treatment photo (i.e., Left (L) image or Right (R) image based on image location).
- If the assessor sees no visibly observable tissue lift, the assessor will mark "No change" on the data sheet and will not choose which image is the post-treatment photo.

**Figure 20-9: Example of Masked Reviewer Assessment Data Sheet**

| Masked ID Number | Improvement | Post-Treatment Screen Location (L or R) | No Change |
|------------------|-------------|---|-----------|
| #####            | X           | R                                       |           |
| #####            | X           | R                                       |           |
| #####            | X           | L                                       |           |
| #####            |             |   | X         |

Since the position of the pre- and post-treatment photos on the right or left side of the screen for a given patient was randomly determined by Ulthera and study personnel, the positions were recorded on a list ("reference key").

**Figure 20-10: Example of Reference Key**

| Masked ID Number | Pre -Treatment Screen Location (L or R) | Post-Treatment Screen Location (L or R) |
|------------------|---|---|
| #####            | L                                       | R                                       |
| #####            | L                                       | R                                       |
| #####            | L                                       | R                                       |
| #####            | R                                       | L                                       |

The three masked reviewers' assessments were recorded on a data sheet for all 23 evaluable subjects. The results of the image assessments for each masked clinician were analyzed by comparing the clinician's results with the reference key.

If the reviewer identified the correct image as the post-treatment image, based on the reference key, the result was recorded as be “improved”.

- If the reviewer observed no change, the result was recorded as “no change”.
- If the reviewer identified the wrong image as the post-treatment image, based on the reference key, the result was recorded as “incorrect”.

Table 20-9 provides an example of how each masked reviewers results were recorded.

**Table 20-9: Example of One Masked Assessor Results**

| Masked ID Number | Reference Key Post-Treatment Photos | Masked Reviewer 1 Assessment | Results   |
|------------------|-------------------------------------|------------------------------|-----------|
| #####            | R                                   | R                            | Improved  |
| #####            | R                                   | R                            | Improved  |
| #####            | R                                   | L                            | Incorrect |
| #####            | L                                   | No Change                    | No Change |

After the three masked reviewers completed their assessment independently, the majority opinion was determined based on the following criteria:

- If the masked reviewers had different assessments, the majority opinion was recorded.
- If the masked reviewers had three different responses (improved, no change, and incorrect) were recorded as the middle response (no change).

**Table 20-10: Example of Three Masked Assessment Results**

| Masked ID | Masked Reviewer 1 Result | Masked Reviewer 2 | Masked Reviewer 3 | Final Result |
|-----------|--------------------------|-------------------|-------------------|--------------|
| #####     | Improved                 | Improved          | Improved          | Improved     |
| #####     | Improved                 | Incorrect         | Improved          | Improved     |
| #####     | Incorrect                | Incorrect         | No Change         | Incorrect    |
| #####     | No Change                | Incorrect         | Improved          | No Change    |

During the course of the study, the results from the reference key and the outcome (percentage of success) of the masked reviewers’ assessments were not shared with the reviewers

### 20.4.3. Qualitative Validation Results

The masked reviewers' assessments were recorded on a data sheet for all 23 evaluable subjects. The results of the image assessments for each masked clinician were analyzed by comparing the clinician's results with the reference key to determine if the clinician selected the correct image as the post-treatment image.

- If the correct image was identified as the post-treatment image, based on the reference key, the subject's result was recorded as be "improved".
- If the reviewer observed no change, the result was considered to be "no change".
- If the reviewer identified the wrong image as the post-treatment image, the result was recorded as "incorrect".

The majority response of the three masked assessors was recorded. If each masked reviewer chose a different response, the majority opinion was recorded as "no change."

The results of the validation study for the masked clinician assessment of pre- and post-treatment photographs for improvement in the lower two-thirds of the face and neck are shown in Table 20-11.

**Table 20-11: Validation Results for Masked Clinician Assessment**

| Patient S/No | Masked Review Number (MRN) | Two Unmasked Reviewers | Three Masked Reviewer Majority Assessment |
|--------------|----------------------------|------------------------|---|
| 1            | 247756                     | Improved               | Improved                                  |
| 2            | 261569                     | Improved               | Improved                                  |
| 3            | 274408                     | Improved               | No Change                                 |
| 4            | 403677                     | Improved               | No Change                                 |
| 5            | 438073                     | Improved               | No Change                                 |
| 6            | 484603                     | Improved               | Improved                                  |
| 7            | 497098                     | Improved               | Improved                                  |
| 8            | 506482                     | Improved               | Improved                                  |
| 9            | 527442                     | Improved               | Improved                                  |
| 10           | 537377                     | Improved               | Improved                                  |
| 11           | 613899                     | Improved               | Improved                                  |
| 12           | 693068                     | Improved               | Improved                                  |
| 13           | 700435                     | Improved               | Improved                                  |
| 14           | 714738                     | Improved               | Improved                                  |
| 15           | 727967                     | Improved               | Improved                                  |
| 16           | 770763                     | Improved               | Improved                                  |
| 17           | 812839                     | Improved               | Improved                                  |
| 18           | 843978                     | Improved               | Improved                                  |

|    |        |           |          |
|----|--------|-----------|----------|
| 19 | 857171 | No Change | Improved |
| 20 | 930483 | Improved  | Improved |
| 21 | 939951 | No Change | Improved |
| 22 | 944878 | No Change | Improved |
| 23 | 948265 | Improved  | Improved |

The validation of the masked assessment is based on the calculation of a kappa statistic from these data, as follows:

$K = (I_o - I_e) / (1 - I_e)$ , where  $I_o$  and  $I_e$  are the observed agreement and the expected agreement under the assumption of independence, respectively. The strength of agreement will be assessed based on the proposed criteria as follows:

**Table 20-12: Kappa Statistic Strength of Agreement**

| Kappa Statistic | Strength of Agreement |
|-----------------|-----------------------|
| <0.00           | Poor                  |
| 0.00 - 0.20     | Slight                |
| >0.20 - 0.40    | Fair                  |
| >0.40 - 0.60    | Moderate              |
| >0.60 - 0.80    | Substantial           |
| >0.80 - 1.00    | Almost Perfect        |

The data were analyzed using kappa statistics. Agreement between masked and unmasked reviewers was 74%. The kappa statistic for the validation of the masked assessment shows there is a substantial strength of agreement, thus validating this method.

#### 20.4.4. Qualitative Results

Based on the masked review conducted by three experienced clinicians of pre- and post- Qualitative Methodology treatment image pairs, clinician-assessed improvement was noted in the lower two-thirds of the face and neck in 68.6% of the subjects (see Table 20-13).

**Table 20-13: Qualitative Results**

| Patient S/No | Masked ID | Three Masked Reviewer Majority Assessment |
|--------------|-----------|---|
| 1            | 364664    | Improved                                  |
| 2            | 506851    | Improved                                  |
| 3            | 143594    | Improved                                  |

| Patient S/No | Masked ID | Three Masked Reviewer Majority Assessment |
|--------------|-----------|---|
| 4            | 281786    | No Change                                 |
| 5            | 810511    | Improved                                  |
| 6            | 990881    | Improved                                  |
| 7            | 710936    | Improved                                  |
| 8            | 734634    | Improved                                  |
| 9            | 309406    | Improved                                  |
| 10           | 554757    | Improved                                  |
| 11           | 465683    | Improved                                  |
| 12           | 435811    | Improved                                  |
| 13           | 629222    | Improved                                  |
| 14           | 840899    | Improved                                  |
| 15           | 775550    | Incorrect                                 |
| 16           | 199312    | No Change                                 |
| 17           | 854016    | Improved                                  |
| 18           | 931529    | No Change                                 |
| 19           | 418900    | Improved                                  |
| 20           | 937724    | No Change                                 |
| 21           | 923432    | Improved                                  |
| 22           | 576805    | No Change                                 |
| 23           | 946834    | Improved                                  |
| 24           | 616379    | Improved                                  |
| 25           | 917439    | No Change                                 |
| 26           | 461179    | Incorrect                                 |
| 27           | 141661    | Incorrect                                 |
| 28           | 125105    | Improved                                  |
| 29           | 511912    | Improved                                  |
| 30           | 750601    | No Change                                 |
| 31           | 276689    | Incorrect                                 |
| 32           | 359113    | Improved                                  |
| 33           | 572794    | Improved                                  |
| 34           | 709208    | Improved                                  |
| 35           | 811646    | Incorrect                                 |
| 36           | 252891    | Improved                                  |
| 37           | 463369    | No Change                                 |
| 38           | 549999    | Improved                                  |
| 39           | 487259    | Incorrect                                 |

| Patient S/No                             | Masked ID | Three Masked Reviewer Majority Assessment |
|--|-----------|---|
| 40                                       | 567449    | Improved                                  |
| 41                                       | 686205    | Improved                                  |
| 42                                       | 968722    | Improved                                  |
| 43                                       | 567089    | Improved                                  |
| 44                                       | 923407    | Improved                                  |
| 45                                       | 902310    | Improved                                  |
| 46                                       | 843156    | Improved                                  |
| 47                                       | 116074    | Improved                                  |
| 48                                       | 963641    | Improved                                  |
| 49                                       | 707506    | Improved                                  |
| 50                                       | 360239    | Incorrect                                 |
| 51                                       | 518293    | Improved                                  |
| 52                                       | 626898    | Improved                                  |
| 53                                       | 733357    | Incorrect                                 |
| 54                                       | 340008    | Incorrect                                 |
| 55                                       | 640436    | Improved                                  |
| 56                                       | 707299    | Incorrect                                 |
| 57                                       | 340338    | Improved                                  |
| 58                                       | 307430    | Improved                                  |
| 59                                       | 345839    | Improved                                  |
| 60                                       | 854790    | Improved                                  |
| 61                                       | 880701    | Improved                                  |
| 62                                       | 931610    | Improved                                  |
| 63                                       | 932611    | Improved                                  |
| 64                                       | 698638    | No Change                                 |
| 65                                       | 126224    | Improved                                  |
| 66                                       | 758248    | Improved                                  |
| 67                                       | 899886    | Incorrect                                 |
| 68                                       | 122021    | Improved                                  |
| 69                                       | 691534    | Improved                                  |
| 70                                       | 272788    | No Change                                 |
| <b>Response Rate for Improvement (%)</b> |           | <b>68.6%</b>                              |

Based on the masked assessment of three clinicians, 68.6% of patients had improvement in the submental (beneath the chin) and neck.

## 20.5. Patient Satisfaction Methodology and Results

### 20.5.1. Patient Satisfaction Methodology

Patients independently completed a questionnaire assessing patient satisfaction at three months (D90) post Ultherapy treatment. Pre- and Day 90 post-treatment photographs were available for viewing during the assessment. Patients had a mirror in hand for real time assessment in comparison to the pre- and day 90 post-treatment photographic images.

### 20.5.2. Patient Satisfaction Results

Based on the patient satisfaction questionnaire, 67% of the subjects indicated that they saw an improvement in face and neck characteristics.

## 20.6. Summary of Results

The quantitative assessment for the right and left side of the face yielded a 75.7% response rate of subjects that had a tissue lift  $\geq 10.0 \text{ mm}^2$ . There was  $71.97 \text{ mm}^2$  and  $71.69 \text{ mm}^2$  average area of tissue lift on the left and right side, respectively in the responding patients. The quantitative results were consistent for both the right and left side of the face.

Based on the masked assessment of three clinicians, 68.6% of subjects had improvement (visibly observable tissue lift) in the submental (beneath the chin) and neck.

The patient satisfaction questionnaire indicated that 67% of the subjects saw an improvement in face and neck characteristics.

### 20.6.1. Supplemental Analysis

The qualitative assessment results and patient satisfaction results were determined for those subjects identified as responders in the quantitative assessment (tissue lift  $\geq 10.0 \text{ mm}^2$ ). The results for this subset for this subset of subjects are as follows:

- 83.0% had improvement (visibly observable tissue lift) in the submental (beneath the chin) and neck based on the qualitative assessment.
- 75.5% noticed improvement in face and neck characteristics based on the patient satisfaction survey.

Overall it can be seen that, subjects that experienced tissue lift  $\geq 10.0 \text{ mm}^2$  also yielded positive patient satisfaction and quantitative results.

## 20.7. Safety Results

### 20.7.1. Sensory Response

The subjects' sensory response to the treatment exposures was recorded for each anatomical region, using a visual analog scale of 0-10 with 1 representing no pain and 10 representing the highest degree of pain.

It is important to note that the pain scores recorded for each section of the face and neck were recorded as the highest sensory response for that particular area: for example, when the clinician was treating the cheek area, the patient was asked to indicate the highest sensory score in that particular area, but the highest sensory score did not necessarily apply to each and every treatment line or pulse delivered within that area. The average patient age is 49.5 and the average sensory response is as follows: cheek is 5.7, submental (lower chin) is 6.1 and submandibular (neck) is 6.6. Sensory responses were moderate and only occurred during the treatment procedure. It is also important to note that pain scores were recorded during actual delivery of ultrasound energy and pain subsided immediately upon cessation of energy delivery. No post treatment medication was required by the subjects.

To achieve consistent aesthetic improvement from a non-invasive therapy, with no post-treatment recovery period, aesthetic treatment patients commonly endure temporary discomfort during the treatment.

In addition, physician sponsored pain studies determined that 800mg of ibuprofen is effective at pain control with lower pain scores during Ultherapy treatments (average is less than 5 out of 10). These following studies are included in Appendix 4.

- *Prospective Double-Blind, Randomized Pilot Study Comparing Ibuprofen to a Narcotic for Pain Management During Micro-Focused Ultrasound Treatment* performed by Hema Sundaram, M.D. and Ashley Lodha.
- *Double-Blind, Randomized, Controlled Split-Face Trial to Assess the Efficacy and Safety of a Liposomal Lidocaine Topical for Pain Management During Micro-Focused Ultrasound Treatment* performed by Vincent R. Fowler and Steven M. Gitt.

### 20.7.2. Adverse Events

A total of seven adverse events were reported. All of the events resolved with no residual sequelae. Four of the adverse events were considered unrelated to the device or the procedure. Five of the adverse events were considered mild and two were considered moderate. It is important to note that none of the device related adverse events received an assessment of moderate.

All of the potential adverse events listed in Table 20-14 are associated with similar aesthetic procedures. The Ulthera System presents no additional risks compared to FDA approved devices used for similar indications.

Many risks associated with aesthetic procedures are related to the condition of the patient's skin, the patient's overall physical health, pre-existing medical conditions, and the clinician's overall skill level.

Table 20-14 provides a complete listing and description of the adverse events.

**Table 20-14: Adverse Events in UTSW Subjects**  
n = 70

| Subject ID | Treatment Date | Onset Date | Relationship to Device | Severity | Action Taken | Outcome               | Adverse Event Description                  |
|------------|----------------|------------|------------------------|----------|--------------|-----------------------|--|
| 0005Y      | 7/6/2010       | 7/7/2010   | Possible               | Mild     | None         | Resolved, no sequelae | Went on right cheek and went on right neck |
| 0027Y      | 7/13/2010      | 7/14/2010  | Possible               | Mild     | None         | Resolved, no sequelae | Went on left cheek                         |
| 0065Y      | 7/31/2010      | 10/23/2010 | Unrelated              | Mild     | Medication   | Resolved, no sequelae | Cold                                       |
| 0079Y      | 8/5/2010       | 10/22/2010 | Unrelated              | Moderate | Medication   | Resolved, no sequelae | Pneumonia                                  |
| 0079Y      | 8/5/2010       | 10/22/2010 | Unrelated              | Moderate | Medication   | Resolved, no sequelae | Cracked rib                                |
| 0091Y      | 8/9/2010       | 8/10/2010  | Probable               | Mild     | None         | Resolved, no sequelae | Went on left side of neck                  |
| 0095Y      | 8/11/2010      | 10/29/2010 | Unrelated              | Mild     | None         | Resolved, no sequelae | Flu  |

Adverse Event is unrelated to the device.

### 20.7.3. Skin Types

For all 70 study subjects, the skin surface remained intact and there was no damage to the skin epidermis. All subjects tolerated the procedures well.

No incidents of acute skin damage or long-term sequelae such as scarring, burns, hypopigmentation, hyper-pigmentation, or ulceration were reported during the course of the study. The absence of any serious adverse effects indicates a very good device safety profile.

Ultherapy has been used on the face with the brow indication since 2009 in approximately 90,000 treatments worldwide. The Ulthera System is sold into Asian countries, Middle Eastern countries, and South American countries as well as other areas where higher Fitzpatrick skin types are the norm. There have been no reported incidents of hyperpigmentation or hypopigmentation or any other skin color related adverse events.

Please see Appendix 5 for additional studies supporting Ulthera's safety profile regarding skin of color. Please note that there were no adverse events related to higher Fitzpatrick skin types during the following studies:

- *An Evaluation of Micro-Focused Ultrasound for Obtaining Lift and Tightening of the Cheek Tissues and Improvement in Jawline Definition and Submental Skin Laxity in Patients*
- *Intense Focused Ultrasound Tightening in Asian Skin: Clinical and Pathologic Results*
- *Multicenter Study of Non-Coagulative Radiofrequency for Periorbital Tissue Tightening*

## 20.8. Conclusion

It is well established in the scientific literature that controlled thermal injury to facial skin leads to acute tissue contraction, followed by a tissue remodeling phase, leading to tightening, fullness, and a favorable cosmetic outcome.<sup>17,18,19,20,21,22,23,24</sup> The Ulthera<sup>®</sup> System produces a similar tissue effect by delivering targeted thermal coagulation to multiple zones in the skin tissue resulting in overall tightening of the tissue, while sparing the epidermis.<sup>10,25</sup> This favorable clinical effect improves lift and tightening of the cheek tissue and improvement in submental skin laxity after treatment with the Ulthera<sup>®</sup> System.<sup>12</sup> This study demonstrated clinical efficacy for the above stated indication resulting from selective thermal coagulation of tissue using the Ulthera<sup>®</sup> System by the high success rate of improvement determined by results of the masked clinician assessment, quantitative assessment and the patient satisfaction questionnaire. This clinical effect results from tightening skin tissue, which is one of numerous mechanisms described in the literature.<sup>18,20,21,23,24</sup>

This safety and efficacy study successfully achieved all the goals stated in the protocol. The study demonstrated that Ulthera<sup>®</sup> System procedures can be safely performed on the face and neck in a clinical setting. Delivery of ultrasound energy using the Ulthera<sup>®</sup> System produces a clinically favorable cosmetic result based on comparative review of the pre- and post-procedure photographs. The masked clinician assessment, quantitative analysis and patient assessment improvement scores all indicated improvement in lifting of the submental (lower chin) and neck tissue.

The predicate device 510(k) provided clinical support based on full face treatments. The study utilized the same methods: qualitative masked assessment, a quantitative analysis and patient satisfaction questionnaire.

The studies for the predicate and subject device utilized the same methodology and yielded acceptable results. The predicate device's indication for the upper face and the subject device's indication for lower face support the indication for lifting lax tissue to achieve a desired aesthetic effect for the full face and neck after the Ulthera<sup>®</sup> procedure.

The Ulthera<sup>®</sup> System provides a single, safe treatment alternative to other aesthetic procedures.

CONFIDENTIAL—Proprietary Information

06/07/2012

Appendix 6 includes representative unretouched photos of two patients who have been treated with the Ulthera® System, one subject who was a non-responder and one subject who achieved significant results.

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**Appendix 1: Proposed Instructions for Use**



Ulthera® System

# Instructions for Use

Featuring

DeepSEE® Technology

for

Ultherapy®

PROCESSED DRAFT

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PROPOSED DRAFT

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Various features of the Ulthera® System are covered by U.S. Patents 6,049,159 and 7,758,524, and contemplated features may be covered by one or more of the following U.S. Patents: 5,820,564; 6,036,646; 6,050,943; 6,120,452; 6,213,948; 6,440,071; 6,500,121; 6,540,679; 7,142,905; 7,229,411; 7,393,325; 7,491,171; 7,530,958; 7,571,336; 7,615,016; and 7,824,348. More than 100 other U.S. and International patents to which Ulthera has rights are issued, published, or pending.

EC REP

MedPass International Limited  
Windsor House Barnett Way  
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United Kingdom

CE

PROPOSED DRAFT



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## Ulthera® System

CAUTION: UNITED STATES FEDERAL LAW RESTRICTS THIS DEVICE TO SALE BY OR ON THE ORDER OF A PHYSICIAN.

THE ULTHERA® SYSTEM IS INTENDED FOR USE ONLY BY PROPERLY TRAINED PHYSICIANS AND PROPERLY TRAINED PERSONS UNDER THE SUPERVISION OF SUCH A TRAINED PHYSICIAN (HENCEFORTH "THE USER").

PRIOR TO OPERATING THE SYSTEM, THE USER MUST THOROUGHLY READ AND UNDERSTAND THIS INSTRUCTIONS FOR USE. IMPROPER USE OF THE SYSTEM MAY CAUSE PERSONAL INJURY AND/OR DAMAGE TO THE SYSTEM THAT MAY INVALIDATE THE WARRANTY AGREEMENT.

NOTE: THIS INSTRUCTIONS FOR USE DESCRIBES THE OPERATION OF THE ULTHERA SYSTEM ONLY. IT IS NOT A SUBSTITUTE FOR THE REQUIRED CLINICAL TRAINING ON THE PROCEDURE THAT UTILIZES THE SYSTEM.

PROCESSED UNDER FOIA

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PROPOSED DRAFT

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# 1. Introduction to Instructions for Use

## 1.1. Purpose

This Instructions for Use (IFU) provides a description of the System components, its controls and displays, instructions for its operation, and other equipment information important to the user.

**Warning:** Do NOT operate the Ulthera System before reading this IFU thoroughly AND being trained on the clinical procedure by an authorized Ulthera representative. This IFU is not a substitute for clinical treatment guidelines and training provided by the Company. For more information on training available please contact your local representative.

## 1.2. Conventions

 **Note:** Notes designate information of special interest

 **Caution:** Cautions alert the user to precautionary steps necessary to properly operate the system. Failure to observe these cautions may void the warranty.

 **Warning:** Warnings alert the user to information that is of the highest importance and vital to the safety of the patient and user.

All procedures are broken down by numbered steps. Steps must be completed in the sequence they are presented.

Bulleted lists indicate general information about a particular function or procedure. They do not imply a sequential procedure.

Control names are spelled as they are on the system, and they appear in **Bold** text.

---

## 2. Medical Safety

### 2.1. Indications for Use

The Ulthera System is indicated for non-invasive dermatological aesthetic treatment to:

- lift the eyebrow
- lift lax submental (beneath the chin) and neck tissue
- lift lax tissue to achieve a desired aesthetic effect for the full face and neck

### 2.2. Contraindications

The Ulthera System is contraindicated for use in patients with

- open facial wounds or lesions
- severe or cystic acne on the face and/or neck

### 2.3. Precautions

When not in use by trained personnel, the Ulthera System User Access Key should be removed from the system to help prevent unauthorized use. Keep the Ulthera System User Access Key in a designated place accessible only to authorized and trained personnel.

The Ulthera System has not been evaluated for use over various materials. Therefore, treatment is not recommended directly over those areas with any of the following:

- Mechanical implants
- Dermal fillers
- Implanted electrical devices
- Metal stents in the face and neck area

Treatment energy is not recommended for use directly on an existing keloid.

The Ulthera System has not been evaluated for use in patients on an anticoagulant treatment plan.

The Ulthera System has not been evaluated for use in the following patient populations:

- Pregnant or breast feeding women
- Children
- Those with the following disease states
  - A hemorrhagic disorder or haemostatic dysfunction
  - An active or local skin disease that may alter wound healing
  - Herpes Simplex
  - Autoimmune Disease
  - Diabetes
  - Epilepsy
  - Bell's Palsy

#### 2.4. Patient Safety



**Warning:** Ulthera should not be used on a patient's eyes or in a location or technique where ultrasound energy can reach the eye.



**Warning:** Use this system only if you are trained and qualified to do so.



**Warning:** If any problems occur during system operation, take immediate action(s): lift the transducer off the patient's skin, press the **See** pushbutton on handle to discontinue treatment in progress, and/or press the red emergency **Stop** button to completely halt system operation.

#### 2.5. Potential Side Effects

Side effects reported in the clinical evaluation of the Ulthera System were mild and transient in nature. These were limited to:

- Erythema (redness): The treated area may exhibit erythema immediately following treatment. This typically resolves within a few hours of treatment.

- Edema (swelling): The treated area may exhibit mild edema following treatment. This typically resolves within a few days of treatment.
  - Pain: Momentary discomfort may be experienced during the procedure while energy is being deposited.
  - Bruising: Mild bruising, which is caused by damage to soft tissue blood vessels, may occur occasionally and typically resolves within a few days of treatment.
  - Nerve Effects:
    - Transient local muscle weakness may result after treatment due to inflammation of a motor nerve.
    - Transient numbness may result after treatment due to inflammation of a sensory nerve.
- No permanent injuries to facial nerves have been reported.
- Scarring: The possibility for scar formation (which will respond to medical care) may exist if incorrect treatment technique is used.

## 2.6. Complaints and Adverse Events

No serious adverse events were observed during the clinical study evaluation of the Ulthera System.

Ulthera follows MDR (Medical Device Reporting) rules for handling complaints and adverse events. Should an adverse event be suspected or reported, contact Ulthera, Inc. at the number on the cover page of this document; for those outside the U.S., contact your local Ulthera representative.

---

## 3. System Overview

### 3.1. System Description

The Ulthera System integrates the capabilities of ultrasound imaging with those of ultrasound therapy.

The imaging feature allows the user to visualize the skin and sub-dermal regions of interest before treatment. It also allows the user to assure proper skin contact in order to deliver the energy at desired depths.

The therapy feature directs acoustic waves to the treatment area. This acoustic energy heats tissue as a result of frictional losses during energy absorption, producing discrete points of coagulation.

### 3.2. System Components and Features

The Ulthera System consists of three primary components: the control unit with integrated touchscreen, the handpiece with cable, and interchangeable transducers (see Figure 3.1).

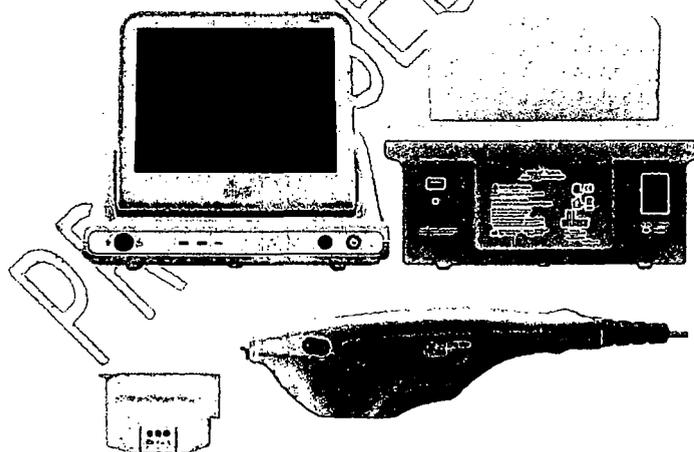


Figure 3.1. Main components of the Ulthera® System: Control Unit (top), Handpiece (bottom right), Image/Treat Transducer (bottom left) that inserts into the handpiece receptacle.

### 3.2.1. Control Unit

The control unit is the tabletop information center for the Ulthera System. It houses the touchscreen monitor and Graphical User Interface (GUI) that allows the user to interact with the device. This screen sets and displays the operating conditions, including equipment activation status, treatment parameters, system messages and prompts, and ultrasound images. Figure 3.2 illustrates the physical features of the control unit, such as the various connector ports and power controls.

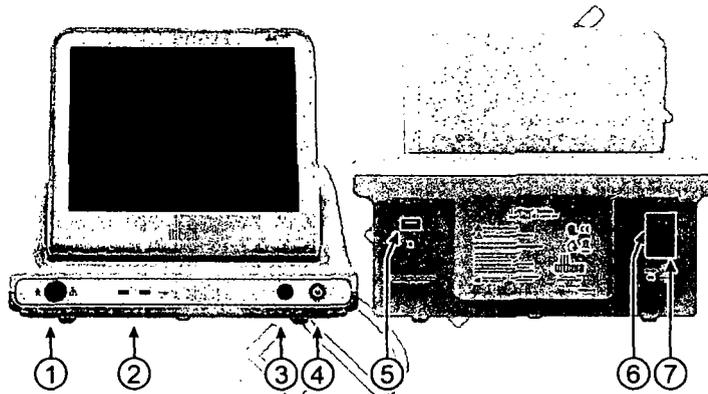


Figure 3.2 Control Unit front view (left) and rear view (right). See Table 3.1 for a description of the controls and connector ports of the control unit.

Table 3.1 Control Unit connector ports and controls (See Figure 3.2)

| Item                             | Description  |
|----------------------------------|--|
| 1 Handpiece Connector Receptacle | Socket for plugging in handpiece cable   |
| 2 USB Ports (two)                | For optional USB removable storage device  |
| 3 Emergency Stop                 | Halts system operation if pressed  |
| 4 On / Off Button                | <ul style="list-style-type: none"> <li>• Momentarily press to turn system ON</li> <li>• Momentarily press to turn system OFF</li> <li>• Press and hold to force system shutdown</li> </ul> |
| 5 Rear Panel USB port            | For Ulthera System User Access key   |
| 6 Main Power Switch              | Supplies power to system. Leave ON (symbol "I" pressed in)   |
| 7 Power Cord Receptacle          | Socket for attachment of power cord  |

Below the monitor, on the front panel of the control unit is a handpiece connector receptacle that interfaces with the handpiece cable. On the front right of the panel is an **On/Off** button and an emergency **Stop** button. When turned OFF via the **On/Off** button the system goes into a very low power standby mode unless the Main Power Switch is also turned to the OFF position by pressing the 'O' symbol. The front of the control unit also has two Universal Serial Bus (USB) ports: both ports may be used for the Ulthera System User Access Key or for an optional removable storage device ("thumb drive").



**Warning:** When not in use by trained personnel, the Ulthera System User Access Key should be removed from the system to help prevent unauthorized use. Keep the Ulthera System User Access Key in a designated place accessible only to authorized and trained personnel.

The rear of the control unit has a USB port, an AC power receptacle and the main power switch. The main power switch should be left in the powered position (with the 'I' pressed inward). In such a configuration, the control unit may be turned ON via the front panel **On/Off** button and can be turned OFF via either the front panel **On/Off** button or the graphical user interface.

### 3.2.2. Handpiece

The handpiece is a handle with an integrated receptacle for insertion of a transducer on one end and an electrical cable for attachment to the control system on the other end. The handpiece has two types of buttons: one to image (**SEE**) and the other to deliver therapy (**TREAT**). Figure 3.3 provides two views of the handpiece, including one showing it connected to an Image/Treat transducer. Table 3.2 is a description of the various components and features illustrated in Figure 3.3.

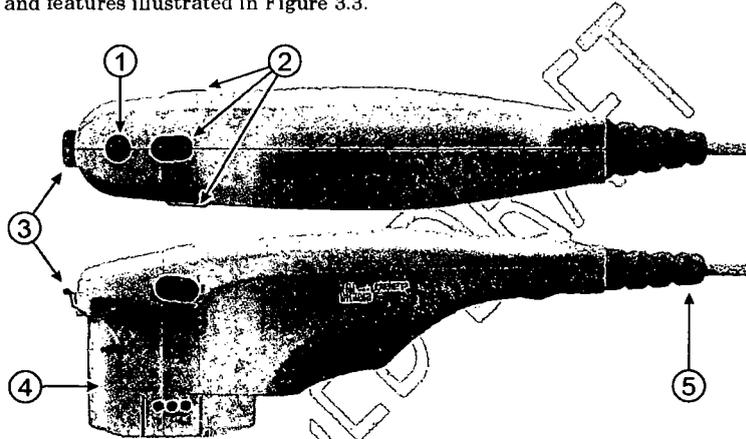


Figure 3.3 Handpiece with transducer inserted, top and side views.

Table 3.2 Handpiece and Transducer Description

| Item                    | Description   |
|-------------------------|---|
| 1 SEE Pushbutton        | <ul style="list-style-type: none"> <li>Engages IMAGING state (if not already imaging)</li> <li>Places system in READY state (times out in 40 seconds)</li> <li>Stops TREATING if treatment in progress</li> </ul> |
| 2 TREAT Pushbuttons     | <ul style="list-style-type: none"> <li>Engages TREATING state</li> </ul>  |
| 3 Latch                 | Locks transducer into handpiece   |
| 4 Transducer            | Image/treat transducer  |
| 5 Strain Relief / Cable | Connects handpiece to Control Unit  |

### 3.2.3. Transducers

Figure 3.4 is an illustration of an image/treat transducer. The transducer can image and treat a region of tissue up to 25 mm long and can image a depth of up to 8 millimeters. Treatment occurs along a line less than or equal to the transducer's active length, which is indicated by guides on the sides of the transducer, as described in Table 3.3. An additional guide at the front tip of the transducer represents the center of the treatment line. In therapy mode, bursts of sound energy create a linear sequence of individual, discrete, thermal coagulation zones. A label atop the transducer provides the transducer type, expiration date, and other information.

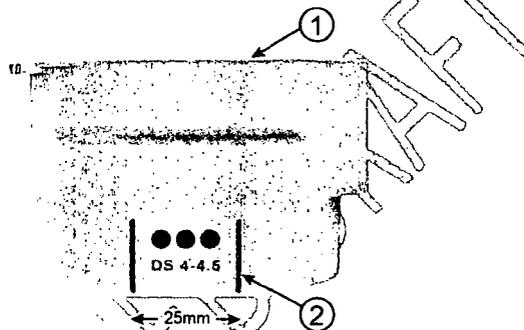


Figure 3.4 (Image/Treat) Transducer, separated from handpiece (see Table 3.3)

Table 3.3 Transducer Description

| Item            | Description  |
|-----------------|--|
| 1. Labeling     | Transducer type and other information  |
| 2. Treat guides | Markers denoting maximum treatment line length and center of treatment line (center of transducer) |

The types of transducers reflect variations in frequencies and treatment depths as shown in Table 3.4.

Table 3.4 Transducer Types

| Transducer Type | Treat Frequency | Treat Depth | Image Depth | Scan Length |
|-----------------|-----------------|-------------|-------------|-------------|
| DS 7 - 3.0      | 7 MHz           | 3.0 mm      | 0 - 8 mm    | 25 mm       |
| DS 7 - 3.0N     | 7 MHz           | 3.0 mm      | 0 - 8 mm    | 14 mm       |
| DS 4 - 4.5      | 4 MHz           | 4.5 mm      | 0 - 8 mm    | 25 mm       |
| DS 7 - 4.5      | 7 MHz           | 4.5 mm      | 0 - 8 mm    | 25 mm       |
| DS 10 - 1.5     | 10 MHz          | 1.5 mm      | 0 - 8 mm    | 25 mm       |
| DS 10 - 1.5N    | 10 MHz          | 1.5 mm      | 0 - 8 mm    | 14 mm       |

### 3.2.4. Essential Accessories

Other essential components provided for operation of the Ulthera System are the power cord that connects the Ulthera System to an AC power outlet, and the proprietary Ulthera System User Access Key.

Ultrasound gel to facilitate transmission of the acoustic energy is also required but is not provided as part of the system.

## 4. System Safety

The following precautions and warnings must be reviewed and observed:

### 4.1. Electrical and Fire Safety



**Warning:** To avoid risk of electric shock, always inspect the Ulthera transducer, handpiece and cable before use. Do not use a damaged cable or a transducer that has been damaged or is leaking fluid.

The Ulthera System is intended for indoor, dry location use. Avoid liquid spills and splashes. Keep coupling gel away from the handpiece transducer connections.

The Ulthera System comes with a three-conductor AC power cord and plug. Use a properly grounded outlet and always plug the Ulthera System directly into the outlet. Never remove the ground conductor or compromise the ground conductor via any AC adapter plugs or extension cords.

Disconnect the power cord from the outlet by pulling on the plug not the cord.

AC powered USB printers or storage devices may pose a shock hazard. Do not touch the USB connectors and the patient at the same time.

Turn off the AC power switch and disconnect the AC power supply before cleaning the control unit.

Do not remove the covers on the control unit or handpiece, the control unit contains hazardous voltages. The Ulthera System contains no user-serviceable components. If the system requires service, contact Ulthera, Inc.

No modification of this equipment is allowed.

The Ulthera System should not be used near flammable gases or anesthetics. Fire or explosion can result. The Ulthera System is not AP or AFG rated.

Avoid restricting ventilation under and behind the Ulthera control unit. Maintain an open space of at least 4 inches/ 10 cm around the control unit. If ventilation holes are obstructed, the system could overheat.

The Ulthera transducer and handpiece is rated as a Type B patient-applied part. It may provide a connection between the patient and protective earth. This may present a hazard if the patient becomes connected to other equipment with excessive electrical current leakage.

Do not touch the handpiece electrical contacts and patient simultaneously.

To avoid a burn hazard, remove the transducer from the patient before performing HF electrosurgical procedures.

#### 4.2. Equipment Use and Care



**Caution:** Failure to observe these precautions may void the warranty.

The Ulthera handpiece connectors must be kept clean and dry. Do not use the transducer if the connectors have been immersed in liquid. See the instructions for cleaning the transducer.

Every effort has been made to make the transducers as rugged as possible; however, they may be permanently damaged if dropped onto a hard surface or if the membrane is punctured. Transducers damaged in this manner are not covered by the warranty.

The Ulthera System has no user-serviceable components. Do not attempt to open the control unit enclosure or transducers. Contact Ulthera, Inc. if service is required.

When not in use by trained personnel, the Ulthera System User Access Key should be removed from the system to help prevent unauthorized use. Keep the Ulthera System User Access Key in a designated place accessible only to authorized and trained personnel.

#### 4.3. Ergonomic Safety



**Warning:** Ultrasound scanning has been associated with repetitive motion injuries such as carpal tunnel syndrome. To reduce chances of such injury, maintain a balanced, comfortable posture while scanning, avoid gripping the handpiece too tightly, and keep hands and arms in a comfortable position while using.

#### 4.4. Medical Ultrasound Safety



**Warning:** Use this system only if you are trained and qualified to do so.

The Ulthera System has a fixed, non-adjustable output power level for imaging, well below the limits set by FDA guidelines. However, ultrasound exposure times should be limited to the shortest amount of time needed to complete the treatment. The ALARA principle (As Low As Reasonably Achievable) can be followed by minimizing the examination time.

If the system displays unusual / inconsistent behavior, discontinue use and contact Ulthera, Inc.

Under some conditions (for example, high ambient temperature and long scanning period), the transducer surface temperature may exceed 41°C. Scanning will be automatically disabled if the internal transducer temperature reaches 49°C.

#### 4.5. Electromagnetic Compatibility and Immunity

The Ulthera System's RF emissions are very low and are not likely to cause interference in nearby electronic equipment.

Ulthera is suitable for use in all establishments other than domestic and those directly connected to the public low voltage power supply network that supplies buildings used for domestic purposes.

Mains (AC) power quality should be that of a typical commercial or hospital environment.

Floors should be wood, concrete or ceramic tile. If floors are covered with synthetic material, the relative humidity should be at least 30% to avoid excessive static electricity.

**Warning:** The Ulthera System should not be situated adjacent to, or stacked with, other electronic equipment. If the system must be installed in close proximity to other equipment, both the Ulthera System and the nearby equipment should be observed to verify normal operation in that configuration.

**Caution:** EMI (Electro-Magnetic Interference) from other electronic systems may cause degradation of the ultrasound image. Ulthera has been designed to meet the standards of IEC60601-1-2 for electromagnetic compatibility, however some computer equipment unintentionally emits strong interfering RF signals. Portable RF communication devices may also affect Ulthera. If image quality is degraded by EMI, the system may need to be relocated or reconfigured.

**Warning:** Use of accessories other than those specified, may result in increased emissions, or decreased immunity of this system.

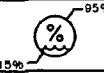
#### 4.6. Disposal

Depleted transducers should be disposed of in accordance with federal, state, and local regulations. For expired transducers (past expiration date), please contact your local Ulthera representative.

4.7. Safety Symbols

A variety of symbols appear on the transducer, handpiece, and control unit in accordance with regulatory guidance.

| SYMBOL  | DEFINITION  |
|---|---|
|    | Type B Applied Part   |
|    | CE marking indicating manufacturer's declaration of compliance with appropriate EU product directives |
|    | Canadian Standards Agency   |
|    | Consult instructions for use  |
|    | Date of Manufacture   |
| SN  | Serial Number   |
|   | Emergency Stop  |
|  | Power Standby Switch  |
|  | Indoor Use Only   |
|  | Keep electrical waste separate from municipal waste   |
|  | Recycle Packaging   |
| IPx1  | Mated handpiece and transducer protected from the effects of vertically dripping water                |

|  |                                  |
|--|----------------------------------|
|   | Catalogue Number                 |
|   | Manufacturer                     |
|   | Storage Range                    |
|   | Keep Dry                         |
|   | Fragile Contents                 |
|   | Relative Humidity                |
|   | Use By, Expiration Date          |
|   | Lot Number                       |
|   | Atmospheric Pressure Limits      |
|  | Recycle Packaging (Polyethylene) |

PROPRIETARY

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## 5. Setting Up for First-Time Use

### 5.1. Unpacking

The control unit and handpiece are shipped together in one container. Transducers are packaged and shipped separately from the control unit and handpiece, in ready-to-use, non-sterile pouches. Transducer gel is also packaged and shipped separately.

### 5.2. Physical Environment

#### 5.2.1. System Base

The System may be placed on a cart or counter with the depth to accommodate the control unit, handpiece and power cord provided. A cart is recommended to offer maximum mobility for the user when treating the patient and provide a more secure housing for the handpiece.

Space should be provided around the back, sides, bottom and top of the System for cooling. In continuous use for extended periods of time, it is normal for the System to be warm.

#### 5.2.2. Electromagnetic Environment

The System is not likely to cause interference in nearby electronic equipment; however, other electronic equipment should not be stacked or placed immediately adjacent to the System.

Flooring should be wood, concrete or ceramic tile. If covered with synthetic material, the relative humidity should be at least 30%.



**Warning:** The Ulthera System should not be situated adjacent to, or stacked with, other electronic equipment. If the system must be installed in close proximity to other equipment, both the Ulthera System and the nearby equipment should be observed to verify normal operation in that configuration.



**Caution:** EMI (Electro-Magnetic Interference) from other electronic systems may cause degradation of the ultrasound image. The Ulthera System has been designed to meet the standards of IEC60601-1-2 for electromagnetic compatibility; however, some computer equipment unintentionally emits strong interfering RF signals. Portable RF communication devices may also affect the Ulthera System. If image quality is degraded by EMI, the system may need to be relocated or reconfigured.

### 5.3. Electrical Requirements

The Ulthera System has an international power supply and may be used with 100-240 VAC, 50-60 Hz power systems. See Section 4.1 Electrical and Fire Safety for additional information.

### 5.4. Connecting Components

#### 5.4.1. Connecting the Handpiece

The handpiece connector receptacle is located on the left side of the control unit's front panel as shown in Figure 5.1. To attach the handpiece connector, align it with the white dot facing up and push it into the receptacle. It will latch when seated properly.

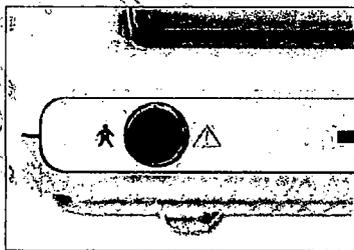


Figure 5.1 Handpiece Connector Receptacle.

To disconnect the handpiece, twist the coupling ring on the connector counterclockwise while pulling outwards.

### 5.4.2. Identifying and Connecting Transducers

Transducers are identified by the label on the top of the transducer which includes the name of the transducer (Ulthera DeepSEE), treatment frequency and treatment depth (DS X-X), a unique serial number, a part number, and date of manufacture.

The Treatment Guidelines on the control unit interface will display the recommended transducer to utilize based on the anatomical area you have selected to treat.

Remove the transducer indicated from its protective pouch. To connect the transducer, slide the transducer into the handpiece as shown in Figure 5.2. When the transducer is fully seated you will hear a tone indicating that it has been correctly inserted.

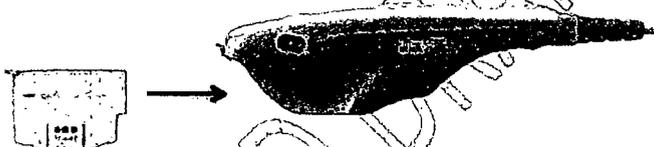


Figure 5.2 Connecting a Transducer

To disconnect the transducer, lift the latch at the tip of the handpiece and slide the transducer straight out of the handpiece.



**Caution:** Do not apply force/displacement to latching cantilever without a transducer installed in the handpiece.

When the transducer is inserted, the control unit automatically detects it and updates the graphical user interface.

### 5.4.3. Connecting Accessories

The Ulthera System User Access Key should be inserted into one of the available USB ports otherwise the message "No Key" will appear and the software will not allow user access.

An optional portable USB storage device, i.e. a "thumb drive", can be inserted into another USB port but not for downloading images or treatment records.

## 6. System Operation

### 6.1. Overview of System Functions

The Ulthera System's Graphical User Interface is divided into three general functions (tabs): Settings, Patient Info, and DeepSEE. The **Settings** function allows you to recall patient treatment information and to change general system settings.

The **Patient Info** function contains the controls and information instrumental in planning a treatment. This function allows you to build patient treatment information when starting a new treatment or to drive selecting regions during a treatment in progress.

The **DeepSEE** function contains the controls and information needed for imaging soft tissue and for treating pertinent soft tissue. An overview of this screen is seen in Figure 6.1

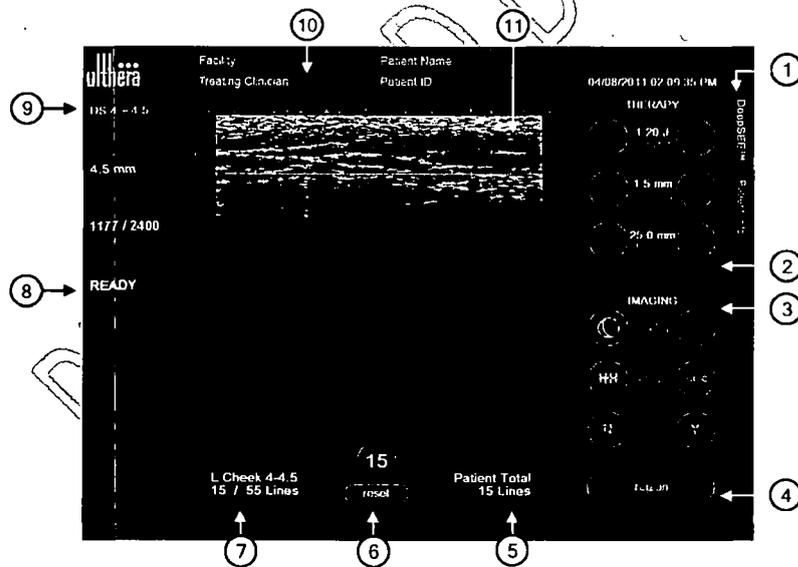


Figure 6.1 Imaging/Therapy Screen (DeepSEE Tab) in READY (to treat) state. See Table 6.1. for description

Table 6.1 Imaging/Therapy Screen Description

| Item |                          | Description   |   |                              |
|------|--------------------------|---|---|------------------------------|
| 1    | System Function Tabs     | DeepSEE   | Imaging/Therapy screen (described in this table)  |                              |
|      |                          | Settings (not scanning)   | Patient and Facility information, Treatment Records and Images, Help, Volume, and System Shutdown controls and dialogs                                      |                              |
|      |                          | Patient Info  | Allows entering of patient information, selection of treatment guidelines and selecting regions during treatments, which automatically set therapy controls |                              |
| 2    | Therapy Controls         | Energy  | Sets acoustic energy level  |                              |
|      |                          | Spacing   | Sets distance between thermal coagulation points  |                              |
|      |                          | Length  | Sets the length of the treatment line   |                              |
| 3    | Imaging Controls         | Marker (not scanning)   | Distance Icon   | Activates distance calipers  |
|      |                          |   | Text  | Activates text annotation    |
|      |                          | Display (scanning)  | Sun icon  | Increases display brightness |
|      |                          |   | Moon icon   | Decreases display brightness |
|      |                          | Image   | Treat ruler icon  | Toggles treat ruler ON/OFF   |
|      |                          |   | Save  | Saves image                  |
|      |                          | Scan  | Y   | Starts scanning (IMAGING)    |
| N    | Stops scanning (IMAGING) |   |   |                              |
| 4    | Region Control           | Launches dialog below image to select tissue region   |   |                              |
| 5    | Patient Total Line Count | Cumulative number of treatment lines delivered  |   |                              |
| 6    | Reset Counter            | Line counter that is reset to "0" by pressing the <b>reset</b> button or by changing regions  |   |                              |
| 7    | Treat Region Line Count  | <ul style="list-style-type: none"> <li>• Treat region selected (e.g. forehead, submental, etc.)</li> <li>• Lines delivered to region / (vs.) recommended lines per guidelines</li> </ul>                            |   |                              |
| 8    | System Status            | READY or TREATING   |   |                              |
| 9    | Probe Information Area   | <ul style="list-style-type: none"> <li>• Name of attached transducer</li> <li>• Treat depth of transducer</li> <li>• Number of treatment lines spent / (vs.) Total treatment line capacity of transducer</li> </ul> |   |                              |
| 10   | Header Information       | <ul style="list-style-type: none"> <li>• Ulthera logo</li> <li>• Facility, Clinician, Patient Name and Patient ID (if entered)</li> <li>• Date and Time</li> </ul>  |   |                              |

|    |                    |  |
|----|--------------------|--|
| 11 | Image/Treat Region | <ul style="list-style-type: none"> <li>• Ultrasound image</li> <li>• Horizontal and vertical (depth) rulers with 1 mm tick marks</li> <li>• Treat ruler indicating spacing, length and depth of treatment</li> </ul> |
|----|--------------------|--|

## 6.2. Activating the Control Unit

**Step 1** Ensure the power cord on the back of the system is plugged into the wall socket.

**Step 2** Ensure the main power switch on the back of the control unit is in the ON position.

 **Note:** This switch may be left in the ON position even when the system is not in use.

 **Warning:** While running, this switch should not be used to shut down the system.

**Step 3** Insert the Ulthera System User Access Key into the USB port on the back of the control unit.

 **Note:** The Ulthera System must be used only with the authorized Ulthera System User Access Key.

**Step 4** Press the green On/Off button on the front of the control unit.

- The system will perform a brief self-test. After passing the self-test, a "NO KEY" message will be displayed if the Ulthera System User Access Key has not yet been inserted; otherwise the starting screen will be displayed.

 **Warning:** If the self-test screen displays any information messages, turn the system OFF and follow the instructions in Section 7.

### 6.3. Setting Up a Treatment Record

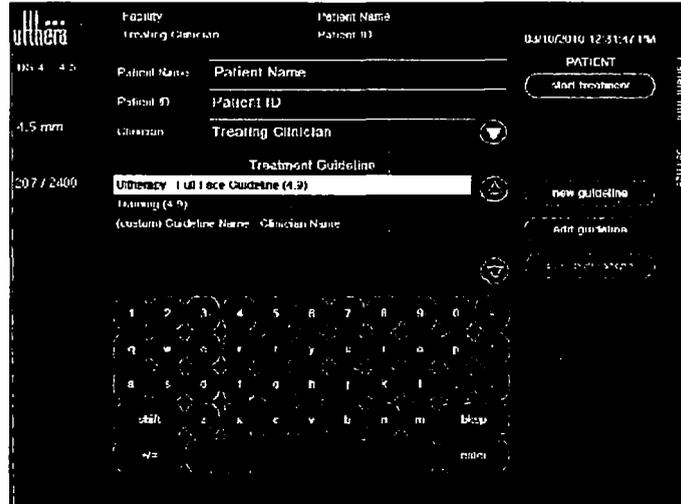


Figure 6.2. Patient Info - Treatment Setup Screen

**Note:** The Patient Info screen is the startup screen.

**Step 1** Enter the patient name, patient ID and the clinician performing the treatment, using the touch pad at the bottom of the screen.

**Note:** A patient name or patient ID along with the selection of a treatment guideline is necessary to start a treatment.

**Note:** Unwanted clinician names stored in the dropdown menu may be deleted by:

- 1) selecting the name to be deleted from the dropdown menu
- 2) pressing the **+/-** key
- 3) pressing the **del** key followed by the **enter** key

**Step 2** Select the desired Treatment Guideline

- An overview of the various regions within the treatment guideline is visible at the bottom of the screen

**Step 3** Tap the Start Treatment button



**Note:** Once the **Start Treatment** button has been pressed the treatment guideline, patient name and patient ID may not be changed until the treatment is ended.

#### 6.4. Selecting a Transducer



**Note:** The Treatment Guideline displays an overview of the various treatment regions with recommended treatment parameters for each, as shown in Appendix A. These treatment parameters are based on results from clinical trials conducted by Ulthera that demonstrated a safe and effective treatment for the treatment region selected.



**Caution:** It is the responsibility of the physician to fully understand the indications for use and safety considerations associated with the Ulthera System.



**Note:** An alternative way to access the treatment region menu is to tap the **Region** button on the **DeepSEE** screen. This approach bypasses the **Patient Info Tab** with the regions listed.

**Step 1** Decide which region you will be treating, and obtain the necessary transducer for that region as depicted on the Patient Info screen.

- The DS 10 – 1.5 transducer has a lower level of energy and a 1.5 mm focal depth.
- The DS 10 – 1.5N transducer has a lower level of energy, 1.5mm focal depth and a narrower patient contact footprint than the DS 10 – 1.5. The DS 7 – 3.0 transducer has a lower level of energy and a 3.0 mm focal depth.
- The DS 7 – 3.0N transducer has a lower level of energy, a 3.0 mm focal depth and a narrower patient contact footprint than the DS 7 – 3.0.
- The DS 7 – 4.5 transducer has an intermediate level of energy and a 4.5 mm focal depth.
- The DS 4 – 4.5 transducer has a higher level of energy and a 4.5 mm focal depth.

**Step 2** After checking the expiration date on the transducer package, open the sealed pouch and connect the transducer by pushing the handpiece latch up and sliding the transducer into the handpiece. When the transducer is fully seated, push the handpiece latch down to lock the transducer into place. You will hear a tone indicating that the transducer has been correctly inserted.



**Caution:** If a "Transducer **Not Connected**" or any **Warning** or **Caution** screen appears when a transducer is attached, there could be a problem with the

transducer or system. Try disconnecting then reconnecting the transducer. If the problem persists, contact your local representative.

**Step 3** On the **Patient Info** screen, the regions available for treatment with the inserted transducer will be displayed in white under “Treatment Guidelines”. Tap the region to be treated from the available regions displayed. This will take you automatically to the **DeepSEE** screen.

- The Therapy settings on the right-hand side of the screen (i.e., energy, spacing and length) are automatically set to the appropriate levels for the treatment region selected, based on the treatment guideline.

### 6.5. Imaging and Treating

The **DeepSEE** screen displays as shown in Figure 6.3.

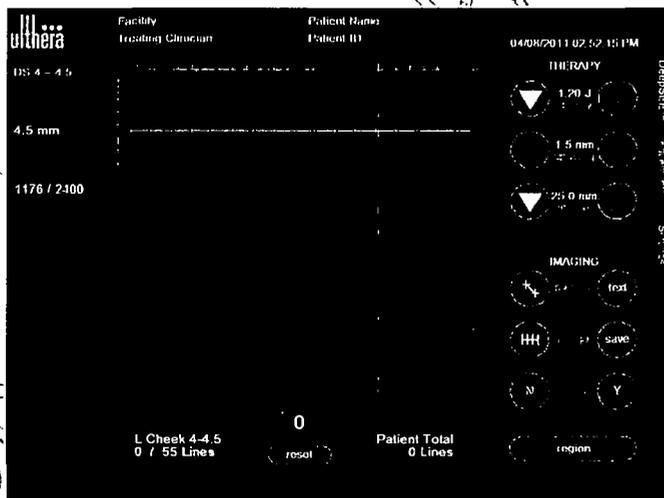


Figure 6.3. DeepSEE screen with treatment region selected (Cheek).

The region you selected from the treatment region menu will be displayed in white on the bottom left/center of the **DeepSEE** screen. The number of recommended treatment lines for the region is displayed underneath as the denominator in yellow, and the cumulative number of treatment lines delivered in that region is displayed as the numerator, in yellow. When the recommended number of treatment lines for the region have been delivered, these numbers will change color to white to signify completion for that region.

A counter for the total number of treatment lines for the patient visit is displayed on the bottom right/center of the screen.

In addition, the appropriate energy level is preset, based on treatment guidelines (see Appendix A – Treatment Guidelines) and can be adjusted down as needed to manage the patient's comfort level.



**Warning:** In the event of damage to any part of the system, as in the handpiece or transducers being dropped, broken, or leaking fluids, the equipment should be disconnected from the power source outlet prior to touching any part of the equipment. Before reconnecting the equipment it should be thoroughly inspected for external damage. Do not use damaged transducers or handpiece on a patient.

### 6.5.1. Treatment Steps

- Step 1** Ensure the face and neck have been cleansed thoroughly.
- Step 2** Carefully apply a thin layer of ultrasound gel to the transducer window. Too much or too little gel will result in poor skin contact. (Use aqueous ultrasound gel only, as other lubricants or lotions can damage the transducers and cables).
- Step 3** Place the transducer treatment window flush with the patient's skin and press the See button on the handpiece to activate the IMAGING state.

An image of the patient's soft tissue appears. The green "treat ruler" that is overlaid upon the image shows the depth that coagulative points will be formed. Green tick marks along the treat ruler show the lateral positions where the coagulative points will be placed along the horizontal plane. For example, with Length set to 25 mm, and Spacing set to 1.5 mm (center to center), a total of 17 coagulative zones would be produced in a treatment line. Verify sufficient coupling between the transducer and the skin by ensuring there are no dark, vertical artifact bars on the image.



**Note:** If the transducer is jostled, dropped or shaken while scanning, it may momentarily pause in order to recalibrate position. It should then resume normal scanning.

- Step 4** Press the See button on the handpiece while in the IMAGING state to activate the READY (to treat) state.



**Note:** The Treat buttons on the handpieces will become lit and a tone is emitted momentarily when the system enters (or exits) the READY state.

The "READY" state turns off after 40 seconds if the **Treat** button is not pressed, but can be reactivated by pressing the **See** button again.

If you would like to freeze the image, tap the Scan N (No) button in the Imaging section on the right hand side of the screen. To resume scanning, press the Scan Y (yes) button (or press the See button again).

To control the image brightness, use the Display buttons to decrease/increase the overall display brightness. These user controls appear only while the system is actively scanning (i.e. in the IMAGING state). When not in the imaging state the controls become distance measurement calipers and text annotation markers (described in Section 6.7) that can be applied to static (frozen) images.

To save a displayed image, next to Image tap Save. The image will be stored on the system and can be recalled, viewed or transferred to an external USB storage device via Images on the Settings Tab.

**Step 5** Verify sufficient coupling between the transducer and the skin by ensuring there are no dark, vertical artifact bars, as indicative of air pockets between the face of the transducer and patient. A properly coupled image should look similar to that in Figure 6.4. Reapply gel as needed to afford ample coupling. A poorly coupled image looks similar to that in Figure 6.5.

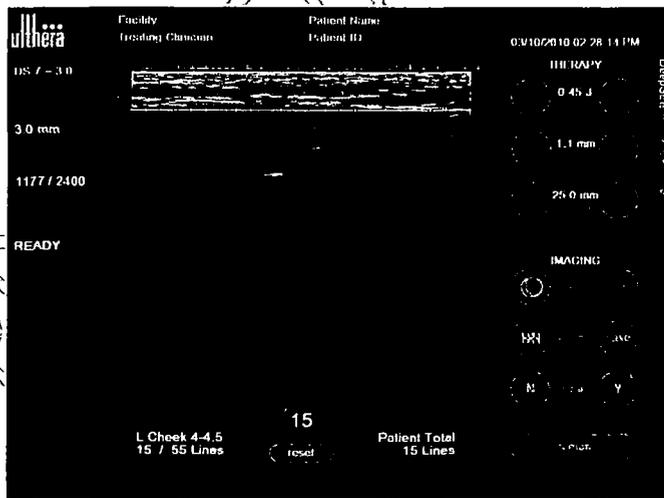


Figure 6.4. Sample image of transducer well-coupled. No vertical dark lines appear.

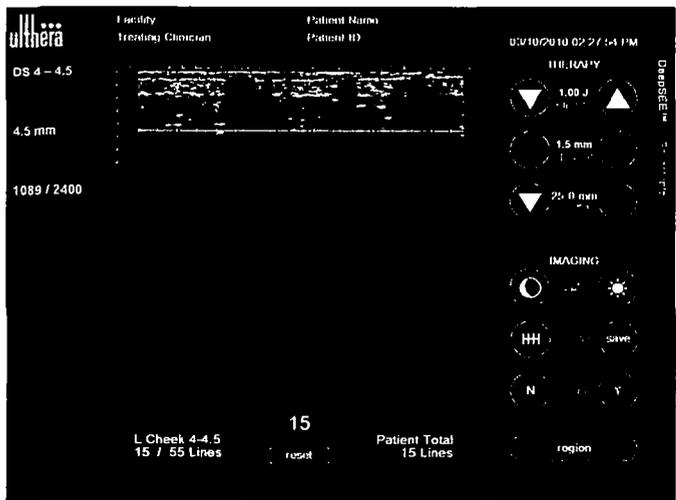


Figure 6.5. Sample Image of Transducer with Poor Coupling on the Cheeks. Large, vertical dark bars are present.

**Step 6** Press a Treat button on the handpiece to activate the TREATING state and deliver the energy between the Treat Guides. Take care that the hand remains still and the handpiece remains in place while the energy is being delivered. In addition a light constant pressure should be maintained between the transducer and the patient's skin. The Treat button's lighting will turn off and the See button will light up momentarily to indicate the system is in the TREATING state. As the energy is delivered a tone is sounded for each coagulation point being created and the green treat ruler will change to a yellow color momentarily. This is shown in Figure 6.6.

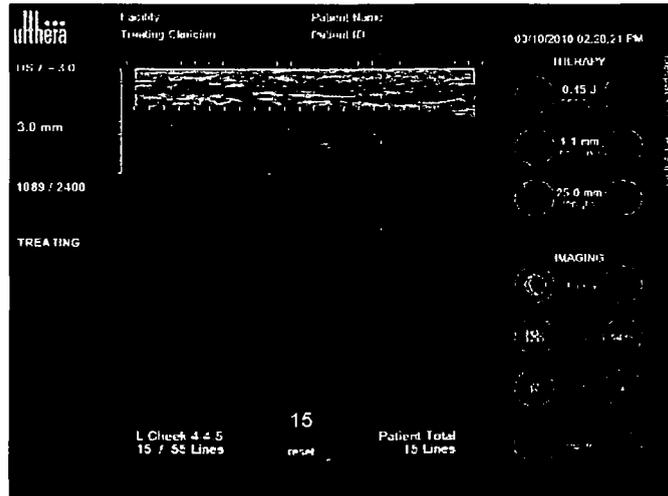


Figure 6.6. TREATING state. A yellow treat progress line is superimposed over the green treat ruler.



**Warning:** If desired, therapy may be cancelled at any time by pressing the **See** button on the handpiece, or the system can be halted by pressing the red Emergency Stop button on the front panel of the control unit. Also, the transducer can be simply lifted off the patient's skin quickly.



**Note:** If an adjustment in the volume of the audio signals is desired, tap the **Settings** tab and use the **Volume** up/down arrows as needed.



**Note:** The settings tab is not available while in the imaging mode.

**Step 7** To deliver the next treatment line of energy within the same treatment region, advance the transducer 2-3 mm to adjacent tissue and press a **Treat** button. If 40 seconds have elapsed since delivering the last treatment line of energy, press the **See** button on the handpiece to restore the READY state, then press a **Treat** button to deliver an additional line of therapy.

**Step 8** After 5 treatment lines are delivered, do a visual check of the transducer window to ascertain if gel needs to be reapplied such that a small bead of gel covers the window.

**Step 9** Continue in this fashion until the recommended number of treatment lines for the region (as shown on the bottom/left of the screen) has been delivered. When the correct number of treatment lines is delivered, the treatment line count color turns from yellow to white.

**Step 10** To continue treatment in another region, tap the **Region** button on the lower right hand of the **DeepSEE** screen. This will prompt the menu of treatment regions and appropriate treatment line counts to be displayed.

 **Note:** If the next treatment region desired is grayed out, change the transducer to the one depicted on the guideline.

 **Note:** If the Treatment Guidelines indicate that the transducer is to be changed in order to treat another section, turn scanning off by pressing the "N" (No) button on the main screen prior to switching transducers.

**Step 11.** Tap the region you will be treating next and proceed as outlined above in Steps 1 through 9.

**Step 12** When all targeted regions have been treated, tap the **End Treatment** button. If all desired treatment lines have been delivered, tap the **Confirm End** button to end the treatment session and to save the treatment record to the system. If further treatment lines are still necessary, you may tap the **Resume Treatment** button to return.

 **Warning:** The **End Treatment** button *must* be tapped at the end of each patient's procedure in order to reset the treatment line counters and maintain an accurate count of treatment lines delivered to any one patient or treatment region.

 **Note:** A treatment record is automatically generated during the procedure, which is ended via the **End Treatment** button. Accessing this Record, or any saved images, is described in Section 6.8 Record Keeping.

**Step 13** The system places you back to the starting screen, **Patient Info**, where you may begin another treatment with a new patient. If treatments are finished or if you desire to review or print records from previous treatments tap the **Settings** tab. From this screen you may review records, images or tap **Shutdown** to turn OFF the system.

**Step 14** Follow cleaning and maintenance instructions in Section 8.0.

## 6.6. Adjunctive Functions

### 6.6.1. Distance Measurements

The Ulthera System allows you to make distance measurements on ultrasound images when the system is not in the active IMAGING state. Tap **Scan N** to stop scanning if necessary.

- Step 1** While you are on the DeepSEE Screen, tap the distance icon, **+ — +** button, in the IMAGING section. A starting point marker will appear near the center of the image.
- Step 2** Touch the screen and the marker will drag along above your finger. Once you have placed the starting point marker where you want then lift your finger off of the screen. At that point an ending point marker will appear, along with a line between the two points.
- Step 3** Touch the screen again to move the ending point marker where you wish to. When you lift your finger the straight line distance between the points will be displayed.
- Step 4** To place a second distance measurement on the screen tap the distance measurement button **+ — +** again, and repeat the above steps.

**Note:** To clear the first distance measurement, off of the screen tap the distance measurement button again, and then a second time if desired to delete the second distance measurement. In fact, tapping the distance measurement button cycles through distance measurements D1 and D2 in the order: *D1 (add), D2 (add), D1 (delete), D2 (delete), and then repeats.*

**Note:** When imaging is restarted by pressing the **Bus** button or **Scan Y** all distance measurements are deleted from the image.

### 6.6.2. Text Annotations

The Ulthera System allows you to add information such as comments atop ultrasound images when the system is not in the active IMAGING state. Tap **Scan N** to stop scanning if necessary.

- Step 1** While you are on the DeepSEE Screen, tap the TEXT button in the IMAGING section. A text box will appear near the center of the image and a keyboard will appear below the image.
- Step 2** Type any comments and/or move the text box where desired by tapping the screen – the box will track your finger.

**Step 3** Hit Enter on the keyboard when finished entering the desired comments and when the text box is in the desired position.



**Note:** Tapping the **Text** button cycles through text annotations Text1 and Text2 in the order: Text1 (add), Text2 (add), Text1 (delete), Text2 (delete), and then repeats.

## 6.7. Record Keeping

The Ulthera System uses a proprietary Ulthera Database for storing a limited number of images and treatment record information. These images are readily accessible to browse, or export to another storage device.

It is strongly recommended that you properly maintain the database by regularly exporting and/or deleting unused or old images and treatment records. Excessive numbers of records and images become difficult to search and maintain on a system primarily dedicated to patient treatment, and thereby reduce productivity and system performance.

The number of images and/or treatment records that can be stored is limited to 200. At startup, if more than that are stored, the user is asked to optionally delete some of them. If not, additional storage is disabled. However, if a procedure is already in progress as the system reaches its 200 mark additional records may be stored, the user will simply be asked to reduce the number of images and/or treatment records in the database the next time the system is started.



**Note:** All image compression methods used by Ulthera System are lossless. This produces small image file size without losing any image resolution or creating any image artifacts.

### 6.7.1. Saving Records in the Database

**Step 1** To save images in the database use the Save button on the DeepSEE tab to save the current display as a single image. Treatment records will automatically be saved assuming it has been set up as stated in Section 6.3 Setting Up a Treatment Record. For accessing images and/or treatment records at a later date see 6.8.3 and 6.8.4 respectively

### 6.7.2. Browsing the Database

**Step 1** Tap the **Settings** tab then tap on either **Records** (to view stored treatment data) or **Images** (to view scans). From here you can browse the data on screen, save to a USB thumb drive, or delete items.



**Note:** It is advisable to store records on an accessory device before deleting.

### 6.7.3. Exporting Images

**Step 1** On the **Settings** screen, tap **Images** to view the menu of treated patients. A screen similar to Figure 6.8. will appear.

**Step 2** Tap a specific **Patient ID** to call up the image stored for that patient or tap **Select All** to call up all stored images.

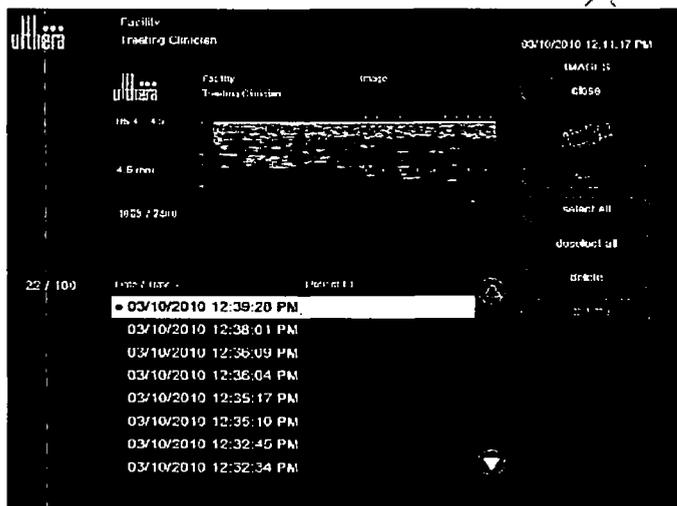


Figure 6.8. Image Export screen. Stored images are listed in the bottom dialog box and the most recently user selected image is displayed above it. If an external storage device is attached then SAVE is enabled.

**Note:** If you inadvertently selected an item or items, tap that item again or tap **Deselect All** to clear the selection(s).

**Step 3** Connect the generic USB storage device (as described in Section 5.4.3 Connecting Accessories).

- The icon for this appears on the right hand side of the screen; it will be grayed out if the accessory is disabled and will be displayed in white if enabled.

**Step 4** Tap **Save** to export image(s) to USB thumb drive

6.7.4. Exporting Records

**Step 1** On the **Settings** screen, tap **Records** to view the menu of treated patients. A screen similar to Figure 6.9. will appear.

**Step 2** Tap a specific **Patient ID** to call up the records stored for that patient or tap **Select All** to call up all stored records.

**Note:** If you inadvertently selected an item or items, tap that item again or tap **Deselect All** to clear the selection(s).

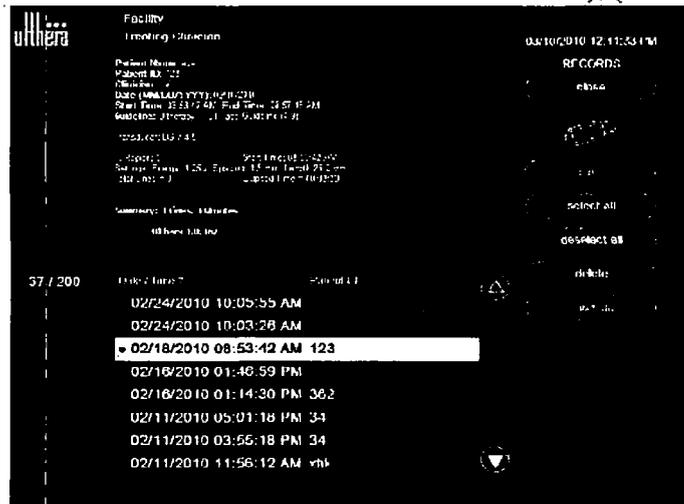


Figure 6.9 Treatment Records screen.

**Step 3** Connect the generic USB storage device (as described in Section 5.4.3 Connecting Accessories).

- The icon for this appears on the upper right hand side of the screen; it will be grayed out if the accessory is disabled and will be displayed in white if enabled.

**Step 4** Tap **Save** to export record(s) to USB thumb drive.

**Step 5** For the information to remain on the System after exporting the desired information tap **Close** to return to the Settings screen. To delete the information from the System after exporting it, see the next Section, 6 8 5.

### 6.7.5. Deleting Records from the Database



**Note:** It is advisable to store records on an accessory device before deleting information.

**Step 1** To remove one or more item(s) from the database, select the item(s) and tap **Delete**; to remove *all* items from the database, tap **Select All** and then tap **Delete All**.



**Note:** If you inadvertently delete an item or items, tap **Undelete** to restore the item(s).

Records in the **Undelete** dialogue may be permanently erased by selecting the items to be permanently erased and then tapping the **Erase** button.

**Step 2** Tap **Close** to return to the **Settings** screen.

### 6.7.6. Recovering Deleted Records/Images from the Database



**Note:** Only the 50 previously deleted records or images may be recovered.

**Step 1** To recover one or more of the 50 previously deleted records or images tap **Undelete**.

**Step 2** Select the images or records that you would like to undelete and tap **Undelete** once more.

The records or images will have now returned to the current database.

## 6.8. Troubleshooting

### 6.8.1. Ulthera System Warning and Caution Dialogs



**Warning:** These dialogs indicate that a problem was detected. See System Messages section for more details.

An example of a system warning appears in Figure 6.10. In such cases the user is given instructions on how to resolve the issue. Please follow the guidance to help solve the problem as quickly as possible and to provide proper information in case Technical Support is needed.

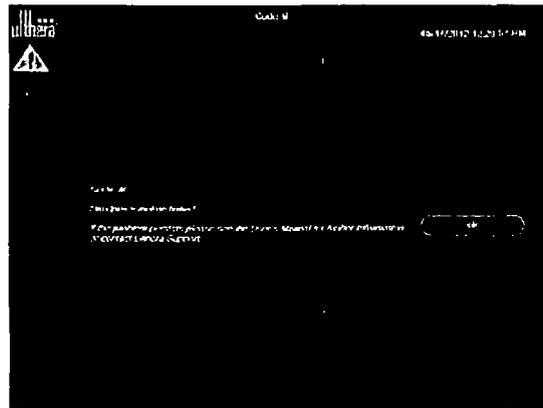


Figure 6.10 Example of System Caution Dialog

### 6.8.2. Unsatisfactory Image Quality

#### Action Required:

- Check that the display brightness is set appropriately for the transducer that is connected and the area being imaged via the **Display** controls.
- Check that enough gel is applied to the transducer.
- If the problem is not resolved, contact Ulthera, Inc. or your country representative for assistance.

### 6.9. Shutting Down the System

- Step 1** Stop any imaging and/or treatment in progress prior to shutting down the system
- Step 2** On the **Settings** screen, tap **Shutdown**
- Step 3** Remove the Ulthera System User Access Key to prevent unauthorized usage



**Note:** The main power switch on the rear panel of the control unit should be left in the ON position; however, it may be switched off when moving the system between rooms or for storage or cleaning.

## 7. System Messages

The Ulthera System is designed with internal checks to ensure that all aspects of the device are functioning appropriately. In the event that an information message presents itself during use, please follow the instructions on the screen or refer to the information listed below.

These messages are classified as INFORMATION SIGNALS per IEC 60601-1-8.

| Info Code | Message Displayed   | Description  |
|-----------|---|--|
| <b>B</b>  | <p>Code B</p> <p> Internal handpiece temperature is too high</p> <p>If the problem persists please see the User's Manual for further information or contact Ulthera Support.</p>   | The internal handpiece temperature is above its limit. Allow the handpiece to cool down.   |
| <b>C</b>  | <p>Code C</p> <p> Hardware halted</p> <p>Please restart the system.</p> <p>If the problem persists please see the User's Manual for further information or contact Ulthera Support.</p>                                  | Hardware was halted due to an event detected in the control unit.  |
| <b>E</b>  | <p>Code E</p> <p> Communication halted</p> <p>Please restart the system.</p> <p>If the problem persists please see the User's Manual for further information or contact Ulthera Support.</p>                             | Communication was halted due to an initialization event detected in the control unit.  |
| <b>G</b>  | <p>Code G</p> <p> Hardware halted</p> <p>Please restart the system.</p> <p>If the problem persists please see the User's Manual for further information or contact Ulthera Support.</p>                                | Hardware was halted due to an event detected in the control unit.  |
| <b>H</b>  | <p>Code H</p> <p> Transducer motion not detected</p> <p>Please remove and reinsert the transducer.</p> <p>If the problem persists please see the User's Manual for further information or contact Ulthera Support.</p> | Transducer motion was not detected. Ensure that the transducer is properly mounted in the handpiece. Please be sure to always hit Scan N before removing transducer. Remove and reinsert the transducer. |
| <b>I</b>  | <p>Code I</p> <p> Communication halted</p> <p>Please restart the system.</p> <p>If the problem persists please see the User's Manual for further information or contact Ulthera Support.</p>                           | Communication halted due to an event detected in the control unit.   |

| Info Code | Message Displayed  | Description  |
|-----------|--|--|
| J         | <p>Code J</p> <p> Handpiece communication halted</p> <p>Please restart the system.</p> <p>If the problem persists please see the User's Manual for further information or contact Ulthera Support.</p>          | Communication halted due to an event detected in the control unit.   |
| K         | <p>Code K</p> <p> Software halted</p> <p>Please restart the system.</p> <p>If the problem persists please see the User's Manual for further information or contact Ulthera Support.</p>                         | Software was halted due to an event detected in the control unit.  |
| L         | <p>Code L</p> <p> Transducer out of lines</p> <p>Please replace transducer and continue.</p> <p>See User's Manual for further information.</p>  | The Transducer's remaining line count is zero. Remove and replace the Transducer.  |
| M         | <p>Code M</p> <p> Handpiece motion halted</p> <p>If the problem persists please see the User's Manual for further information or contact Ulthera Support.</p>   | Inspect handpiece. Ensure that the transducer is properly mounted and latched in the handpiece.  |
| N         | <p>Code N</p> <p> USB flash memory connectivity</p> <p>Please check flash drive and continue.</p> <p>See User's Manual for further information.</p>   | A problem was detected with the attached USB flash memory drive. Make sure the drive is properly formatted and has enough free space. Do not remove the drive while the system is communicating with it. |
| P         | <p>Code P</p> <p> Hardware halted</p> <p>Please restart the system.</p> <p>If the problem persists please see the User's Manual for further information or contact Ulthera Support.</p>                       | Hardware was halted due to an event detected in the control unit.  |
| S         | <p>Code S</p> <p> The red STOP button has been pressed.</p> <p>Please restart the system.</p> <p>If the problem persists please see the User's Manual for further information or contact Ulthera Support.</p> | The red Stop button was pressed.   |
| T         | <p>Code T</p> <p> Internal transducer temperature is too high</p> <p>If the problem persists please see the User's Manual for further information or contact Ulthera Support.</p>                             | The internal transducer temperature is above its limit. Allow the transducer to cool down or use another transducer.   |
| U         | <p>Code U</p> <p> Control unit temperature too high</p> <p>If the problem persists please see the User's Manual for further information or contact Ulthera Support.</p>                                       | The internal control unit temperature is above its limit. Allow the control unit to cool down. Provide proper ventilation.   |

| Info Code | Message Displayed  | Description   |
|-----------|--|---|
| V         | <p>Code V</p> <p> Transducer energy delivery halted</p> <p>Tap Scan Y to resume scanning</p> <p>If the problem persists please see the User's Manual for further information or contact Ulthera Support.</p>      | <p>Excessive reflected power has been detected. If the problem persists, please try another transducer and contact Ulthera Support. Use Transducer only as instructed. Tap Scan Y to resume scanning.</p> |
| W         | <p>Code W</p> <p> Unauthorized transducer.</p> <p>Please replace the transducer and continue.</p> <p>Please contact your local representative for further assistance.</p>   | <p>The transducer connected is not an authorized transducer. Contact your local representative for further assistance.</p>  |
| X         | <p>Code X</p> <p> Transducer cannot be read</p> <p>Please remove and reinsert the transducer.</p> <p>If the problem persists please see the User's Manual for further information or contact Ulthera Support.</p> | <p>The transducer cannot be read. Remove and reinsert the transducer. Check that the transducer contact area is clean.</p>  |

PROPOSED DRAFT

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## 8. Cleaning and Care

### 8.1. Cleaning the Transducer and Handpiece



**Note:** Transducers are packaged and shipped non-sterile and ready to use.

Because the transducer will come in contact with the skin of a patient, the standard practice for cleaning and low level disinfection of transducers between patients is to gently but thoroughly wipe the transducers with a standard 70% isopropyl alcohol prep pad. One may also use a standard 70% isopropyl alcohol prep pad to gently wipe the handpiece and cable. Neither the transducers nor the handpiece should be submerged in liquid. Place the transducer back into its original packaging between uses.



**Warning:** Use only this procedure for cleaning. Do not use acetone or other solvents as this can damage the transducer.

### 8.2. General Care of the System

To get the best possible performance, treat the equipment carefully by adhering to the following guidelines:

1. Inspect the handpiece and connectors regularly for any problems.
2. Turn scanning off before changing transducers to ensure proper identification of transducers and to prolong the life of the system.
3. Do not drop the handpiece or transducers on the floor or other hard surfaces. This can cause permanent damage.
4. Do not twist or pull the transducer cables. This could cause damage to internal wires and connections.
5. Use aqueous ultrasound gel only. Other lubricants or lotions, particularly mineral oil, could eventually damage transducers or cables.
6. Do not use acoustic standoff pads or any objects between the transducer and patient.
7. Apply ultrasound gel only to the window of the transducer and wipe it from the transducer after completing a treatment. Avoid getting the gel on the handpiece or control unit.
8. Transducers should be cleaned between procedures. See cleaning procedure information immediately preceding this subsection.
9. Keep new transducers in sealed pouches until ready for use.

10. Place transducers back into original pouch and reseal for storage between procedures.
11. Do not hold the handpiece in a manner that can damage the chord or strain relief while removing or inserting transducers.



**Caution:** Always check the expiration date on the transducer before using.

PROPOSED DRAFT

## 9. Re-order Information

Please contact Ulthera, Inc. or your country representative to order transducers, accessories, or other items for your system.

| Description                               | Catalog/<br>Reorder Number |
|---|----------------------------|
| Ulthera Control Unit                      | UC-1                       |
| Ulthera® DeepSEE® Handpiece               | UH-2                       |
| Ulthera® DeepSEE® Transducer DS 7-3.0     | UT-1                       |
| Ulthera® DeepSEE® Transducer DS 7-3.0N    | UT-1N                      |
| Ulthera® DeepSEE® Transducer DS 4-4.5     | UT-2                       |
| Ulthera® DeepSEE® Transducer DS 7-4.5     | UT-3                       |
| Ulthera® DeepSEE® Transducer DS 10-1.5    | UT-4                       |
| Ulthera® DeepSEE® Transducer DS 10-1.5N   | UT-4N                      |
| Ulthera System Cart                       | UR-1                       |
| (Optional) Ulthera System Case            | US-1                       |
| (Optional) Ulthera System User Access Key | UK-1                       |
| (Optional) USB Storage Device             | UD-1                       |

## 10. Safety Standards and Regulatory Classifications

|   |
|---|
| FDA Product Classification 878.4590   |
| UL60601-1, IEC60601-1 Medical Electrical Equipments Part 1: General Requirements for Safety.                    |
| Class I device, type B applied part, non AP/APG rated.  |
| Ingress protection: IPx0 ("Ordinary Equipment") for Control Unit; IPx1 for mated transducer and handpiece.      |
| Mode of operation: Continuous.  |
| IEC60601-1-2, Electromagnetic Compatibility, CISPR 11 class A, Group 1.   |
| IEC60601-1-4, Programmable electrical medical systems   |
| IEC60601-2-37, Particular requirements for the safety of ultrasonic medical diagnostic and monitoring equipment |
| Patient contacting materials comply with ISO 10993-1  |
| NRTC Certification: Canadian Standards Association (CSA)  |
| ISO 13485 Quality Assurance Standard  |

# Appendix A – Treatment Guidelines

As displayed on the user interface and as notated in Tables A.1. & A.2. guidelines are set forth for the levels of energy, available transducer and the number of treatment lines to be delivered for each treatable region.

Table A.1. Treatment Guideline (5.0)

| Ultherapy – Guideline (5.0) |                     |            |                   |      |      |      |       |
|-----------------------------|---------------------|------------|-------------------|------|------|------|-------|
| Area                        | Region              | Transducer | Energy Levels [J] |      |      |      | Lines |
| Medial Neck                 | Medial Neck 4-4.5   | DS4-4.5    | 1.20              | 1.00 | 0.90 | 0.75 | 14    |
|                             | R Neck 4-4.5        | DS4-4.5    | 1.20              | 1.00 | 0.90 | 0.75 | 18    |
| Right Side<br>4.5           | R Cheek 4-4.5       | DS4-4.5    | 1.20              | 1.00 | 0.90 | 0.75 | 55    |
|                             | R Brow 7-4.5        | DS7-4.5    | 1.05              | 0.90 | 0.75 | 0.66 | 10    |
|                             | R Orbit 7-4.5       | DS7-4.5    | 1.05              | 0.90 | 0.75 | 0.66 | 10    |
| Medial Neck                 | Medial Neck 7-3.0   | DS7-3.0    | 0.45              | 0.35 | 0.30 | 0.25 | 14    |
| Right Side<br>3.0           | R Neck 7-3.0        | DS7-3.0    | 0.45              | 0.35 | 0.30 | 0.25 | 18    |
|                             | R Cheek 7-3.0       | DS7-3.0    | 0.45              | 0.35 | 0.30 | 0.25 | 40    |
|                             | R Brow 7-3.0        | DS7-3.0    | 0.45              | 0.35 | 0.30 | 0.25 | 10    |
|                             | R Orbit 7-3.0       | DS7-3.0    | 0.45              | 0.35 | 0.30 | 0.25 | 10    |
|                             | R Infraorbital 3.0N | DS7-3.0N   | 0.45              | 0.35 | 0.30 | 0.25 | 9     |
| Left Side<br>4.5            | L Neck 4-4.5        | DS4-4.5    | 1.20              | 1.00 | 0.90 | 0.75 | 18    |
|                             | L Cheek 4-4.5       | DS4-4.5    | 1.20              | 1.00 | 0.90 | 0.75 | 55    |
|                             | L Brow 7-4.5        | DS7-4.5    | 1.05              | 0.90 | 0.75 | 0.66 | 10    |
|                             | L Orbit 7-4.5       | DS7-4.5    | 1.05              | 0.90 | 0.75 | 0.66 | 10    |
| Left Side<br>3.0            | L Neck 7-3.0        | DS7-3.0    | 0.45              | 0.35 | 0.30 | 0.25 | 18    |
|                             | L Cheek 7-3.0       | DS7-3.0    | 0.45              | 0.35 | 0.30 | 0.25 | 40    |
|                             | L Brow 7-3.0        | DS7-3.0    | 0.45              | 0.35 | 0.30 | 0.25 | 10    |
|                             | L Orbit 7-3.0       | DS7-3.0    | 0.45              | 0.35 | 0.30 | 0.25 | 10    |
|                             | L Infraorbital 3.0N | DS7-3.0    | 0.45              | 0.35 | 0.30 | 0.25 | 9     |
| Right Side<br>1.5           | R Cheek             | DS10-1.5   | 0.25              | 0.20 | 0.18 | 0.15 | 75    |
|                             | R Brow              | DS10-1.5   | 0.25              | 0.20 | 0.18 | 0.15 | 15    |
|                             | R Orbit 10-1.5      | DS10-1.5   | 0.25              | 0.20 | 0.18 | 0.15 | 15    |
|                             | R Infraorbital 1.5  | DS10-1.5   | 0.25              | 0.20 | 0.18 | 0.15 | 15    |
|                             | R Infraorbital 1.5N | DS10-1.5N  | 0.25              | 0.20 | 0.18 | 0.15 | 15    |
|                             | R Oral 1.5          | DS10-1.5   | 0.25              | 0.20 | 0.18 | 0.15 | 25    |
| Left Side<br>1.5            | L Cheek             | DS10-1.5   | 0.25              | 0.20 | 0.18 | 0.15 | 75    |
|                             | L Brow              | DS10-1.5   | 0.25              | 0.20 | 0.18 | 0.15 | 15    |

|               |                     |            |      |      |      |      |    |
|---------------|---------------------|------------|------|------|------|------|----|
|               | L Orbit 10-1.5      | DS 10-1.5  | 0.25 | 0.20 | 0.18 | 0.15 | 15 |
|               | L Infraorbital 1.5  | DS 10-1.5  | 0.25 | 0.20 | 0.18 | 0.15 | 15 |
|               | L Infraorbital 1.5N | DS 10-1.5N | 0.25 | 0.20 | 0.18 | 0.15 | 15 |
|               | L Oral 1.5          | DS 10-1.5  | 0.25 | 0.20 | 0.18 | 0.15 | 25 |
|               | L Oral 1.5N         | DS 10-1.5N | 0.25 | 0.20 | 0.18 | 0.15 | 25 |
| Medial Option | Medial Neck 7-4.5   | DS 7-4.5   | 1.05 | 0.90 | 0.75 | 0.66 | 14 |
| Right Option  | R Neck 7-4.5        | DS 7-4.5   | 1.05 | 0.90 | 0.75 | 0.66 | 18 |
|               | R Cheek 7-4.5       | DS 7-4.5   | 1.05 | 0.90 | 0.75 | 0.66 | 55 |
|               | R Brow 7-3.0N       | DS 7-3.0N  | 0.45 | 0.35 | 0.30 | 0.25 | 10 |
|               | R Orbit 7-3.0N      | DS 7-3.0N  | 0.45 | 0.35 | 0.30 | 0.25 | 10 |
|               | R Infraorbital 3.0  | DS 7-3.0   | 0.45 | 0.35 | 0.30 | 0.25 | 9  |
| Left Option   | L Neck 7-4.5        | DS 7-4.5   | 1.05 | 0.90 | 0.75 | 0.66 | 18 |
|               | L Cheek 7-4.5       | DS 7-4.5   | 1.05 | 0.90 | 0.75 | 0.66 | 55 |
|               | L Brow 7-3.0N       | DS 7-3.0N  | 0.45 | 0.35 | 0.30 | 0.25 | 10 |
|               | L Orbit 7-3.0N      | DS 7-3.0N  | 0.45 | 0.35 | 0.30 | 0.25 | 10 |
|               | L Infraorbital 3.0  | DS 7-3.0   | 0.45 | 0.35 | 0.30 | 0.25 | 9  |

Table A.2. Treatment Guideline (5.0 PLUS)

| Ultherapy – Guideline (5.0 PLUS) |                     |            |                   |      |      |      |       |
|----------------------------------|---------------------|------------|-------------------|------|------|------|-------|
| Area                             | Region              | Transducer | Energy Levels [J] |      |      |      | Lines |
| Medial Neck                      | Medial Neck 4-4.5   | DS 4-4.5   | 1.20              | 1.00 | 0.90 | 0.75 | 18    |
| Right Side<br>4.5                | R Neck 4-4.5        | DS 4-4.5   | 1.20              | 1.00 | 0.90 | 0.75 | 26    |
|                                  | R Cheek 4-4.5       | DS 4-4.5   | 1.20              | 1.00 | 0.90 | 0.75 | 77    |
|                                  | R Brow 7-4.5        | DS 7-4.5   | 1.05              | 0.90 | 0.75 | 0.66 | 10    |
|                                  | R Orbit 7-4.5       | DS 7-4.5   | 1.05              | 0.90 | 0.75 | 0.66 | 10    |
| Medial Neck                      | Medial Neck 7-3.0   | DS 7-3.0   | 0.45              | 0.35 | 0.30 | 0.25 | 18    |
| Right Side<br>3.0                | R Neck 7-3.0        | DS 7-3.0   | 0.45              | 0.35 | 0.30 | 0.25 | 26    |
|                                  | R Cheek 7-3.0       | DS 7-3.0   | 0.45              | 0.35 | 0.30 | 0.25 | 56    |
|                                  | R Brow 7-3.0        | DS 7-3.0   | 0.45              | 0.35 | 0.30 | 0.25 | 10    |
|                                  | R Orbit 7-3.0       | DS 7-3.0   | 0.45              | 0.35 | 0.30 | 0.25 | 10    |
|                                  | R Infraorbital 3.0N | DS 7-3.0N  | 0.45              | 0.35 | 0.30 | 0.25 | 9     |
| Left Side<br>4.5                 | L Neck 4-4.5        | DS 4-4.5   | 1.20              | 1.00 | 0.90 | 0.75 | 26    |
|                                  | L Cheek 4-4.5       | DS 4-4.5   | 1.20              | 1.00 | 0.90 | 0.75 | 77    |
|                                  | L Brow 7-4.5        | DS 7-4.5   | 1.05              | 0.90 | 0.75 | 0.66 | 10    |
|                                  | L Orbit 7-4.5       | DS 7-4.5   | 1.05              | 0.90 | 0.75 | 0.66 | 10    |
| Left Side<br>3.0                 | L Neck 7-3.0        | DS 7-3.0   | 0.45              | 0.35 | 0.30 | 0.25 | 26    |
|                                  | L Cheek 7-3.0       | DS 7-3.0   | 0.45              | 0.35 | 0.30 | 0.25 | 56    |
|                                  | L Brow 7-3.0        | DS 7-3.0   | 0.45              | 0.35 | 0.30 | 0.25 | 10    |
|                                  | L Orbit 7-3.0       | DS 7-3.0   | 0.45              | 0.35 | 0.30 | 0.25 | 10    |

|                   |                     |             |      |      |      |      |    |
|-------------------|---------------------|-------------|------|------|------|------|----|
|                   | L Infraorbital 3.0N | DS 7 - 3.0N | 0.45 | 0.35 | 0.30 | 0.25 | 9  |
| Right Side<br>1.5 | R Check             | DS 10-1.5   | 0.25 | 0.20 | 0.18 | 0.15 | 75 |
|                   | R Brow              | DS 10-1.5   | 0.25 | 0.20 | 0.18 | 0.15 | 15 |
|                   | R Orbit 10-1.5      | DS 10-1.5   | 0.25 | 0.20 | 0.18 | 0.15 | 15 |
|                   | R Infraorbital 1.5  | DS 10-1.5   | 0.25 | 0.20 | 0.18 | 0.15 | 15 |
|                   | R Infraorbital 1.5N | DS 10-1.5N  | 0.25 | 0.20 | 0.18 | 0.15 | 15 |
|                   | R Oral 1.5          | DS 10-1.5   | 0.25 | 0.20 | 0.18 | 0.15 | 25 |
|                   | R Oral 1.5N         | DS 10-1.5N  | 0.25 | 0.20 | 0.18 | 0.15 | 25 |
| Left Side<br>1.5  | L Check             | DS 10-1.5   | 0.25 | 0.20 | 0.18 | 0.15 | 75 |
|                   | L Brow              | DS 10-1.5   | 0.25 | 0.20 | 0.18 | 0.15 | 15 |
|                   | L Orbit 10-1.5      | DS 10-1.5   | 0.25 | 0.20 | 0.18 | 0.15 | 15 |
|                   | L Infraorbital 1.5  | DS 10-1.5   | 0.25 | 0.20 | 0.18 | 0.15 | 15 |
|                   | L Infraorbital 1.5N | DS 10-1.5N  | 0.25 | 0.20 | 0.18 | 0.15 | 15 |
|                   | L Oral 1.5          | DS 10-1.5   | 0.25 | 0.20 | 0.18 | 0.15 | 25 |
|                   | L Oral 1.5N         | DS 10-1.5N  | 0.25 | 0.20 | 0.18 | 0.15 | 25 |
| Medial<br>Option  | Medial Neck 7-4.5   | DS 7-4.5    | 1.05 | 0.90 | 0.75 | 0.66 | 18 |
| Right<br>Option   | R Neck 7-4.5        | DS 7-4.5    | 1.05 | 0.90 | 0.75 | 0.66 | 26 |
|                   | R Check 7-4.5       | DS 7-4.5    | 1.05 | 0.90 | 0.75 | 0.66 | 77 |
|                   | R Brow 7-3.0N       | DS 7 - 3.0N | 0.45 | 0.35 | 0.30 | 0.25 | 10 |
|                   | R Orbit 7-3.0N      | DS 7 - 3.0N | 0.45 | 0.35 | 0.30 | 0.25 | 10 |
|                   | R Infraorbital 3.0  | DS 7 - 3.0  | 0.45 | 0.35 | 0.30 | 0.25 | 9  |
| Left Option       | L Neck 7-4.5        | DS 7-4.5    | 1.05 | 0.90 | 0.75 | 0.66 | 26 |
|                   | L Check 7-4.5       | DS 7-4.5    | 1.05 | 0.90 | 0.75 | 0.66 | 77 |
|                   | L Brow 7-3.0N       | DS 7 - 3.0N | 0.45 | 0.35 | 0.30 | 0.25 | 10 |
|                   | L Orbit 7-3.0N      | DS 7 - 3.0N | 0.45 | 0.35 | 0.30 | 0.25 | 10 |
|                   | L Infraorbital 3.0  | DS 7 - 3.0  | 0.45 | 0.35 | 0.30 | 0.25 | 9  |

PRO

**Appendix 2: Overview of Previous Clinical Testing from  
K072505**

## Overview of Previous Clinical Studies

Two previous clinical studies have been conducted using the Ulthera® System: 1) a clinical safety study at MEEI (Protocol Number 05-06-032); 2) a pivotal study at Northwestern University in Chicago (Protocol Number 1253-014, IDE G060261). During these studies, in which the Ulthera® System was extensively used, safe and efficacious energy delivery protocols were established.

This section of the 510(k) submission provides only a brief overview of the previous clinical testing of the Ulthera® System because Ulthera provided this information in detail in its previous cleared premarket notification (K072505). Previous studies have demonstrated that the Ulthera® System has a significant safety profile and is safe for the device's expanded use indication. This information is available via cross-reference to K072505.

### 1.0 Summary of Human Safety Study (MEEI, Boston)

This open-label, prospective, pilot phase-I clinical trial was conducted to evaluate the clinical safety of the Ulthera® System in the treatment of the dermis and subcutaneous tissues in the face and neck with regard to skin inflammation, pain, adverse events, and histology. Study subjects scheduled to undergo a limited rhytidectomy (mini-facelift) procedure were enrolled, and tissue that had been treated with the Ulthera® System was removed during the rhytidectomy and submitted for histopathology.

#### 1.1 Study Summary

- Fifteen subjects were treated
- Seven subjects underwent facelift surgery within 24 hours of treatment
- Eight subjects underwent facelift surgery 4 to 12 weeks after treatment
- The pre-auricular area was exposed to more than 1,300 ultrasound pulses
- Three transducer types were used
- No epidermal disruption was observed
- No adverse responses were reported
- No delayed sequelae in the treated skin occurred

#### 1.2 Study Objective

The objectives of this study were to confirm that the Ulthera® System creates controlled thermal coagulation zones in the dermis, while sparing the epidermis, and to evaluate the effects of different doses of energy with regard to pain, inflammation, and visual changes on facial skin.

#### 1.3 Conclusions

In this first human clinical study with the Ulthera® System to treat facial-tissue, the device provided safe and well-tolerated delivery of thermal coagulation to precise and consistent regions in the dermis and subcutaneous tissues while sparing the epidermis.

## 2.0 Summary of Face-Neck Study (Northwestern University, Chicago)

This open-label clinical trial was conducted to establish the safety and efficacy of the Ulthera<sup>®</sup> System for non-invasive treatment to achieve eyebrow elevation resulting from tissue coagulation and tightening in patients with all skin types (Fitzpatrick I – VI).

### 2.1 Study Summary

- Thirty-five subjects were treated.
- Three transducer types were used.
- No epidermal disruption was observed.
- No adverse events were reported through the follow-up period (minimum of 90 days).
- There was no evidence of skin hyper- or hypo-pigmentation in patients up to 10 months post-treatment.
- Twenty-four subjects completed a patient satisfaction questionnaire at 8 to 10 months post-treatment and 75% of them were either satisfied or very satisfied with the improvement in their eyebrow position.
- The cumulative result of the three masked reviewers was an 85.7% “Improved” evaluation for all 35 subjects.

### 2.2 Study Objective

The objective of this study was to demonstrate that the Ulthera<sup>®</sup> System can be safely used on the face and neck in a clinical setting and achieve a clinically significant cosmetic effect of eyebrow elevation.

### 2.3 Conclusion

This clinical study demonstrated that the Ulthera<sup>®</sup> System can provide safe and efficacious delivery of ultrasound energy. The thermal coagulative tissue effect in skin resulted in clinically significant improvement in eyebrow position in a majority of subjects. The data support the intended use of the system for non-invasive dermatological treatment to produce eyebrow lift through tissue coagulation and tightening; and imaging of skin and sub-dermal tissue.

**Appendix 3: Facial Anatomical Articles**

# Essentials of ORTHOGNATHIC Surgery

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To my wife, Ingrid, and children, Johan and Mignon

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## Esthetic Facial Evaluation

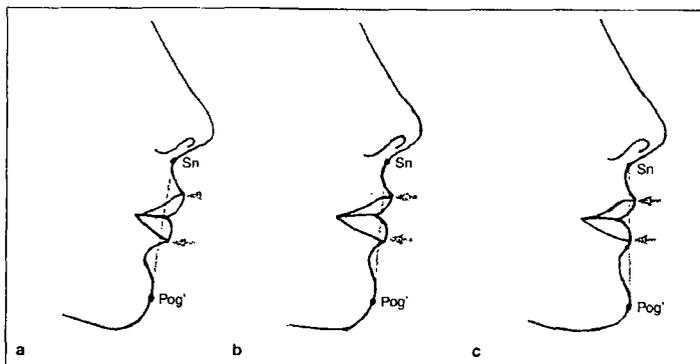


Fig 2-27 Effect of the chin position on the subnasale-pogonion line (Sn-Pog'). (a) Effect in an individual with mandibular anteroposterior deficiency (lips ahead of the line). (b) With the chin in normal horizontal relationship to the maxilla, the upper lip should be 5.5 mm and the lower lip 2.5 mm ahead of Sn-Pog'. (c) Effect in an individual with mandibular prognathism (lips on the line). In all three cases, the upper lip position has not changed; however, a change in Pog' position results in a change in the lip position relative to the Sn-Pog' line.

### Lower third of the face

A systematic examination of the lower third of the face includes evaluation of the lips, labiomental fold, nasolabial angle, chin, and chin-throat area.

#### Lips

The protrusion, retrusion, and soft tissue thickness of each lip is evaluated with the lips in repose. The upper lip usually projects slightly anterior to the lower lip. The lips' positions relate to the underlying dental position, such as maxillary dental protrusion or lack of upper lip support caused by, for example, Class II, division 2 malocclusion or excessive orthodontic retraction of maxillary incisors. An individual with an excessive increase in lower lip vermilion and a deep labiomental fold often also has a Class II, division 1 malocclusion.

The anteroposterior lip position may be assessed with the help of the E-line or S-line as guidelines (see the following sections on cephalometrics). The subnasale-pogonion line, also called the *lower facial plane*, is an impor-

tant guide in assessing the lip position and planning orthodontic and surgical positioning of the incisors, as well as surgical positioning of the chin. The upper lip should be  $3 \pm 1$  mm ahead of this line and the lower lip  $2 \pm 1$  mm ahead of this line. Extractions followed by retraction of incisors behind the subnasale-pogonion line should be avoided. Keep in mind that this assessment is influenced by the anteroposterior position of the chin and the soft tissue thickness of the lips (Fig 2-27).

#### Labiomental fold

The lower lip-chin contour should have a gentle S-curve, with a lower lip-chin angle of at least 130 degrees (Fig 2-28). The angle is often acute in cases of Class II mandibular anteroposterior deficiency because of impingement of the maxillary incisor on the lower lip or macrogenia. The angle is flattened in individuals with microgenia or lower lip tension caused by Class III malocclusion. The surgeon considering genioplasty should assess not only the anteroposterior position of the pogonion but also the chin shape and the labiomental fold.

## 2 | Systematic Patient Evaluation

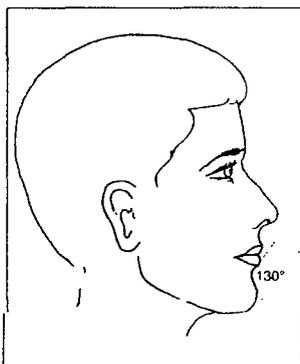


Fig 2-28 Labiomental fold.

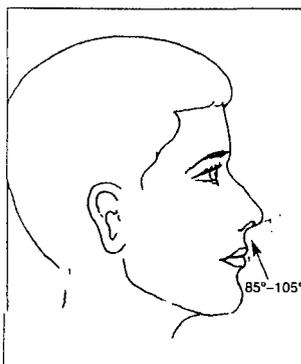


Fig 2-29 The nasolabial angle, measured between the columella of the nose and the upper lip (Sn-Ls), should be 85 to 105 degrees.

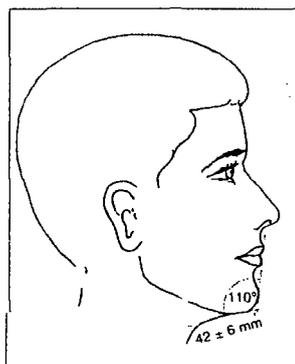


Fig 2-30 Chin-throat angle and length.

**Nasolabial angle**

The nasolabial angle, which is measured between the inclination of the columella and the upper lip (Fig 2-29), should be in the range of 85 to 105 degrees. In females a slightly larger angle is acceptable, while a smaller angle is considered esthetically pleasing in males. Patients with mandibular anteroposterior deficiency have increased nasolabial angles, while this angle is usually acute in individuals with Class III relations. Surgical or orthodontic retraction of maxillary incisors should be avoided in individuals with large nasolabial angles. Where crowding necessitates tooth extraction, the nasolabial angle should influence the decision to extract first versus second premolars. Surgical repositioning of the maxilla also affects the nasolabial angle. In general, the maxilla should never be moved posteriorly, especially in combination with superior repositioning. This surgical movement leads to loss of lip support, increase in nasolabial angle, increase in nasal projection, and flattening of the nasal base. These changes result in poor esthetics and a premature aging effect. The maxilla should be moved posteriorly only in individuals with true maxillary protrusion, which occurs very rarely.

**Chin**

Chin projection should be in good balance with the entire profile. At this stage, the middle third should be masked and the chin's relation to the rest of the facial structures evaluated. Various soft tissue cephalometric analyses are available to assist in clinical evaluation of the anteroposterior chin position. The chin should, however, be evaluated in all three dimensions. The width of the chin should be assessed in relation to the overall facial shape. A narrow chin often has a knobby appearance, and if surgical advancement of the chin is planned, widening of the chin should be contemplated. The labiomental fold, chin shape, relation to the dental midline, symmetry, and cant of the lower border should be considered.

**Chin-throat area**

The presence of a "double" chin and adipose tissue should be noted. The chin-throat angle (normally 110 degrees) provides chin definition (Fig 2-30). The distance from the neck-throat angle to the soft tissue pogonion should be approximately 42 mm. These observations are pertinent when considering mandibular setback or advancement procedures, genioplasty (advancement or reduction), or submental liposuction.

## 2 | Systematic Patient Evaluation

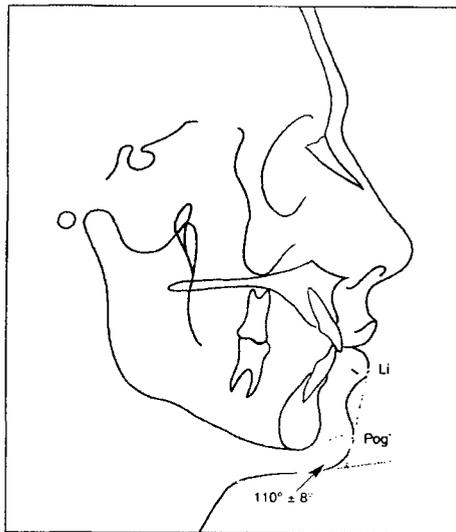


Fig 2-40 Lower lip-chin-throat angle.

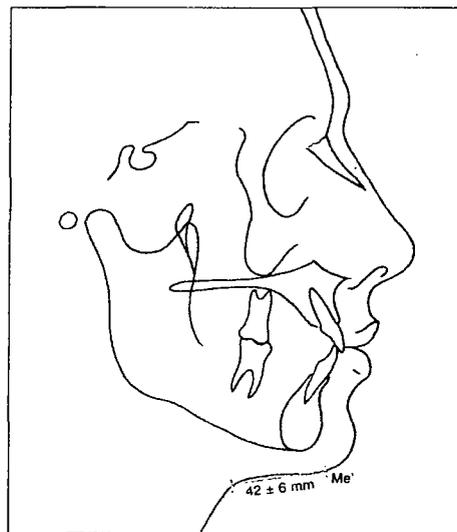


Fig 2-41 Chin-throat length.

**Lower lip-chin-throat angle**

The lower lip-chin-throat angle is contained between a line drawn from Li to Pog' and a submental tangent line. An angulation of  $110 \pm 8$  degrees is considered normal. For this assessment, the radiograph must be taken in natural head posture (Fig 2-40).

This angle will be more acute in patients with mandibular anteroposterior excess and/or macrogenia. It will be more obtuse in cases of mandibular anteroposterior deficiency and/or microgenia.

**Chin-throat length**

The chin-throat length is measured from the angle of the throat to Me' (Fig 2-41). A distance of  $42 \pm 6$  mm is considered normal. This measurement is only meaningful with the patient's head in natural posture.

The distance will be excessive in individuals with mandibular prognathism and short in mandibular recessive cases. This measurement is significant in differentiating between mandibular

anteroposterior excess and maxillary deficiency. Mandibular setback would obviously reduce this length.

**Facial contour angle**

The angle of facial convexity is formed by lines drawn from G' to Sn and from Sn through Pog'. The line from G' to Sn is also called the *upper facial plane* (UFP), while the lower facial plane (LFP) is formed by the line from Sn to Pog'. The mean angulation is estimated to be  $-12$  degrees. A clockwise angle is expressed as positive, while a counterclockwise angle is negative. Males tend to have a straighter profile ( $-11 \pm 4$  degrees), while a slightly more convex profile is considered esthetically pleasing for females ( $-13 \pm 4$  degrees) (Fig 2-42). It is important, however, to differentiate among the various facial deformities that may produce the same facial contour angle. The measurement of the angle does not reveal the localization of the deformity.

In Fig 2-43, both individuals have normal anteroposterior relations according to the facial con-

## Lateral Cephalometric Radiographic Evaluation

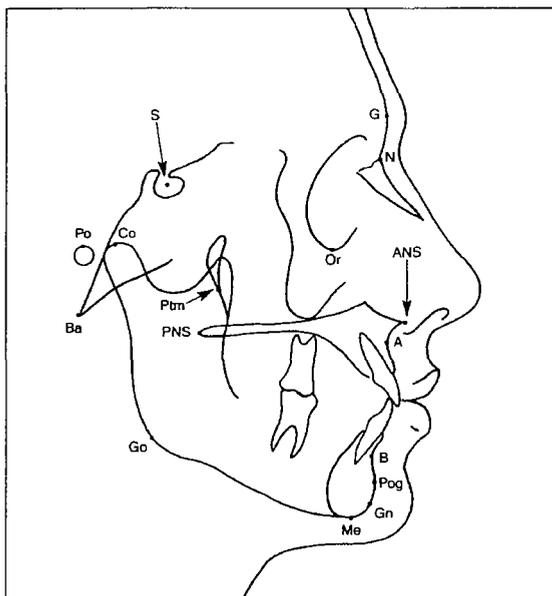


Fig 2-50 Hard tissue cephalometric landmarks

**Skeletal analysis****Hard tissue landmarks**

Hard tissue landmarks, shown in Fig 2-50, include the following:

- Glabella (G):** The most anterior point of the frontal bone
- Nasion (N):** The most anterior point on the frontal nasal suture in the midsagittal plane
- Orbitale (Or):** The lowest point on the inferior orbital rim
- Sella (S):** The center of the sella turcica, as on the lateral cephalogram, which is located by inspection
- Pterygomaxillare (Ptm):** The apex of the teardrop-shaped pterygomaxillary fissure (lowest point of the opening)
- Basion (Ba):** The point where the median sagittal plane of the skull intersects the lowest

point in the anterior margin of the foramen magnum

**Anterior nasal spine (ANS):** Anterior tip of the nasal spine

**Posterior nasal spine (PNS):** The most posterior aspect of the palatal bone

**A-point, or subspinale:** The most posterior midline point in the concavity where the lower anterior edge of the anterior nasal spine meets the alveolar bone overlying the maxillary incisors

**B-point, or supramentale:** The most posterior midline point in the concavity of the mandible between the alveolar bone overlying the mandibular incisors (infradentale) and the pogonion

**Pogonion (Pog):** The most anterior point of the chin

**Gonion (Go):** The point defined by using two lines, one tangent to the inferior border of the mandible and the other tangent to the posterior border of the ramus; found by bi-

## 2 | Systematic Patient Evaluation

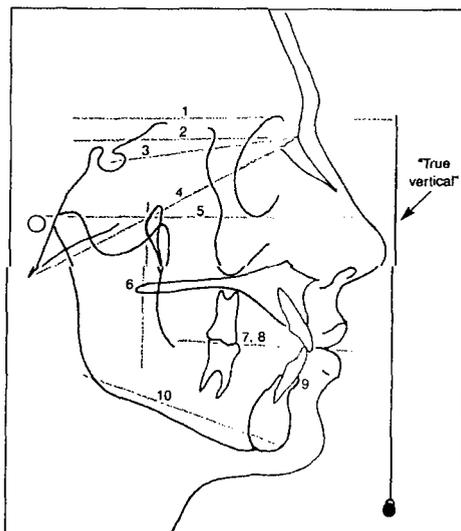


Fig 2-51 Hard tissue planes. (1) "True horizontal" plane (HP). (2) Constructed horizontal plane (cHP). (3) Anterior cranial base (S-N). (4) Basion-nasion (Ba-N) plane. (5) Frankfort horizontal (FH) plane. (6) Pterygoid vertical (Ptv). (7) Functional occlusal plane. (8) Occlusal plane. (9) Dental plane (A-Pog). (10) Mandibular plane (Go-Gn).

secting the angle formed by the two lines and extending the bisector through the curvature of the mandible

**Gnathion (Gn):** The lowest, most anterior midline point on the symphysis of the mandible (midway between the menton and the pogonion)

**Menton (Me):** The most inferior point on the symphysis of the mandible in the midline

**Porion (Po):** The most superior point of the external auditory meatus (anatomic point); the machine porion is the uppermost point on the outline of the rods of the cephalometer

**Condylion (Co):** The most posterosuperior point on the head of the condyle

### Hard tissue planes

Hard tissue planes, shown in Fig 2-51, include the following:

**"True horizontal" plane (HP):** A line perpendicular to a plumb line on the radiograph will be the HP for a specific patient.

**Constructed horizontal plane (cHP):** A horizontal

plane constructed by drawing a line through nasion at an angle of 7 degrees to S-N (see point 2 in Fig 2-51). This plane tends to be close to true horizontal.

**Anterior cranial base (S-N):** Formed by a line drawn from sella to nasion

**Basion-nasion (Ba-N) plane:** Extends between basion and nasion and divides the face and the cranium

**Frankfort horizontal (FH) plane:** Extends from porion to orbitale

**Pterygoid vertical (Ptv):** A vertical line perpendicular to the Frankfort horizontal plane and drawn through the distal outline of the pterygomaxillary fissure

**Functional occlusal plane:** A line through the cusp contacts of the molars and premolars defines this plane

**Occlusal plane:** Formed by a line drawn through the mesial cusp contact of the molars and dividing the incisor overbite

**Dental plane:** Extends between A-point and pogonion

**Mandibular plane:** Extends from gonion to gnathion

# 11 Aesthetic Facial Proportions

Marion B. Ridley and Steven M. VanHook

During every recorded age of history, and undoubtedly even earlier, humankind has sought to define and measure beauty and thereby be enabled to create it. Indeed, it has been stated that the prime requisites of a civilization are intellectual energy, freedom of the mind, and a sense of beauty.<sup>1</sup> *Aesthetic* is derived from the Greek word *aisthesis*, which means having a sense or love of that which is beautiful. Individuals have unique perspectives on aesthetics that are related to their personalities and environmental milieu.<sup>2</sup> Thus no two people would likely describe their concept of beauty in exactly the same way. Although a universal canon of beauty cannot be established because of differences in time, culture, ethnicity, and age, there are found proportion and harmony among the parts of certain faces, which confer on the whole a timeless beauty.<sup>3</sup>

Defining an ideal beauty has been an elusive, unattainable goal of every civilization. In interpreting the definition of ideal beauty from civilizations past, we are limited in the resources available. Often we are left to interpret the most popular artistic creations of the time and assume that this is how society felt beauty should be portrayed. At other times, we are able to read the historical record and writings about the subject from the people of those eras. The people of ancient Greece attempted to describe beauty through the perfection of the mind and body in an ordered universe. Their civilization focused on art, literature, and politics, while also valuing the value of beauty in society. There were rewards for those of society with beauty, and often people were referred to with names that described specific aspects of their beauty.<sup>4</sup> Attempts were made to define beauty through mathematical equations and geometric formulas (i.e., laws by which much of nature seemed to abide).<sup>5</sup> The Athenian philosopher Plato stated that "the qualities of measure and proportion invariably constitute beauty and excellence." He wrote that there are three wishes of every man: to be healthy, to be rich by honest means, and to be beautiful. Although Plato started defining beauty in terms of mathematics, he also realized that beyond physical proportions, beauty was also the result of good taste and balance.

## History of Beauty in Art

Several other Greek figures played important roles in helping to define ideal beauty. Polyclitus developed a canon of proportions in the fifth century BC that he felt

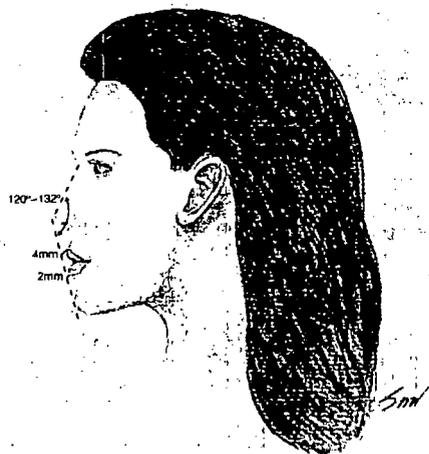
produced a figure with a flawless body. He experimented with proportions taken from nature and from those proportions created figures appearing more aesthetically pleasing to onlookers. Even more influential in the development of an ideal beauty was the Greek sculptor Praxiteles. His work in the fourth century BC led to a depiction of ideal beauty that held for the next 100 years.<sup>4</sup> He sculpted the figure of Aphrodite, the goddess of love, in what is considered the first completely nude image of the goddess created. In his interpretation he crafted a female figure that appeared much more gentle than previous sculptures, in which females seemed more like males with breasts attached to their chests.<sup>6</sup> His Aphrodite showed human expression, and this figure, modeled after a well-known woman of his society, was to be imitated and revered for many years.

In the first century BC the Roman architect Marcus Vitruvius Pollio wrote that the proportions of humans should be used when creating sacred buildings. He reasoned that the human body is a model of perfect proportions; thus architecture would benefit if buildings were modeled on nature. He described the proportions of humans who he felt created the most ideal figure. He also attempted the task of trying to contain the human figure within a circle and square by having the figure with arms and legs extended (later to be referred to as the Vitruvian man). Although his work was not appreciated in his time, he provided a great influence for several of the Italian Renaissance painters.

The late fourteenth century through the middle of the sixteenth century in western Europe was referred to as the Renaissance period. During this time there was a renewed interest in ancient Greece, and the ideals of classic beauty reappeared. Women were starting to receive formal education and were attaining some increased degree of independence. People were also regarding female intelligence as compatible with beauty.<sup>4</sup> This increased reverence for women was also met with new advances in artistic techniques. Masaccio (1401–1428) developed the artistic technique of perspective, allowing the creation of figures that appeared more realistic and human.<sup>6</sup> Artists during this time found that copying beauty was no longer the goal; they wanted to *perfect* beauty. Female faces would often be created with the combination of various features from different models.<sup>4</sup>

Leonardo da Vinci (1452–1519) devised a new version of the Vitruvian man and developed an obsession with the infinity of geometric transformation as exhibited by his

## 130 | Principles of Facial Plastic and Reconstructive Surgery



**Fig. 11.18** The nasomental angle is formed by the intersection of the line of the nasal dorsum and the nasomental line. The upper lip should fall 4 mm posterior to this line and the lower lip 2 mm behind it.

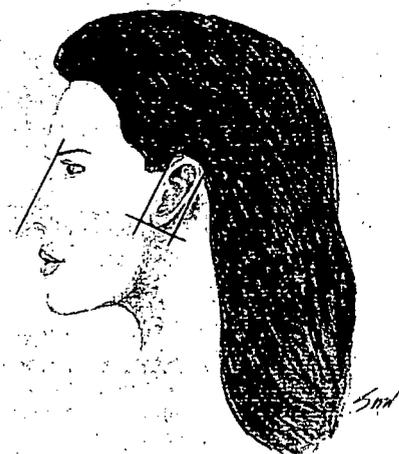
A second method of assessing horizontal lip position is to construct a line between the nasal tip (T) and the pogonion (Pg) termed the nasomental line (Fig. 11.18). The lips should lie posterior to this line. The lower lip ideally falls 2 mm posterior to this line and upper lip 4 mm behind it. This concept was described by Ricketts as the E-line and has been incorporated into the aesthetic triangle by Powell and Humphreys.<sup>20</sup>

### Chin

The chin is the aesthetic unit that confers strength to the face. The anterior limit is at a vertical dropped from the brow. For the chin to have pleasing form it must be well defined from both frontal and lateral views without appearing knoblike.<sup>19</sup> There should be a definite, but gentle, mentolabial sulcus separating the cutaneous lower lip from the chin.

The chin is included in measurement of the lower portion of the face (Sn to Me), as well as being part of the length of the lower lip (to Me). The lower lip and chin compose two thirds of the lower portion of the face.

When measured from a line drawn between the vermilion border of the lower lip (labrale inferius, LI) to the pogonion (Pg), the deepest point of the mentolabial sulcus (Si) should lie 4 mm behind this line (Fig. 11.17).



**Fig. 11.19** The long axis of the ear is parallel to the line of the nasal dorsum. Ear width should be 55 to 60% of its length.

### Ears

An additional facial feature to be considered is the ear. This flaplike, cartilaginous appendage has multiple convolutions and is attached to the scalp approximately one ear length posterior to the lateral brow. The superior aspect of the ear is at the level of the brow, and its inferior aspect is at the level of the ala nasi.

The width of the ear is 55 to 60% of its length. The line of the posterior aspect of the auricle roughly parallels the dorsal plane of the nose.<sup>28</sup> The long axis of the ear is posteriorly rotated 15 degrees from the vertical plane (Fig. 11.19). The auricle produces an angle of 20 degrees with the mastoid posteriorly. The superior portion of the helix should rest at 15 to 20 mm from the squamous portion of the temporal bone.

### Neck

Although the neck is not usually considered one of the major aesthetic units of the face, its shape, especially in the upper portion, can have a marked impact on the appearance of the chin and lower portion of the face. A low-lying hyoid bone, excessive submental fat, or laxity of the platysma can cause the neck-chin contour to be obtuse and create the perception of a chin deformity that does not exist.

Powell and Humphreys<sup>20</sup> have defined the mentocervical angle (MC), which relates the line of the neck to that of the entire face. The angle is produced by constructing

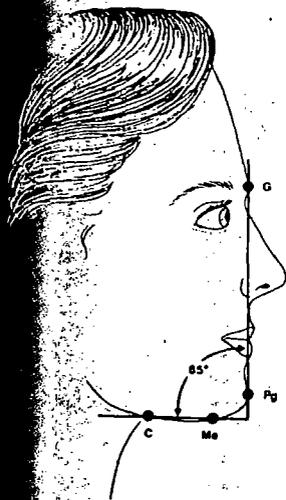


Fig. 11.20 The mentocervical angle. Relative degree of upper, middle, and lower facial protrusion or retrusion. This method does not take into account the angle of the neck or the projection of the nose in the facial analysis. C, cervical point; G, glabella; Me, menton; Pg, pogonion.

the facial plane from the glabella (G) to the pogonion (Pg), and intersecting a line drawn from the menton (Me) to the innermost point between the submental area and the neck (the cervical point, C). This angle should ideally be between 80 degrees and 95 degrees (Fig. 11.20).

**Aesthetic Analysis of the Face**

Gonzales-Ulloa<sup>29,30</sup> based his method of facial profileplasty on the relationship of the facial structures to the facial plane, which he termed the zero meridian (Fig. 11.21). In the ideal facial profile, the facial plane lies 85 to 92 degrees relative to the Frankfort horizontal when constructed through the nasion (N). On the forehead, the glabella (G) lies just anterior to the plane and then slopes gently posteriorly. The alar crease is posterior to the plane. In the lower face, the anteriormost point of the chin should lie within the plane. Using this concept a plane constructed approximately perpendicular to the Frankfort horizontal through the nasion (N) will indicate the relative degree of upper, middle, and lower facial protrusion or retrusion. This method does not take into account the angle of the neck or the projection of the nose in the facial analysis.

The aesthetic triangle was described by Powell and Humphreys in 1984.<sup>20</sup> This method of facial analysis allows for consideration of all of the major aesthetic

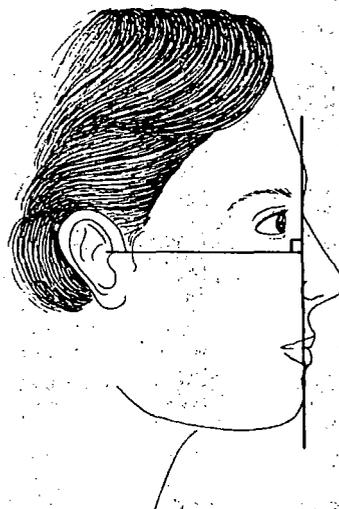


Fig. 11.21 The zero meridian of Gonzales-Ulloa.

masses of the face and illustrates their interdependence. Angles that have been considered separately can now be assessed simultaneously to evaluate facial harmony. It is first necessary to define one additional angle that has not yet been considered. The nasomental angle is formed by the intersection of the dorsal line of the nose and the nasomental line (Fig. 11.18).

The analysis begins at the forehead, which is relatively stable and the least amenable to surgical alteration. The facial plane is constructed between the glabella (G) and the pogonion (Pg). The facial plane determined by this method should intersect the Frankfort horizontal plane at an angle of 80 to 95 degrees. The glabella (G) is used as the reference point on the forehead rather than the nasion (N) (as used by Gonzales-Ulloa) because the position of the nasion (N) can be changed relatively easily by deepening the nasofrontal angle (NFr).

The nasofrontal angle (NFr) is then drawn as described previously. This angle should ideally be between 115 degrees and 135 degrees. The nasofacial angle (NFA) can now be measured from these lines as well. This angle should lie in the range of 30 to 40 degrees (Fig. 11.22).

The nasomental line is then constructed between the pogonion (Pg) and nasal tip (T). This creates the most important angle of the aesthetic triangle, the nasomental angle. The ideal range for this angle is 120 to 132 degrees. The upper line of this angle, the dorsal line of the nose, is primarily dependent on nasal projection. The lower line,

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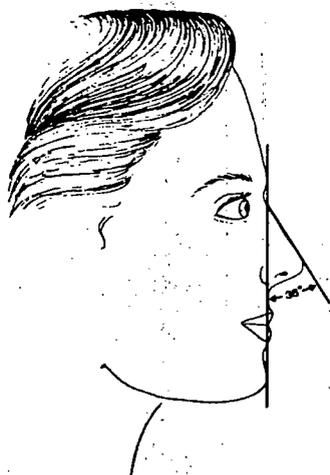


Fig. 11.22 Facial analysis using the aesthetic triangle of Powell and Humphreys. Components include the following: (1) the facial plane, (2) the nasofrontal angle (NFr), (3) the nasomentalar angle, and (4) the mentocervical angle (MC).

the nasomentalar line, is readily modified by the position of the chin. The nasomentalar line also allows horizontal position of the lips to be assessed. The upper lip should lie ~4 mm behind this line and the lower lip ~2 mm behind it (Fig. 11.18).

Finally, the mentocervical angle (MC) is measured. This angle evaluates the neck line and its relationship to the lower face. It is determined by constructing a line between the cervical point (C) and the lowermost point on the chin (Me) to intersect the facial plane. This angle should measure between 80 and 95 degrees (Fig. 11.20).

The aesthetic triangle is therefore affected by the nasofrontal angle (NFr) or depth of the nasion (N); the degree of nasal projection, and the position of the chin. Its appropriateness can be confirmed by the range of normal values for the primary, or nasomentalar, angle and by the relationship of its upper and lower lines to the facial plane; that is, the nasofacial angle (NFa) and to the horizontal position of the lips (i.e., 4 mm to the upper lip and 2 mm to the lower lip).

### Summary

Numerous methods have been presented for assessment of the individual aesthetic units of the face and for the determination of their relative proportions in evaluating the face as a whole. Other factors, such as age, ethnicity,

body habitus, and personality, must also be taken into account in the aesthetic assessment of the face. Although no precise algorithm for the determination of facial beauty exists, preoperative facial measurements assist in the determination of which facial features need to change to produce harmony with the face as a whole. Postoperative determination of the same measurements allows for assessment of the adequacy and appropriateness of the change.

### Glossary

**alar groove** junction of the ala nasi with the cheek

**cervical point (C)** innermost point between the submental area and the neck

**columella point (Cm)** anteriormost soft tissue point on the nasal columella

**dorsal line** line passing through the nasion (N) and the nasal tip (T); should be drawn through any dorsal hump that exists

**facial plane** coronal plane passing through the face at the glabella (G) and pogonion (Pg)

**Frankfort horizontal** line drawn from the superior aspect of the bony external auditory canal to the inferior most aspect of the infraorbital rim on a lateral radiograph, approximated on photograph by a line from the superior tragus to lower eyelid-cheek skin junction

**glabella (G)** most prominent point of the forehead on profile; usually at the level of the supraorbital rim

**gonion** most inferior, posterior, and lateral point on the external angle of the mandible

**labrale inferius (LI)** vermilion border of the lower lip

**labrale superius (LS)** vermilion border of the upper lip

**mentocervical angle (MC)** angle of a line drawn from the menton (Me) to the cervical point (C) relative to the facial plane

**menton (Me)** lowest contour point of the chin

**nasion (N)** point of deepest depression at the root of the nose

**nasofacial angle (NFa)** incline of the dorsum of the nose in relation to the facial plane

**nasofrontal angle (NFr)** angle defined by a tangent passing from the nasion (N) through the glabella (G) and the dorsal line of the nose

**nasolabial angle (NL)** angle between the line of the nasal columella (Sn-Cm) and the line of the upper lip (Sn-LS)

**nasomentalar angle** intersection of the dorsal line of the nose and a line from the pogonion (Pg) to the nasal tip (T)

**nasomentalar line** a line connecting the pogonion (Pg) and the nasal tip (T)

**pogonion (Pg)** anteriormost point of the chin

**stomion inferius (stmi)** uppermost point on the vermilion of the lower lip

**stomion superius (stms)** lowermost point on the vermilion of the upper lip

**subnasale (Sn)** point at which the nasal columella merges with the upper cutaneous lip

**tip nasal (T)** anterior-most point on nasal profile

**trichion (Tr)** anterior hairline at the midline; may be determined in those with a receding hairline as the superiormost point of action of the frontalis muscle.

#### Acknowledgments

Illustrations by Steven M. VanHook, MD, and Renée Clements, BAA.

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#### Appendix 4: Sensory Response Studies

**Double-Blind, Randomized, Controlled Split-Face Trial to Assess the Efficacy and Safety of a Liposomal Lidocaine Topical for Pain Management During Micro-Focused Ultrasound Treatment.**

Fowler, Vincent R. and Gitt, Steven M.

**Purpose:**

The primary purpose of this study was to assess the safety and level of pain control provided by commercially available liposomal lidocaine topical compared to control used prior to micro-focused ultrasound (MFU) treatments. Efficacy of the MFU treatment will also be, secondarily, to ensure the topical has no effect on treatment outcomes.

**Methods:**

N=15. Liposomal lidocaine topical (active) and a control cream (of similar consistency and color) was applied in a split-face design and in random order to right and left sides of the face. Treating investigators and subjects were blinded to which side was treated with active. All patients were also given 800mg of ibuprofen 60 minutes prior to MFU treatments. 30 minutes after application of topical and control cream, one side of the face was washed, wiped with alcohol to remove residual tackiness, and treated with MFU per guidelines. The same steps were then completed on the other side. Subjects were asked to report an average Numeric Rating Scale (NRS) pain scores for each facial region immediately after treatment and for each depth treated (3.0mm or 4.5mm). Efficacy based on masked-observer ratings will be assessed at 90 and 180 days. Safety, based on AE incidence, was also assessed.

**Results:**

At this interim time point, for active/control (presented in this order) average scores were  $4.8 \pm 2.3/5.5 \pm 2.5$  (peri-orbital),  $4.1 \pm 2.6/4.6 \pm 2.0$  (cheek), and  $3.8 \pm 1.9/4.1 \pm 2.4$  (submandibular), for the 3.0mm depth and  $5.7 \pm 2.3/6.0 \pm 2.5$  (peri-orbital),  $4.6 \pm 2.2/4.9 \pm 2.4$  (cheek), and  $2.7 \pm 1.8/3.5 \pm 1.7$  (submandibular) for the 4.5mm depth. Combined average pain scores for all regions of the face were  $3.8 \pm 1.9$  and  $4.1 \pm 2.4$ , for active and placebo control, respectively. The incidence of AEs did not differ between sides treated with active versus control.

**Conclusion:**

Liposomal lidocaine topical pre-treatment did not result in significant differences between facial region or combined pain scores when compared to control. There was no significant difference in adverse events at this interim time point. In these subjects who were administered 800mg of ibuprofen as a pre-treatment to micro-focused ultrasound procedures, average pain scores were <5 on a 10 point scale. This finding is promising and suggests a single high dose of ibuprofen may be an effective means of pain control during MFU treatment.

**NOTE:** Complete pain data and efficacy data at 90 days will be available at the time of presentation.

## Prospective Double-Blind, Randomized Pilot Study Comparing Ibuprofen to a Narcotic for Pain Management During Micro-Focused Ultrasound Treatment

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Hema Sundaram, M.D. and Ashley Lodha  
Research sponsored by Ulthera, Inc.  
Abstract presented at ASDS 2011 Meeting in Washington D.C.

### Background and Objectives

Microfocused ultrasound (MFU) has emerged as a new aesthetic energy technology for skin lifting and tightening, with FDA clearance in 2009 via the de novo 510(k) process as a Class II medical device for non-surgical brow-lifting. Prospective, controlled clinical studies with an evidence level of II using validated, quantified measurement scales have shown the device to be safe and efficacious for non-surgical lifting. A challenge reported by some clinicians is maintaining patient comfort during treatment, which spares the epidermis and creates micro-zones of thermal coagulation at specific depths in the dermis and hypodermis. Patients are typically pre-medicated for pain relief with a single dose of a narcotic such as hydrocodone/acetaminophen. No controlled studies have been performed previously to substantiate anecdotal reports that this improves patient comfort during MFU treatment. Furthermore, an alternative method of pain relief would be advantageous for patients seeking to resume normal daily activities such as driving immediately after MFU (which itself produces no post-procedural recovery time), since this is not possible following pre-medication with a narcotic.

The primary objective of this study was to compare the level of pain control provided by a prescription-strength dose of ibuprofen to the level of pain control provided by a narcotic when used prior to MFU treatment. Variation in the level of pain during treatment of specific facial zones, and safety and efficacy of MFU during a 180 day post-treatment period were assessed as secondary outcomes.

### Study Design / Materials and Methods

20 healthy subjects were enrolled in the study and randomly assigned to two groups, A and B, for MFU treatment to the full face and neck at depths of 3mm and 4.5mm according to a standardized protocol. Group A received 800mg of ibuprofen 60 minutes before treatment, while Group B received 10mg hydrocodone/500mg acetaminophen 60 minutes before treatment. The investigator, treating subinvestigator and study subjects were blinded in regards to the pre-medication that was given. Subjects reported pain scores on a 10-point Numeric Rating Scale (NRS) immediately after treatment of each facial zone (periorbital, cheek, submental and submandibular) and for each depth to which it was treated (3.0mm or 4.5mm). Treatment efficacy was assessed by a masked evaluator at 90 and 180 days after treatment, based on comparison of standardized digital images before and after treatment. Safety, based on incidence of adverse effects, was also assessed during and after treatment.

### Results

Mean pain scores for each facial zone and treatment depth were comparable for Groups A and B. The greatest pain was experienced during treatment of the periorbital zone. Pain scores were similar for the 3mm and 4.5mm treatment depths, except in the periorbital region where the 4.5mm depth produced more discomfort in some subjects. Combined average pain scores were below 5 on the 10-point scale for both groups. Adverse events were minor and temporary, including temporary tenderness of the treated areas, and did not differ between groups. In particular, there was no significant post-treatment ecchymosis in either group. There was no difference between the groups in treatment efficacy at the evaluation time points.

### Conclusion

Pre-medication with either ibuprofen or hydrocodone/acetaminophen resulted in acceptable pain scores (less than 5 out of 10) during MFU treatment of all facial zones except for the periorbital region at the 4.5mm treatment depth. Average combined pain scores were also acceptable (less than 5 out of 10) for all facial zones at both treatment depths (3mm and 4.5mm). The data from this pilot study suggest that a single, prescription-strength dose of ibuprofen may be comparable in efficacy to a single dose of hydrocodone/acetaminophen when administered 1 hour prior to MFU. Both clinicians and patients may prefer the use of ibuprofen instead of a narcotic as pre-medication for MFU, since it allows patients to resume normal daily activities, including driving, immediately after the procedure. Additionally, based on evidence from cold immersion studies that overall pain perception is diminished if the final experience during a procedure is less painful, a secondary recommendation from our study is that the periorbital zone should not be the last area treated during MFU to the full face and neck, since this zone was found to be the most painful by our study subjects.

Further controlled studies with larger numbers of subjects are required to substantiate the findings of this pilot study.

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\*Please Note: Ultherapy is indicated for use as a non-invasive dermatological aesthetic treatment to lift the eyebrow. Other uses of Ultherapy described in this presentation are not FDA approved, and the safety and efficacy of alternate uses has not been established. Healthcare professionals should base patient treatment decisions on the attached FDA approved labeling for Ultherapy, as well as their own clinical judgment. Ulthera does not endorse nor promote any information in the materials contained herein. The materials provided are for medical information purposes only.

Side effects of Ultherapy are as follows: Immediately following Ultherapy®, the skin may appear red for a few hours. It is not uncommon to experience slight swelling for a few days following the procedure or tingling/tenderness to the touch for weeks following the procedure, but these are mild and temporary in nature. Occasional temporary effects can include bruising or welts, which resolve in hours to days, or numbness in a select area, which resolves in days to weeks. As with any medical procedure, there are possible risks associated with the treatment. There is a remote risk of a burn that may or may not lead to scarring, which will respond to medical care, or temporary nerve inflammation, which will resolve in a matter of weeks.

The Ulthera System has not been evaluated for use over various materials. Therefore, treatment is not recommended directly over those areas with mechanical implants, dermal fillers, or implanted electrical devices. The Ulthera System has not been evaluated for use for pregnant or breast feeding women; children; or those with the disease states such as herpes simplex, autoimmune disease, diabetes, epilepsy, or Bell's palsy. The Ulthera System is contraindicated for use in patients with open facial wounds or lesions, severe or cystic acne on the face and/or neck, an active systemic or local skin disease that may alter wound healing, a hemorrhagic disorder or hemostatic dysfunction, or an anticoagulant treatment plan.

### Appendix 5: Skin of Color Studies

**Evaluation of Micro-Focused Ultrasound for Obtaining Lift and Tightening of the Cheek Tissue and Improvement in Jawline Definition and Submental Skin Laxity in Patients with Fitzpatrick Skin Phototypes 3 through 6**

**Background:** Objective of the study was to evaluate efficacy and safety of micro-focused ultrasound (Ultherapy®) for obtaining lift and tightening of the cheek tissue, and improving jawline definition and submental skin laxity in patients with Fitzpatrick skin phototypes 3 through 6.

**Methods:** Fifty-Four subjects meeting inclusion/exclusion criteria were treated on the cheeks, submentum, submandibular regions at two depths, 4.5mm and 3mm, line density was on average of 422 lines per subject. Efficacy measures, masked-observer ratings, physician and subject global aesthetic improvement scales (PGAIS and SGAIS respectively), and patient satisfaction were completed at 90 and 180 days. Safety, based on AE incidence, was assessed.

**Results:** Subjects demographics ; average age 53 years (32-64 years), 98% female, 9.4% Hispanic/Latino, 67.9% African American, 18.8% Asian and 2% other (non-Caucasian). Fitzpatrick skin types III-17%, IV-47.2%, V-30.2 and VI 5.6%. At interim analysis time point (90 d n=48, 180 d n=39), PGAIS, 85.4% and 56.4% improved (improved to very much improved) at 90 and 180 days, respectively. SGAIS, 79.2% and 76.9% improved at 90 and 180 days, respectively. 81.8% of subjects were satisfied to very satisfied at 90 days and 73.2% of subjects were satisfied or very satisfied at 180 days. Masked observer assessments will be completed before time of presentation. Data from all subjects enrolled will be analyzed before time of presentation. No serious adverse events were reported. No treatment related adverse events reported.

**Conclusion:** Micro-Focused ultrasound is valuable for nonsurgical skin lifting and tightening, and a noninvasive alternative to surgery or submental liposuction in selected patients. Although results are positive, higher densities of treatment are currently under investigation and may be warranted to optimize efficacy outcomes. Importantly, results of this study suggest that it is safe for all-skin types.

## Intense Focused Ultrasound Tightening in Asian Skin: Clinical and Pathologic Results

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**BACKGROUND** Laxity and wrinkles of the aging face are common cosmetic concerns. Intense focused ultrasound (IFUS), a novel treatment modality for skin laxity, produces thermal effects at various depths while sparing overlying epidermis.

**OBJECTIVE** To evaluate the safety and efficacy of IFUS in facial skin tightening.

**METHODS AND MATERIALS** Twenty-two Korean patients with facial laxity were analyzed after a single IFUS treatment. Patient assessments were recorded, and two blinded, experienced clinicians who assessed improvement of nasolabial folds and jaw tightening evaluated photographs of patients and rated skin laxity. Skin biopsies were taken from 11 patients before and 2 months after treatment.

**RESULTS** Objectively, nasolabial folds and jaw lines were improved in all patients. Subjectively, 77% of patients reported much improvement of nasolabial folds, and 73% of patients reported much improvement at the jaw line. Histologic evaluation of skin biopsy samples using hematoxylin and eosin and Victoria blue stains showed greater dermal collagen with thickening of the dermis and straightening of elastic fibers in the reticular dermis after treatment.

**CONCLUSION** IFUS is a safe, effective, noninvasive procedure to tighten the facial skin of Asian patients. Improvement is associated with greater production of dermal collagen and straightening of dermal elastic fibers.

*The authors have indicated no significant interest with commercial supporters.*

Nonablative rejuvenation (NAR) lasers have become popular tools in the treatment of facial laxity and wrinkles. NAR devices have been designed to induce thermal injury within the dermis while sparing the overlying epidermis. NAR devices in use include intense pulsed light, radiofrequency (RF), neodymium-doped yttrium aluminum garnet (Nd:YAG), and pulsed dye lasers. Although the incidence of adverse effects is lowest with NAR, cosmetic improvements are subtle and inconsistent, and NAR often requires serial treatments over a 6- to 12-month period.<sup>1-3</sup>

Ultrasound-based imaging systems have been used over several decades for clinical diagnosis. Intense focused ultrasound (IFUS) is an energy modality that propagates through tissues up to depths of several

millimeters. During the past decade, IFUS has been used as a clinical noninvasive surgical tool to treat tumors, including those of the liver, prostate, and uterus.<sup>4-6</sup> IFUS creates well-defined thermal injury zones to the superficial musculoaponeurotic system (SMAS). IFUS is similar to fractional laser resurfacing in that thermal lesions are fractionated at multiple spots, but IFUS is different in that the thermal lesions occur only in deep dermal tissue.

Several studies have reported a novel IFUS approach in human cadaveric facial tissue and porcine tissue.<sup>7-9</sup> These reports have showed that IFUS produced focused thermal collagen denaturation in the SMAS, inducing shrinkage and tissue tightening. Alam and colleagues<sup>10</sup> reported clinical results of ultrasound tightening of facial and neck skin. The present study is

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## INTENSE FOCUSED ULTRASOUND TIGHTENING IN ASIAN SKIN

the first to investigate the safety and efficacy of ultrasound tightening in Asian facial skin with histologic results.

### Materials and Methods

#### Patients

Twenty-two patients (Fitzpatrick skin type III–VI) with facial laxity were enrolled in this study. Mean patient age was 48.5 (range 38–73); two of the 22 patients were male. All patients gave written informed consent for treatment and photographs. Eleven patients agreed to the biopsy procedure. Exclusion criteria were prior cosmetic facial surgery or placement of tissue fillers, scarring in the treatment region, and allergy to topical anesthetics.

#### Intense Focused Ultrasound Device

One IFUS device (Ulthera LLC, Mesa, AZ) was used in this study. The handpiece contained a transducer that was used for imaging the treatment region before delivering a series of ultrasound exposures for treatment. The device contained the following three handpieces (in order of most-superficial focus to deepest focus within tissue): superficial, 7.5 MHz with a focal depth of 3.0 mm; intermediate, 7.5 MHz with a focal depth of 4.5 mm; and 4.4 MHz with a focal depth of 4.5 mm. Lower-frequency handpieces have deeper focal depths. Handpieces delivering energy at 7.5 MHz and a focal depth of 3.0 mm and 4.4 MHz and 4.5 mm were used in this study. Each probe delivers a set of pulses in a linear array, with pulses spaced 1.5 mm apart and an entire linear array of up to 25 mm long. The spacing of pulses within each linear array was set at 1.5 mm, allowing 17 thermal coagulative zones created with each probe discharge. Linear arrays are spaced in parallel at 3-mm intervals. Two available hand pieces with distinct focal depths were used with single passes 1 to 2 mm apart.

#### Pretreatment Preparation

Topical anesthetic cream was applied to the entire face and allowed to sit for 60 minutes. The anes-

thetic cream was washed off with mild soap and water.

#### Selection of Ultrasound Handpieces

All patients were treated only once with IFUS. Ultrasound gel was applied to the skin, and the handpiece was pressed perpendicularly, uniformly, and firmly to the skin surface. The forehead and temples and the thin malar area were treated with the 7.5-MHz, 3.0-mm handpiece at the following energy setting: forehead, 0.3 to 0.35 J; malar, 0.35 J; temple, 0.35 J. The cheeks and submentum were treated with 4.4 MHz, 4.5 mm at the 1.0 J energy setting and at 7.5 MHz with the 3.0-mm handpiece at the highest energy setting, 0.45 J. The spacing of pulses was set at 1.5 to 2.0 mm. Before treatment, imaging was used to confirm that the handpiece was placed firmly on the skin surface and that the predicted skin depth was correct. On average, 30 treatment lines were delivered to the forehead, 10 lines to each temple, 70 lines to each cheek, and 90 lines to the submentum. After treatment, the ultrasound gel was wiped off.

Clinicians and patients analyzed the treatment results subjectively at 2 months. The principal investigator and the patients gathered clinical data. The investigator gathered photographic documentation using identical cameras and camera settings (Canon EOS-40D, 10.1 megapixels, high-resolution setting, 2816 × 1880 pixels, Canon Corp., Tokyo, Japan), lighting, and patient positioning before and 2 months after the treatment. Two blinded dermatologists (one female and one male) evaluated paired before-and-after photographs of the 22 patients in a randomized fashion to determine whether there was discernible clinical improvement. The dermatologists were not aware of which photographs were taken before and which after treatment. Specifically, if a blinded reviewer detected a change in a particular patient, the reviewer was asked to identify the post-treatment image. If the post-treatment image was identified correctly, the reviewers' assessment was considered to be "improved;" if the reviewer

identified the post-treatment image incorrectly, the reviewers' assessment was considered to be "worse." If the reviewer reported no difference between the two photographs, the assessment was considered to be "no change." The criteria for objective evaluations were improved = 1, no change = 0, worse = -1. Objective scores indicating improvement were calculated as the sum of the two clinician's scores. Patients made subjective clinical assessments of skin tightening by evaluating their own photos. Subjective improvement was assessed much improvement = 2, improvement = 1, no change = 0, worse = -1. Side effects of the focused ultrasound treatment were documented at each treatment session and during the follow-up visit.

#### Histological Analysis

Skin biopsies were taken from 11 patients before and 2 months after treatment. The 2-mm punch biopsies were sampled from the lateral side of the cheek. All specimens were stained with hematoxylin and eosin (H&E), Victoria blue, and Masson's trichrome stain. The two blinded evaluators assessed the pathologic results by examining the histologic photographs in random order, viewing six sections per patient. The area fractions of collagen and dermal thickness were determined using Image J software (<http://rsb.info.nih.gov/ij/>) on tissue sections stained with Masson's trichrome.

#### Statistical Analysis

All experimental data were analyzed using paired Student *t*-tests with SPSS 12.0 statistical software (SPSS, Inc., Chicago, IL). All *p*-values were two-tailed, and *p* ≤ .05 was considered statistically sig-

nificant. Summary data are expressed as means ± standard errors of the mean.

## Results

### Clinical Results

All 22 patients completed treatment and received follow-up examinations; no patients did not complete the study due to intolerable treatment or side effects (Figures 1 and 2).

Objectively, all patients demonstrated nasolabial fold and jaw line improvement. Twenty of the 22 patients (91%), showed improvement of two objective score values at the nasolabial fold and jaw line. Two patients (9%) showed nasolabial fold and jaw line improvement of one objective score value. The average objective score of nasolabial fold and jaw line improvement was 1.91. Subjectively, 77% (*n* = 17) of patients reported much improvement of nasolabial folds, and 73% (*n* = 16) reported much improvement of the jaw line. The average subjective scores of nasolabial fold and jaw line improvement were 1.77 and 1.72, respectively.

Patients experienced only minimal pain during the treatment session. No patient reported severe pain requiring additional pain relief with analgesia or sedation. All patients had mild erythema and swelling that persisted for 2 to 3 days. Four patients developed numbness along the mandible after treatment on the cheeks that resolved without sequelae 2 to 3 weeks after IFUS treatment. No other adverse events, including but not limited to nerve and muscle dysfunction, bruising, or bleeding were observed; no



Figure 1. Improvement of the nasolabial fold after a single intense focused ultrasound treatment. (A) Before treatment, (B) 1 month after treatment, (C) 2 months after treatment.

## INTENSE FOCUSED ULTRASOUND TIGHTENING IN A SIAN SKIN

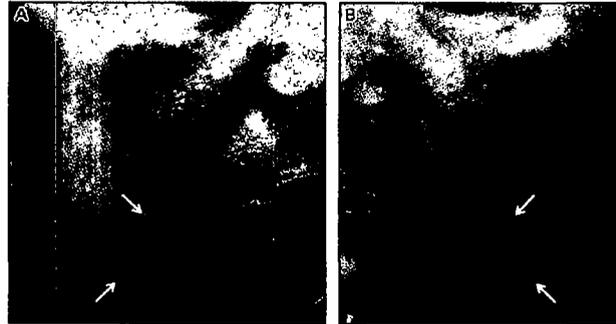


Figure 2. Improvement of jaw line and marionette line after single Intense focused ultrasound treatment. (A) Before treatment, (B) 2 months after treatment.

serious adverse events occurred. Whitish wheals or striations were apparent on the cheek and submentum of two patients.

#### Histologic Results

The mean age of patients from whom skin biopsies were taken was 51.6 (range 39 to 73), and all were female. The histology of skin biopsy samples taken before and 2 months after treatment demonstrated significant differences. There were more dermal collagen fibers of the reticular dermis after treatment than before, resulting in greater dermal thickness; the mean thickness before treatment was  $1.32 \pm 0.18$  mm, versus  $1.63 \pm 0.31$  mm after treatment. The average area fraction of collagen in the reticular dermis increased 23.7%, a change that was statistically significant (Table 1). Neither epidermal changes nor inflammatory reactions, assessed using H&E staining, were noted in any of the cases (Figure 3). In skin biopsy samples taken 2 months after treatment, the elastic fibers of the upper and lower reticular dermis were more parallel and straighter in appearance than samples taken before treatment (Figure 4).

#### Discussion

Various noninvasive devices have been developed in an effort to treat aging skin.<sup>11</sup> These modalities have

primarily focused on treating the superficial layers of the skin because of limitations in penetration depth. One of the most-effective treatments for aging skin is ablative skin resurfacing with carbon dioxide or erbium lasers, which induces sublethal thermal injury to the skin tissue, causing removal of the epidermis, and contraction and remodeling of the dermis. Although ablative skin resurfacing has been proven effective in treating aging skin, patients treated with this modality sometimes have prolonged erythema, infections, and permanent pigmentary changes. For this reason, nonablative skin resurfacing devices, including intense pulsed light, light-emitting diode, RF, Nd:YAG, and pulsed dye lasers have been designed in an effort to reduce the unwanted adverse effects of ablative skin resurfacing.<sup>12</sup> Although these nonablative skin resurfacing modalities have fewer adverse effects than ablative skin resurfacing, the former modality is less efficacious.

Ultrasound waves induce vibration in the composite molecules of a given tissue, and the friction between the molecules generates heat. Ultrasound energy is a new modality in the field of nonsurgical tissue tightening. Deep energy delivery to the level of the SMAS in a fractionated pattern is thought to be most effective in inducing skin tightening.<sup>13</sup> The wedge-shaped thermal defects created by the ultrasound devices investigated reaches beyond the upper layers of the skin into the deep dermis and subcutis. This

**TABLE 1. Average Fraction of Collagen and Dermal Thickness Before and After IF Intense Focused Ultrasound Treatment**

|                                       | Mean ± Standard Deviation |                            | Change, % | P-value |
|---------------------------------------|---------------------------|----------------------------|-----------|---------|
|                                       | Before treatment          | Two months after treatment |           |         |
| Average area fraction of collagen (%) |                           |                            |           |         |
| Papillary dermis                      | 54.38 ± 10.89             | 55.58 ± 8.22               | 2.2       | .26     |
| Reticular dermis                      | 52.70 ± 7.79              | 65.18 ± 7.89               | 23.7      | .001    |
| Dermal thickness (mm)                 | 1.32 ± 0.18               | 1.63 ± 0.31                | 65.9      | .001    |

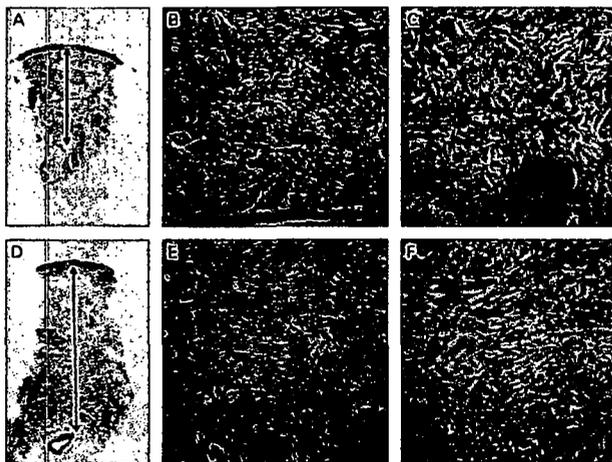
IFUS, intense focused ultrasound.

modality reduces risk of inadvertent cutaneous injury to the extent that this delivery can separate secondary scatter and absorption in the epidermis from those in the dermis.

For many decades, high-intensity focused ultrasound (HIFU) has been investigated as a tool to treat solid benign and malignant tumors and is now emerging as a potential noninvasive alternative to conventional therapies. In contrast to traditional HIFU,

IFUS deposits short pulses within the millisecond domain (50–200 ms). A frequency in the megahertz domain, which avoids cavitation processes, is used instead of the kilohertz domain frequencies commonly used in HIFU. The nominal energy level deposited at each site in IFUS is also significantly lower (0.5–10 J) than with HIFU (100 J).

The IFUS-mediated thermal ablation tissue response is similar to that from other energy-based devices



**Figure 3.** Histology of skin biopsy before (A, B, and C) and after (D, E, and F) intense focused ultrasound based on hematoxylin and eosin (H&E) staining. Treatment resulted in fewer dermal collagen fibers, especially in the lower reticular dermis; dermal thickness was also greater. The collagen fibers exhibit a more-parallel and straighter appearance after treatment (arrow length in A: 600 μm, in D: 1,000 μm). (A, B, and C) Tissue samples taken before treatment and stained with H&E. (A) × 40; (B) upper dermis, × 200; (C) lower dermis, × 200. (D, E, and F) Tissue samples taken after treatment and stained with H&E; (D) × 40; (E) upper dermis, × 200; (F) lower dermis, × 200.

INTENSE FOCUSED ULTRASOUND TIGHTENING IN ASIAN SKIN

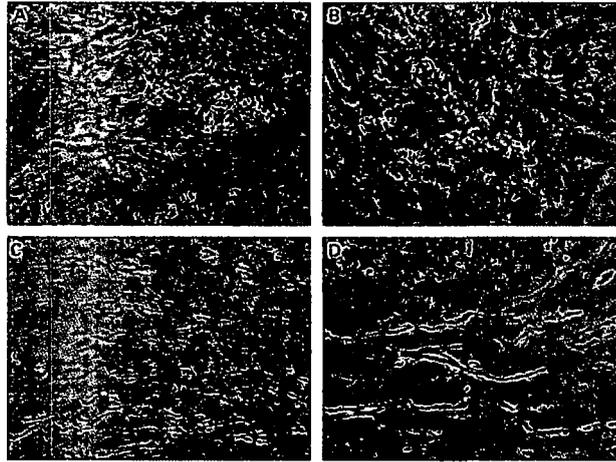


Figure 4. Histology of skin biopsy before (A and B) and after (C and D) intense focused ultrasound based on Victoria blue staining. Treatment showing that the elastic fibers are more parallel and straighter in the upper and lower dermis after treatment. (A and B) Tissue samples taken before treatment and stained with Victoria blue. (A) upper dermis,  $\times 400$ ; (B) lower dermis,  $\times 400$ . (C and D) Tissue samples taken after treatment. C: upper dermis,  $\times 400$ ; (D) lower dermis,  $\times 400$ .

such as lasers, RF, and combination laser-RF devices.<sup>7,8</sup> Thermal imaging has revealed that the energy of RF delivery is much more diffuse, tends to affect the dermis, and travels along connective tissue septae into the subdermis (Table 2).<sup>14</sup> In contrast to monopolar RF (Thermage Inc., Hayward, CA), IFUS is sharply focused.<sup>7</sup> IFUS is able to focus energy within tissue to produce a 25-mm line of discrete thermal injury zones spaced 0.5 to 5.0 mm apart. Thus, most of the energy is deposited in the form of heat in the focal zone of the beam, leaving the surrounding area unaffected. This characteristic allows the induction of numerous unique thermal damage patterns. Using IFUS, tissue may be altered using various arrays of microscopically small focal damage

rather than ablating an entire macroscopic area. IFUS allows a rapid healing response from tissue immediately adjacent to the thermal lesions, which is conceptually similar to laser fractional photothermolysis.<sup>15</sup>

In the present study, 77% and 73% patients reported much improvement of the nasolabial fold and jaw line, respectively, as a result of IFUS-mediated tightening occurring after a single treatment. Patients' subjectively assessed clinical improvement was not significantly different based on age or area treated (e.g., nasolabial folds vs the jaw line). Side effects included transient redness, swelling, temporary numbness, and linear whitish wheals. Linear

TABLE 2. Comparison of Monopolar Radiofrequency (RF) and Intense Focused Ultrasound (IFUS)

|                      | Monopolar RF               | IFUS                                     |
|----------------------|----------------------------|--|
| Depth of target spot | To subcutaneous fat tissue | To superficial musculoaponeurotic system |
| Width of target spot | Volumetric effect          | Fractional effect                        |
| Need for cooling     | Necessary                  | Unnecessary                              |
| Imaging              | Not available              | Available                                |

whitish wheals were noted in two patients during the use of the 4.5-mm focal depth probe on the cheek and submentum. Inadequate uncoupling of the heat energy to the skin during the operations of these two patients is thought to have induced the wheals. Most patients reported feeling pain during the procedure, but none needed analgesics. The pain tolerance differed between the patients and was independent of age or fat thickness of face.

H&E staining of the facial biopsies sampled 2 months after treatment revealed a greater number of collagen fibers in the reticular and deep dermis. Victoria blue staining of the tissue indicated that the number of elastic fibers was also greater in the deep dermis. The skin samples were 2-mm punch biopsies taken from the lateral malar area that did not penetrate to deep tissue. Therefore, any changes in the SMAS were not observed in our study because of the depth of the biopsy samples, which were not deep enough to include fat or the SMAS layer. This investigation is the first ultrasound-induced tissue change study reporting histological data of Asian human skin. We observed increased dermal collagen and rearrangement of elastic fibers in the reticular and deep dermis. These changes are likely due to the heat delivered to the tissue, which subsequently causes collagen regeneration.

A significant advantage of the dermatologic use of IFUS in Asian patients is that the absorption of ultrasound energy is independent of the melanin content of skin. Instead the microscopic and bulk mechanical properties of the tissue determine the absorption in the skin.<sup>16,17</sup> Therefore, in contrast to light-based devices, the action of IFUS is independent of skin color and chromophores. In addition, IFUS creates a sharp focus of the ultrasound beam several millimeters within the skin. The power density of the converging ultrasound beam is therefore much lower as it passes through the epidermis than at its focal point. Only minimal energy absorption and heating of the tissue occurs in the epidermis, which is insufficient to create significant thermal damage. Thermal heating obviates the need for skin

cooling to protect the epidermis of any skin type, as is the case with other devices that induce unexpected thermal alterations within the skin. The data presented here show that the use of IFUS in Asian people appears to be safe and effective.

Another advantage of IFUS is that imaging and targeted energy exposure can be accomplished using the same handpiece. High-resolution diagnostic ultrasound imaging provides excellent intraoperative visualization of the facial tissue layers, facilitating precise treatment. As hypothesized in an earlier cadaveric study,<sup>7</sup> if the "suture-like" points of thermal injury could be delivered at the level of the superficial musculoaponeurotic system, shrinkage and retraction at that level may be achieved with minimal risk to the facial nerve.<sup>10</sup> The deep penetration of IFUS could result in nerve injury, but the present study is the first to investigate the detrimental effect of IFUS exposures on the facial nerve or its branches. The results reported here support the safety of IFUS for treatment of facial tissue, with only four of 22 patients (18%) developing temporary numbness along the mandible, and no sequela were reported. No motor nerve injury was apparent,<sup>18</sup> although marginal mandibular nerve branches are located superficially in the face and should not be aggressively treated.

One limitation of this study is that we did not have a standard photographic device and objective parameters to demonstrate mid- to lower facial tightening, although this study is the first report to combine clinical and histologic data supporting the safety and efficacy of intense ultrasound therapy to the facial tissue of Asian patients. We observed that focused ultrasound induces increased collagen fibers and straightening of elastic fibers in the deep dermis of facial tissue. We conclude that the novel treatment modality IFUS offers a noninvasive treatment option for skin tightening in Asian patients. Because the intense ultrasound system selectively delivers heat energy to thermal injury zones in the SMAS layer, we hypothesize that this system

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also stimulates dermal collagen and elastic fibers in the zone of intense ultrasound treatment.

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## Multicenter Study of Noninvasive Radiofrequency for Periorbital Tissue Tightening

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**Background and Objectives:** This 6-month study evaluated the efficacy and safety of treatment with a nonablative radiofrequency (RF) device.

**Study Design/Materials and Methods:** Eighty-six subjects received a single treatment with the ThermoCool TC™ System (Thermage, Inc., Hayward, CA) and were evaluated for 6 months after treatment.

**Results:** Independent scoring of blinded photographs resulted in Fitzpatrick wrinkle score improvements of at least 1 point in 83.2% (99/119) of treated periorbital areas. Treating physicians, without reference to pre-treatment photographs, noted improvements in 28.9% (48/166) of treatment areas. Fifty percent (41/82) of subjects reported being satisfied or very satisfied with periorbital wrinkle reductions. Objective photographic analysis showed that 61.5% (40/65) of eyebrows were lifted by at least 0.5 mm. Rates and duration of edema/erythema were very low (e.g. vs. ablative procedures). Overall 2nd-degree burn incidence was 0.36% (21 per 5,858 RF applications). Three patients had small areas of residual scarring at 6 months.

**Conclusions:** A single treatment with this RF tissue tightening (RFTT) device produces objective and subjective reductions in periorbital wrinkles, measurable changes in brow position, and acceptable epidermal safety. These changes were indicative of a thermally induced early tissue-tightening effect followed by additional tightening over a time course consistent with a thermal wound healing response. *Lasers Surg. Med.* 33:232–242, 2003.

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**Key words:** nonablative; noninvasive; rhytids; ThermoCool; radiofrequency; skin tightening; skin contraction; tissue contraction; tissue tightening

### INTRODUCTION

Over the past several years, laser technologies have replaced chemical peels and dermabrasion as the treatment of choice to improve photodamaged skin. Resurfacing of the facial skin with CO<sub>2</sub> or erbium:yttrium–aluminum–garnet (Er:YAG) lasers effectively heats and ablates damaged tissue, causing underlying collagen contraction and new

collagen formation that is critical for tissue tightening and wrinkle reduction [1–3]. Although the ablative laser techniques are associated with impressive efficacy in reducing periorbital wrinkles and tightening sagging skin, dermabrasion-type side effects following laser surgery are common [4]. Erythema occurs in practically all patients undergoing CO<sub>2</sub> procedures; the healing time usually lasts 3 months but may persist up to 12 months after some procedures. Risk of pigmentary alteration, infection, dermatitis, and scarring are other well-known drawbacks [4–6].

Enhancements in laser design and experience of the aesthetic procedure specialist can somewhat minimize the risk of injury with the ablative techniques [7]. Nonablative technologies have been developed in an effort to reduce complications, minimize perioperative pain, and shorten the healing time by creating a dermal wound without ablating the epidermis [8]. Examples of these newer noninvasive technologies include CoolTouch infrared laser (1,320 nm), pulsed dye laser (585, 595 nm), intense pulsed light sources (585–1,100 nm), Nd:YAG (1,064 nm), Smoothbeam infrared laser (1,450 nm diode), ultrasound, and microdermabrasion [9,10]. While the incidence of adverse effects is unquestionably lower with nonablative techniques, the cosmetic improvement is subtle and/or inconsistent, and often requires serial treatments over a 6- to 12-month period [9–13].

Radiofrequency tissue tightening (RFTT) is a recently introduced alternative to nonablative laser technology. Early low-energy modifications of traditional ablative RF electrosurgery units have been used with limited success for cosmetic purposes to achieve superficial dermatological changes [14,15]. More recently, a nonablative RFTT device

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(ThermaCool TC™ System [Thermage, Inc., Hayward, CA]) was developed especially for tightening deeper dermal structures without epidermal damage [10,16]. This new device uses a proprietary capacitive coupling method to transfer higher energy fluences through skin to a greater volume of dermal tissue than do nonablative lasers, while protecting the epidermis. Unlike lasers, which convert light to heat and target specific superficial structures or chromophores (selective photothermolysis), RF produces heat when the tissue's electrical resistance converts the electric current to thermal energy deeper within the dermis [10]. Moreover, unlike standard RF devices that concentrate energy at single-dimension points or along two-dimension edges, this new RFTT device uniformly disperses the energy to three-dimensional volumes of tissue at controllable depths. Initial collagen denaturation within these thermally modified deep tissues is thought to be the mechanism for immediate tissue contraction; subsequent neocollagenesis then further tightens the dermal tissue and reduces wrinkles [17]. The epidermis is protected with controlled cryogen cooling before, during, and after volumetric RF tissue heating.

Animal studies have documented that this RFTT device can achieve dermal heating as shallow as the papillary dermis or as deep as the subcutaneous fat [10]. Safety evaluations of this RF device on human abdominal skin have demonstrated a low incidence of transient side effects; histological analysis of the tissue verified minimal signs of scarring as well as preservation of the epidermis with fibroplasia and other indicators of increased collagen formation [16]. Skin tightening is also thought to be the main mechanism of action leading to the eyelid elevation that has been reported with this RF technology in a small series of patients [9]. Preliminary reports on the use of this device for tightening of facial skin (including periorbital wrinkles and acne scars) have been promising, with only 2 of 45 subjects (4.4%) presenting with transient 2nd-degree burns (edema and/or erythema) in 6 of 4,147 total applications (0.1%) [18].

The primary purpose of this multicenter clinical study was to evaluate the efficacy and safety of a single treatment with the RFTT device for the reduction of periorbital wrinkles in order to achieve FDA clearance for an established aesthetic indication. An additional interest of the investigators and the sponsoring company was to characterize the objective and subjective clinical effects of both short-term tissue tightening and subsequent additional tightening due to wound healing over the full course of the study. The study integrated a variety of evaluations (e.g., subjective investigator assessment, a patient questionnaire, and blinded photograph review) in an attempt to assess even subtle clinical changes over the 6-month study period.

## MATERIALS AND METHODS

### Study Design

This blinded, multicenter (IRB-approved) study evaluated the efficacy and safety of a nonablative nonlaser RF-

based device for the treatment of periorbital wrinkles or skin laxity. Each subject received a single course of RF treatment with a standardized algorithm. Investigators evaluated treatment efficacy with the Fitzpatrick Wrinkle Classification System (FWCS), and subjects reported on their overall satisfaction and perceptions at 2, 4, and 6 months. Assessment of wrinkle improvement also included review of a series of baseline and 2-, 4-, and 6-month photographs for each subject; these blinded photographs were separately scored with the FWCS by three independent clinicians, including two facial plastic surgeons and a dermatologic surgeon. In addition, 4- and 6-month photographs were compared with baseline photographs using an objective technique to measure eyebrow lift. During their clinic visits (within 24–72 hours and at 1, 2, 4, and 6 months), subjects were also evaluated for potential adverse effects.

### Study Population

To ensure a diverse mix of subject demographics and clinician experience, the study enrollment goal was set at approximately 80–100 subjects from six separate and geographically diverse practice settings. Enrollment criteria called for subjects of any skin type to be between the ages of 35 and 70 years and to have a desire for improved appearance of periorbital wrinkles or skin laxity in the periorbital area. All surgeons were in private practice and had extensive experience with laser treatments for skin lesion removal or skin resurfacing. Major exclusion criteria included blepharoplasty or chemical peel treatments within 1 year, collagen implants or usage of botulinum toxin type A within 6 months, or recent usage of retinoid either orally (6 months) or topically (2 weeks). Subjects with previous laser surgery were eligible only if the procedure had occurred at least 1 year prior to enrollment.

### RF Device

The ThermaCool TC System heats tissue using a proprietary method of coupling RF to skin by a thin capacitive membrane that distributes RF energy over a volume of tissue beneath the membrane surface. A cryogen system simultaneously cools the epidermal surface for protection. This combination of deep volumetric tissue heating and surface cooling allows sustained delivery of higher energy fluences in a single treatment. The prototype device used in this clinical trial is functionally similar to the device currently marketed as the ThermaCool TC system, but lacks many of the sophisticated features and controls that greatly enhance the usefulness and simplicity of the commercial unit.

The major components of the device include (1) an RF generator producing a 6-MHz alternating-current RF signal, the energy level of which is set by the clinician; (2) a handpiece for directing the RF energy to the skin, delivering cooling cryogen spray, and monitoring temperature, pressure, and RF feedback; (3) an electrode treatment tip, for transferring RF energy to skin and serving as a membrane for contact cooling; and (4) a cooling module that feeds cryogen through a controlled valve on the handpiece

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to the tip's contact cooling membrane. The system components are integrated with an imbedded Pentium®-based computer. User controls and a video screen for read-out of procedure data are located on the generator panel. Like conventional RF tissue heating devices, tissue heat is generated based on tissue's natural resistance to the movement of electrons within an RF field (Ohm's law), rather than photon absorption. As with lasers, the energy output can be stated in terms of joules as calculated by: impedance  $Z$  (ohms ( $\Omega$ )) to the movement of electrons creates heat (joules (J)) relative to the amount of current  $I$  (amps (A)), and time  $t$  (seconds) that current is delivered to tissue.

$$\text{Energy (J)} = I^2 \times Z \times t.$$

The distinguishing tissue-heating feature of the test device is the method of coupling of RF to the skin with a capacitive coupling membrane instead of a standard RF conducting electrode. This capacitive coupling method transforms RF to a volumetric or tissue "zone" heating device, rather than a concentrated "point" heating source as characterized by standard RF electrode heating devices such as a bovie. This unique volumetric heating method allows large amounts of energy (up to 220 J per  $\text{cm}^2$ ) to be distributed in a volume of tissue beneath the skin, without coagulation or burning at the electrode-to-skin interface, though the upper limit for facial skin is about 140 J. It is this novel method of distributing large energy deliveries evenly over a three-dimensional volume of tissue that differentiates the test device from standard RF devices and available light-based devices. In addition, the uniform electrical field distribution present at depths of at least 2.5-mm potentially heats deeper structures to higher temperatures than other tissue heating sources.

#### Treatment Procedure

Before the treatment session, each subject submitted to a series of photographs and a baseline wrinkle evaluation. The periorbital region extending from the wrinkled area at the outer canthus to the area above the eyebrow was targeted for treatment [4]. Topical anesthetic (5% lidocaine) was applied to the designated treatment area, which was then occluded with clear dressing for at least 45 minutes before treatment. After the anesthetic was thoroughly and completely wiped off with a dry gauze, the treatment area was marked in ink with a grid pattern of contiguous squares, each square slightly larger than the selected RF treatment tip (0.25 or 1  $\text{cm}^2$ ). The area of the grid and the planned number of RF applications depended on the size of the targeted treatment area in each subject. At the discretion of the investigator, some subjects received nerve blocks into the forehead area just superior to the eyebrow; this was administered either before or during the procedure. A RF return pad was adhered to the subject's back to create a return path for RF travel. A proprietary coupling fluid was spread over the treatment area to enhance thermal and electrical contact with the treatment tip.

Clinicians treated each ink-grid square of the target area with a separate application from the RF tip, resulting in

approximately 40–80 RF applications per patient. Each application consisted of three continuous and automatic phases: (1) cryogen pre-cooling, (2) simultaneous RF heating and cryogen cooling, and (3) cryogen post-cooling. A specific combination of treatment parameters that included the RF energy level, energy "on" time, and cooling rate for each application was initially set by the clinician by choosing 1 of 9 possible treatment level settings; the settings correlate with a range of 52–220 J delivered through the 1  $\text{cm}^2$  treatment tip surface. The choice of setting was determined mostly by the location and thickness of the skin directly within each targeted grid square. Lower fluences were used for areas directly over thinner wrinkled skin while higher fluences were selected for all other areas where a maximal tightening effect was desired. In addition, clinicians adjusted RF levels or upper limits according to subject pain tolerance during the procedure.

#### Efficacy Outcomes

For objective wrinkle evaluations, photographs obtained at baseline were compared with photographs taken at the 2-, 4-, and 6-month follow-up visits. Five views of the face were taken at each photographic session: front, 3/4 left, 3/4 right, full left, and full right. All photographs were masked to block investigator name, treatment settings, and treatment time. For each subject, sets of the masked photographs taken from the side angles but at different timepoints were then arranged in random (i.e., nonchronological) side-by-side fashion on a storyboard, and the three independent reviewers rated the periorbital wrinkles on each photograph according to the FWCS. After unblinding, the scores were compared to determine inter-rater reliability. Patient effect (outcome) was classified as improved or not on the left and right sides at different timepoints.

Investigator in-clinic evaluations of treatment outcome were assessed using the FWCS (Table 1). Wrinkles were classified into the nine Fitzpatrick subgroups by the investigator at baseline and then again during the post-treatment clinic visits at 2, 4, and 6 months. Clinicians did not refer to pre-treatment photographs while making post-treatment wrinkle assessments. For each subject, wrinkle improvement (reduction of subgroup score  $\geq 1$ ), no change, or worsening was calculated for each eye separately for each post-treatment clinical evaluation.

In accord with a post-hoc addendum to the study protocol, frontal photographs were also assessed objectively to determine the amount of forehead tissue tightening as evidenced by eyebrow lift above each eye. This assessment method was developed by clinical photographers and a research scientist at Thermage, Inc. One of the clinical photographers used Adobe PhotoShop 6.0 software to draw a horizontal reference line that intersected the apex of the inner canthus on each eye. On each side of the face, four measurements (at intervals of 1.5, 2.0, 2.5, and 3.0 cm outward from the inner canthus) were then made from this line up to the superior margin of the eyebrow. The average pre-treatment eyebrow values on each side were compared to the average post-treatment values at various timepoints. Measurements were recorded in 0.1 mm increments. Based

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TABLE 1. The Fitzpatrick Wrinkle Classification System (FWCS)

| Class | Wrinkling   | Score | Degree of elastosis   |
|-------|---|-------|---|
| I     | Fine wrinkles   | 1–3   | Mild (fine textural changes with subtly accentuated skin lines)   |
| II    | Fine to moderate depth wrinkles<br>Moderate number of lines                     | 4–6   | Moderate (distinct papular elastosis [individual papules with yellow translucency under direct lighting] and dyschromia)      |
| III   | Fine to deep wrinkles<br>Numerous lines<br>With or without redundant skin folds | 7–9   | Severe (multipapular and confluent elastosis [thickened yellow and pallid] approaching or consistent with cutis rhomboidalis) |

on pre-trial sensitivity testing, the margin of measurement error in detecting any objective change in brow position was determined to be  $\pm 0.5$  mm. Thus, patients whose average post-treatment eyebrow lift value was above the 0.5 mm sensitivity cutoff were classified as having objective evidence of tissue tightening. The average absolute value of lift was also reported. To meet the specifications of this validated methodology for measuring brow position, precise photographic conditions (including identical head positions and precise camera setup) were required. It was anticipated that many photographs would not be evaluable due to these procedural demands.

Subjects rated their overall satisfaction with the outcome at 2, 4, and 6 months after treatment by assigning a ranking of unsatisfied, neutral, satisfied, or very satisfied at each timepoint. They also rated their perception of skin tightness (looser, same, or tighter) and appearance (worse, same, or better) at 6 months after treatment. The RF brow-lifting effect was not specifically queried and, thus, was not captured in the patient satisfaction scoring.

#### Safety Outcomes

With each RF application, the subject called out the level of procedural pain (on a 5-point scale where 0 = no pain and 4 = intolerable pain). Adverse events were also noted. Thermal injuries were classified by investigators as 1st degree (involving only the epidermis, and characterized by transient erythema and edema without blisters or a break in the skin); 2nd degree superficial or deep (involving destruction of epidermis as well as a variable portion of the dermis [superficial or deep], and characterized by blistering and scabbing that resolved in 1 month [superficial] or longer [deep]); or 3rd degree (involving destruction of the entire thickness of the skin resulting in scarring that did not spontaneously resolve). Investigators documented observations of signs and symptoms related to the treatment area immediately after and within 72 hours of treatment, and then again at 1, 2, 4, and 6 months post-treatment. The photographs used in the efficacy evaluation also provided documentation of reported adverse events.

#### RESULTS

##### Study Population

Of the 87 subjects enrolled into the study, 86 completed the RF treatment course. One subject dropped out just

minutes after initiating RF treatment, citing extreme nervousness. Two subjects were lost to follow-up after 1 month, and another subject was lost to follow-up after 4 months. The number of subjects per clinic ranged from 9 to 20. The study population was fairly diverse in terms of age (mean 54 years) and skin type on the Fitzpatrick scale (19) (Table 2). Skin types were pre-dominantly Type II but ranged from Type I to Type IV. All nine subclasses of wrinkle classifications were represented in the study population at baseline, with an average investigator-assigned FWCS score of 4.7 (Table 3). There were 13 violations of protocol, including eight involving subjects who were enrolled and treated despite being over age 70 years. However, all 86 patients who completed treatment were the basis for all safety evaluations, and all 83 patients who completed 6 months of follow-up were the basis for all efficacy evaluations; full data were not available for all patients at all timepoints due to missing data on case report forms, missing or unevaluable photographs, or missed patient visits.

TABLE 2. Subject Demographics

|                        | Category  | Number of subjects | Percentage of subjects evaluated |
|------------------------|-----------|--------------------|----------------------------------|
| Gender                 | Female    | 79                 | 92                               |
|                        | Male      | 7                  | 8                                |
| Age group              | <40       | 6                  | 7                                |
|                        | 41–50     | 28                 | 33                               |
|                        | 51–60     | 33                 | 38                               |
|                        | > 60      | 19                 | 22                               |
| Ethnicity              | Caucasian | 72                 | 84                               |
|                        | Hispanic  | 13                 | 15                               |
|                        | Asian     | 1                  | 1                                |
| Sun-reactive skin type | I         | 7                  | 8                                |
|                        | II        | 48                 | 56                               |
|                        | III       | 23                 | 27                               |
|                        | IV        | 8                  | 9                                |
| Prior treatments       | Yes       | 4                  | 5                                |
|                        | No        | 82                 | 95                               |
| Smoking history        | Yes       | 16                 | 19                               |
|                        | No        | 70                 | 81                               |

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**TABLE 3. Fitzpatrick Wrinkle Classifications Assigned by Investigator for 86 Subjects at Baseline Clinical Visit**

| Class | Scores | Assigned at baseline |      |
|-------|--------|----------------------|------|
|       |        | Right                | Left |
| I     | 1      | 4                    | 4    |
|       | 2      | 7                    | 7    |
|       | 3      | 5                    | 5    |
| II    | 4      | 30                   | 30   |
|       | 5      | 13                   | 12   |
| III   | 6      | 10                   | 11   |
|       | 7      | 10                   | 10   |
|       | 8      | 5                    | 5    |
|       | 9      | 2                    | 2    |

**RF Treatments**

The average number of RF treatment applications per subject was 68 (range=23–114). The average energy setting for these applications was 16 (range=11–21) (Fig. 1). The amount of energy delivered at these settings was equivalent to approximately 58–140 J/cm<sup>2</sup> area of skin. The 1 cm<sup>2</sup> treatment tip was employed for almost all RF applications; two subjects received a few applications with the 1/4 cm<sup>2</sup> tip in addition to their main treatment with the standard-size tip. Of the 86 subjects completing an RF treatment course, 22 received a nerve block just superior to the eyebrows immediately prior to or shortly after initiation of RF treatment. The average RF setting for these 22 patients was similar to that of the overall patient population.

**Efficacy**

At least one evaluable photograph was available for 62 of the 83 subjects at 6 months. The 6-month photographs were of poor technical quality or unavailable in 21 patients; only a single left or right side photograph was evaluable in five patients. The independent and blinded review of evaluable photographic results documented consistent and, in many patients, progressively increasing improvements in wrinkle scores over the full 6-month study period. At the

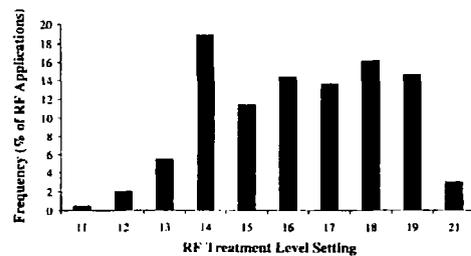


Fig. 1. Distribution of radiofrequency (RF) treatment levels in 86 subjects (1 cm<sup>2</sup> treatment tip only).

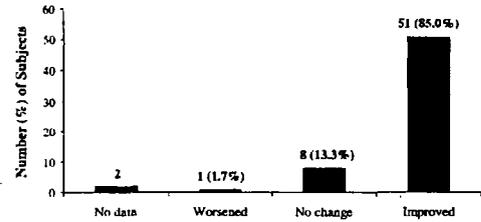


Fig. 2. Number of subjects showing improvement, no change, or worsening 6 months after a single RF treatment based on blinded independent review of photos: right side of face.

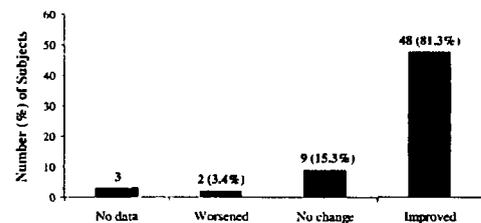


Fig. 3. Number of subjects showing improvement, no change, or worsening 6 months after a single RF treatment based on blinded independent review of photos: left side of face.

interim 4-month timepoint, 79.1% (76/96) of treated periorbital areas showed  $\geq 1$  FWCS score improvement from baseline. A representative photograph of a subject with objective signs of wrinkle diminution after the single RF treatment is shown in Figure 4. Between the 4- and 6-month photographic review, wrinkle improvements were maintained and, in several more subjects, became noticeable for the first time. In the 62 subjects for whom at least one evaluable photograph was available at 6 months, 83.2% (99/119) of treated periorbital areas showed a baseline-to-6-month improvement in wrinkle scores. Results for the left and right sides are shown in Figures 2 and 3. Over this same half-year period, 14.3% (17/119) of treated areas had no change and 2.5% (3/119) worsened. Of the 99 areas showing objective improvement, 64.6% (64/99) of the left and right treated areas improved by one Fitzpatrick point, 31.3% (31/99) improved by two Fitzpatrick points, and 4.0% (4/99) improved by three or more Fitzpatrick points.

Investigator-assigned wrinkle scores were based on in-clinic examinations at baseline, 2, 4, and 6 months; the investigators did not have access to photographs from previous visits. This subjective evaluation of treated left and right periorbital areas at 6 months showed that 92.8% (154/166) had either improved (i.e., by a decrease of at least one Fitzpatrick point) or remained the same (Table 4). Improvements of at least one Fitzpatrick point (e.g., from score 6 at baseline to score 5) were seen in 25.0% (37/148) of treated areas at 2 months, increasing to 28.9% (48/166) at

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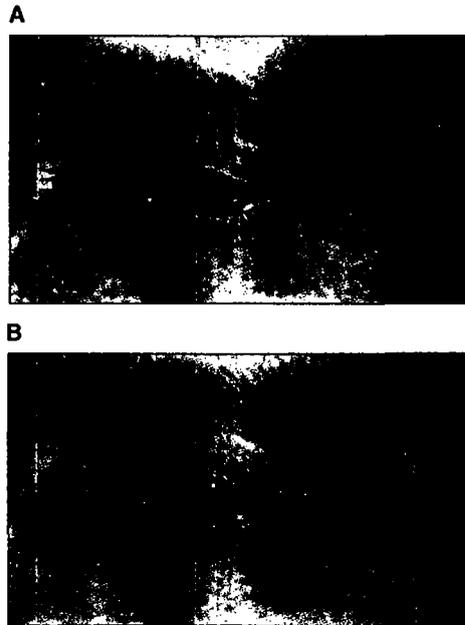


Fig. 4. Example of wrinkle reduction after RF treatment. A: Pre-treatment; (B) 4 months post-treatment. [Figure can be viewed in color online via [www.interscience.wiley.com](http://www.interscience.wiley.com).]

6 months. Wrinkles had worsened in 7.2% (12/106) of the periorbital areas.

Computer-aided measurement of evaluable photographs for post-treatment eyebrow lift was conducted. To meet the specifications of this validated methodology for measuring brow position, precise photographic conditions (including identical head positions and precise camera setup) were required. As a result, only 60 subjects had paired before-and-after pictures that qualified as evaluable for purposes

of the brow measurement, 27 subjects with a 1- to 4-month photograph and 33 subjects with a 6-month photograph. Left and right sides were measured separately and in one subject, only one side of the photograph was suitable for computer analysis. Overall, 66.4% (79/119) of left or right eyebrows had an average lift that was greater than the predetermined minimum threshold for tissue tightening detection ( $\geq 0.5$  mm) from baseline to the time of the follow-up photograph. Average lift was 1.49 mm in all the right sides and 1.30 mm in all the left sides. Representative photographs of a subject with measurable eyebrow lift are shown in Figure 5. Overall, in those subjects with 6-month post-treatment photographs, 61.5% (40/65) of measured eyebrows were raised above the threshold of detection.

Treatment satisfaction data were available from 82 subjects at 6 months (Table 5). Overall, 50% (41/82) of these subjects reported they were satisfied or very satisfied with the treatment outcome, and similar percentages rated their skin to be tighter and their appearance as better. No data on patient satisfaction with the RF brow-lifting effect were collected.

**Safety**

Each subject's application-related pain scores (typically for about 34 applications per side) were averaged. The average pain score on each side was mild or moderate for most patients (Table 6). In those cases when early RF applications produced an uncomfortable level, the clinician could reduce the RF energy level for subsequent applications. Those subjects receiving nerve blocks reported no pain in almost all instances.

The most frequently noted treatment-related events were erythema (36.0% incidence immediately and 16.7% within 72 hours) and edema (13.9% immediately and 6.4% within 72 hours) (Table 7). By 1 month, no subject had signs of edema, and only 3 (3.9%) had lingering signs of erythema. These early and transient 1st degree burns were not unexpected. Scabbing was the next most frequent procedure-related adverse event, seen in 7.7% of subjects at the early clinic visit, in 1.4% at 2 months, and in no subjects at 6 months.

There were no 3rd degree burns, but 15 subjects were reported to have at least one grid-spot of 2nd degree

**TABLE 4. Wrinkle Improvement After a Single Radiofrequency (RF) Treatment: Investigator Clinical Assessments Over Time**

|                                       | Fitzpatrick classification scores over time |            |                      |            |                      |            |
|---------------------------------------|---|------------|----------------------|------------|----------------------|------------|
|                                       | Baseline to 2 months                        |            | Baseline to 4 months |            | Baseline to 6 months |            |
|                                       | Right                                       | Left       | Right                | Left       | Right                | Left       |
| Eyes with data                        | 74  | 74         | 80                   | 80         | 83                   | 83         |
| Number of eyes (%) with improvement   | 19 (25.7%)                                  | 18 (24.3%) | 22 (28.6%)           | 21 (26.2%) | 24 (28.9%)           | 24 (28.9%) |
| Number of eyes (%) remaining the same | 49 (66.2%)                                  | 51 (68.9%) | 51 (66.2%)           | 53 (68.3%) | 53 (63.9%)           | 53 (63.9%) |
| Number of eyes (%) with worsening     | 6 (8.1%)                                    | 5 (6.8%)   | 7 (9.1%)             | 6 (7.5%)   | 6 (7.2%)             | 6 (7.2%)   |

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Fig. 5. Example of eyebrow lift after RF treatment, as described in text. A: Pre-treatment; (B) 6 months post-treatment: average lift 1.7 mm (right) and 2.0 mm (left). [Figure can be viewed in color online via [www.interscience.wiley.com](http://www.interscience.wiley.com).]

TABLE 5. Subject Evaluation of Treatment Outcome

| Visit interval        | 2 Month<br>(N 70) | 4 Month<br>(N 74) | 6 Month<br>(N 82) |
|-----------------------|-------------------|-------------------|-------------------|
| <b>Satisfaction</b>   |                   |                   |                   |
| Very satisfied        | 8 (11%)           | 11 (15%)          | 10 (12%)          |
| Satisfied             | 24 (34%)          | 24 (32%)          | 31 (38%)          |
| Neutral               | 28 (40%)          | 29 (39%)          | 26 (30%)          |
| Unsatisfied           | 10 (14%)          | 10 (14%)          | 16 (20%)          |
| <b>Skin tightness</b> |                   |                   |                   |
| Looser                | 0                 | 2 (3%)            | 2 (2%)            |
| Same                  | 48 (69%)          | 44 (59%)          | 43 (52%)          |
| Tighter               | 22 (31%)          | 28 (38%)          | 37 (45%)          |
| <b>Appearance</b>     |                   |                   |                   |
| Worse                 | 2 (3%)            | 1 (1%)            | 3 (4%)            |
| Same                  | 36 (51%)          | 38 (51%)          | 38 (46%)          |
| Better                | 31 (44%)          | 35 (47%)          | 40 (49%)          |

burning, accounting for 15 burns that were classified as superficial and six as deep. The 21 2nd degree burns resulting from a total of 5,858 RF exposures represented an overall observed burn risk of 0.36% per application. Three clinic sites accounted for all but one of the 2nd degree burns.

TABLE 6. Subject Comfort Level During RF Treatment

| Pain (score)         | Average pain score (N 86) |            |           |            |
|----------------------|---------------------------|------------|-----------|------------|
|                      | Right side                | Percentage | Left side | Percentage |
| No pain (0)          | 10                        | 12         | 3         | 3          |
| Mild pain (1)        | 34                        | 40         | 39        | 45         |
| Moderate pain (2)    | 33                        | 38         | 30        | 35         |
| Severe pain (3)      | 8                         | 9          | 11        | 13         |
| Intolerable pain (4) | 1                         | 1          | 3         | 3          |

The areas of epidermal interruption ranged from 4 to 9 mm in length. Three of the five subjects with deep 2nd degree burns developed residual scars and were offered laser treatment. Another subject developed mild, focal textural changes, and the fifth subject had complete resolution of scarring by 6 months. A representative photographic sequence of a subject with early burning and resolution is shown in Figure 6.

Other adverse events were reported by five subjects. Forehead bruising resolving in 3–4 weeks (three subjects) and altered sensation (two subjects) were both thought to be

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TABLE 7. Clinical Observations After RF Treatment

| Clinical observation  | Time intervals           |            |                          |                          |          |                          |
|---|--------------------------|------------|--------------------------|--------------------------|----------|--------------------------|
|   | Immediate                | Early      | 1 Month                  | 2 Months                 | 4 Months | 6 Months                 |
| Clinical signs  | N = 86                   | N = 78     | N = 76                   | N = 74                   | N = 80   | N = 83                   |
| Abrasion  | 2 (2.3%)                 | 4 (5.1%)   | 0                        | 0                        | 0        | 0                        |
| Edema   | 12 (13.9%)               | 5 (6.4%)   | 0                        | 0                        | 0        | 0                        |
| Erythema  | 31 (36.0%)               | 13 (16.7%) | 3 (3.9%)                 | 1 (1.4%)                 | 0        | 0                        |
| Blistering  | 2 (2.3%)                 | 3 (3.8%)   | 0                        | 0                        | 0        | 0                        |
| Blanching   | 1 (1.2%)                 | 0          | 0                        | 0                        | 0        | 0                        |
| Bruising  | 0                        | 3 (3.8%)   | 0                        | 0                        | 0        | 0                        |
| Crusting  | 0                        | 2 (2.6%)   | 0                        | 0                        | 0        | 0                        |
| Hyperpigmentation   | 0                        | 0          | 1 (1.3%)                 | 1 (1.4%)                 | 1 (1.2%) | 0                        |
| Oozing  | 0                        | 1 (1.3%)   | 0                        | 0                        | 0        | 0                        |
| Purpura   | 1 (1.2%)                 | 2 (2.6%)   | 0                        | 0                        | 0        | 0                        |
| Scabbing  | 0                        | 6 (7.7%)   | 2 (2.6%)                 | 1 (1.4%)                 | 0        | 0                        |
| Ulcer   | 1 (1.2%)                 | 4 (5.1%)   | 1 (1.3%)                 | 0                        | 0        | 0                        |
| Scarring  | 0                        | 0          | 1 (1.3%)                 | 1 (1.4%)                 | 5 (6.3%) | 3 (3.6%)                 |
| Textural change   | 0                        | 0          | 1 (1.3%)                 | 1 (1.4%)                 | 1 (1.2%) | 2 (2.4%)                 |
| Other   | 1 (1.2%)<br>(white area) | 0          | 1 (1.3%)<br>(tenderness) | 1 (1.4%)<br>(tenderness) | 0        | 1 (1.2%)<br>(poison ivy) |
| Totals  | 51                       | 43         | 10                       | 6                        | 7        | 6                        |
| Total number (%) of subjects with observations <sup>a</sup> | 36 (41.9%)               | 24 (30.8%) | 7 (9.2%)                 | 4 (5.4%)                 | 6 (7.5%) | 7 (8.4%)                 |

<sup>a</sup>Some subjects with multiple clinical signs are listed more than once within given time interval.

related to use of nerve block. There was one case of post-treatment urticarial swelling that appeared in a hatched pattern of red ridges, apparently demarcating the edge of the treatment tip movement over the treatment grid; this urticaria occurred in a patient pre-treated with nerve block and receiving higher joule settings. Headaches lasting less than 24 hours (one subject) or persisting for months following treatment (two subjects) were of unknown relationship to the device. One subject presented at the 6-month visit with an allergic reaction that was deemed related to her history of food allergies.

#### DISCUSSION

There is a growing population seeking to minimize signs of aging without the risks or prolonged recovery of laser procedures [11,20] and there are numerous laser and nonlaser technologies being developed and studied to meet this need. This was the first large multicenter evaluation of a new nonablative RFTT device for cosmetic use. This RF method of heating tissue—with controlled volumetric heating of deeper cutaneous tissues resulting in tissue tightening—differs radically from traditional laser methods. In this 6-month trial, the clinical significance of this novel tightening mechanism was demonstrated in subsets of patients evaluated by different techniques: 83% wrinkle improvement was seen in photographic review, 29% by clinical assessment, and 62% of upper eyelids were elevated. While a number of questions remain, this initial study clearly shows the potential for dramatic clinical benefit with RFTT.

A major limitation of this study's design is that it did not attempt to vary treatment factors that are likely to optimize outcome in clinical practice, such as treatment setting titration, patient selection, and treatment algorithm variations. The size and design of this study did not allow, for example, for subgroup analysis of patients receiving lower or higher numbers of RF applications, patients receiving lower or higher fluence levels (especially those receiving high fluences after nerve block), or patients within varying photoaging classes. In future studies, it will be important to correlate such procedural and patient variables with both wrinkle outcome and adverse event frequency. This will be of particular interest to clinicians seeking the best results from this promising technology.

Notwithstanding the nonoptimal study design, the results of this multicenter 6-month clinical study are significant. Most importantly, analysis of photographs showed clear reductions in wrinkles in the majority of the 86 subjects from a single treatment session. The patient questionnaire, which limited patient feedback on efficacy to the periorbital wrinkles revealed that about half of the subjects were very satisfied or satisfied with the wrinkle reduction results at 6 months. This relatively low number is possibly reflective of the narrow scope of the patient questionnaire, which did not capture the changes in brow position or other potential tissue changes, and lack of patient access to the pre-treatment photographs. Further, the modest nature of wrinkle reduction over a 6-month study period may be difficult to discern with daily self-observation. Similarly, the difference between the results

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of the photographic evaluation and the results of the clinician's analysis (again, without reference to the pre-treatment photograph) likely reflects the difficulty in registering subtle changes in a dynamic viewing of the patient versus in a side-by-side comparison of static photographs.

With the recent FDA clearance of this device for cosmetic use—an approval based largely on the generally positive results of this large clinical study—more dermatologists, plastic surgeons, and other aesthetic specialists are now evaluating RF for use in a range of tissue tightening procedures. Clinicians should keep in mind several issues as they consider employing this device for aesthetic procedures, including: the unknown contribution of additional treatment sessions, the likely role of treatment setting titration for each patient and even for each tissue area, and the possibility that certain types of laxity and wrinkles are more likely to respond to a deep volumetric heating effect than others. A better understanding of these variables is likely to lead to more impressive outcomes in the future. Quantifying the efficacy of noninvasive cosmetic procedures is notoriously difficult [8,11]. Histologic

changes, although interesting and objective, do not always correlate with aesthetic improvements. Although patients and clinicians frequently report subjective improvements in skin tone and texture after procedures with nonablative techniques, the degree of this mild improvement is hard to measure objectively (i.e., via photography or other techniques) [10].

To add scientific rigor in the present study, three blinded observers rated the post-treatment wrinkle improvements seen on photographs, and a computer-aided photoanalysis program was created to measure eyebrow lift. As suspected at the study outset, the strict technical criteria of these photography-based outcome measures led to a high number of patients being deemed unevaluable. Still, by both of these more objective outcome measures, the treatment session produced positive results at 6 months, with 83% of treated areas showing wrinkle improvement and 61% of eyebrows being elevated by at least 0.5 mm. Significantly, the wrinkle improvements increased continuously from 2 to 4 to 6 months after a single treatment session, a clinical pattern reflecting the postulated two-phase mechanism of action with RFTT: a short-term initial tightening effect due to

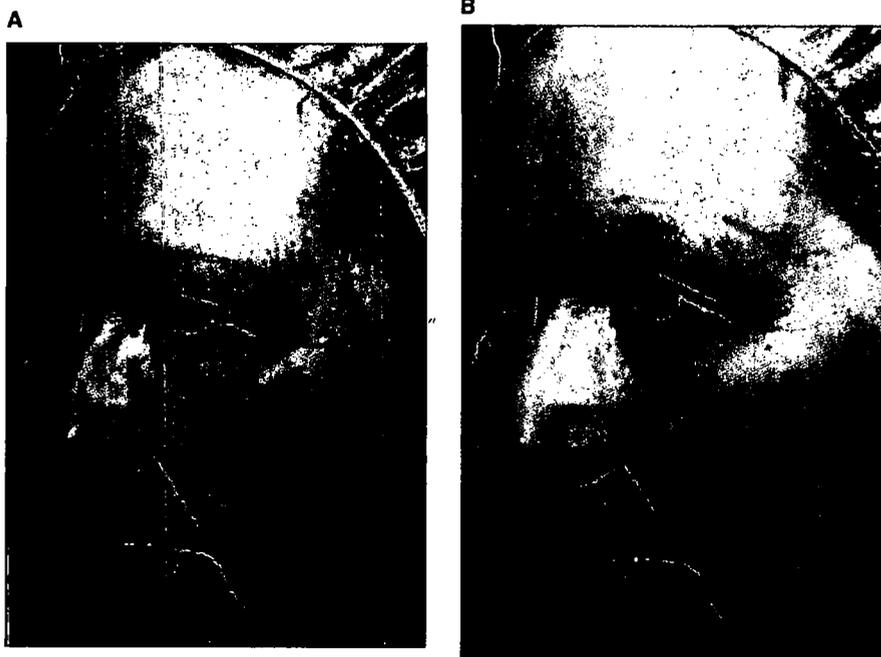


Fig. 6. Example of adverse event after RF treatment, showing small burn and subsequent resolution. A: Pre-treatment; (B) 1 hour post-treatment; (C) 6 months post-treatment. [Figure can be viewed in color online via [www.interscience.wiley.com](http://www.interscience.wiley.com).]

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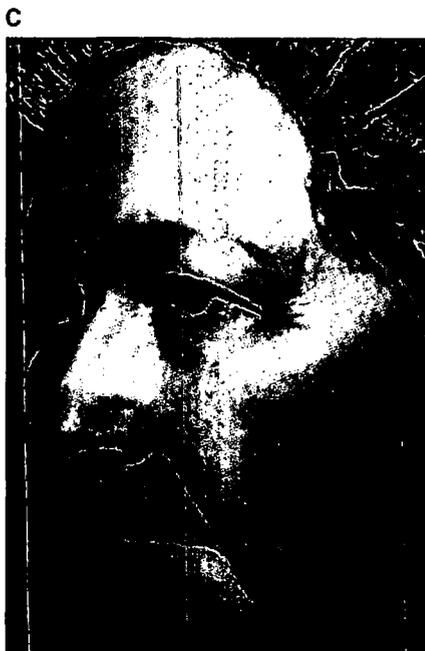


Fig. 6. (Continued)

primary collagen contraction followed by a longer-term (e.g., 6 months or more) remodeling effect with further tightening due to secondary collagen synthesis [1-3,21]. The more subjective interpretations of the investigators and the subjects themselves lend support to the objective evidence of a durable and evolving RF efficacy.

The high degree of safety with this technique is impressive. In this study, the device's simultaneous RF heating and cryogen cooling allowed delivery of energy sufficient to produce good efficacy without also causing long-lasting skin damage. There was considerable center-to-center variation in the rates of 2nd-degree burns following RF treatment, with two clinics reporting no such burns and one clinic accounting for 9 of the 21 reports, suggesting some influence of user technique on safety outcome. Such variations are expected, and may reflect differences in clinic populations or in clinician technique, choice of RF settings, use of nerve block, or reporting accuracy. As previously described, the study was not powered to test the potential correlation between RF setting and either wrinkle outcome or burn frequency. However, the investigators did note a general concordance between higher treatment fluence and higher incidence of burns and by the end of the study had begun developing procedures that might eventually result in even higher

levels of safety. Specifically, investigators (1) decreased treatment fluence over areas of bony prominence, since these areas receive intensified treatment effects, (2) removed lipid-based skin creams and applied adequate coupling gel to avoid epidermal heating, and (3) applied the treatment tip with uniform four-corner pressure to avoid preferential application of energy to any one tissue contact point (an edge-of-tip effect that may account for the single case of urticaria). Refinement of such protocol issues and identification of individuals at highest risk for burns and other adverse effects will result in a very high level of safety for RFTT.

The documentation of eyebrow lift seems to confirm the early general impressions reported by investigators that RF treatment not only smoothed wrinkles but also, in many subjects, led to a more "open" expression. However, it should be noted that this endpoint was not included in the original protocol, but was instead added post-hoc to the results analysis based on investigator feedback. The principle of tightening tissue to "lift" adjacent structures has long been employed with conventional incisional plastic surgical procedures. The apparent potential of this novel RF device to achieve even a fraction of a similar "lifting" or tightening benefit without an incision is of great interest to the aesthetic practitioner and patient, and may well represent a more important application for this novel technology than these carefully studied, but modest wrinkle reduction effects.

The mechanism for this observation of clinical tightening is unknown, though the relatively deep electrical field depth of at least 2.5 mm suggests the potential to heat both dermal and fascia components. We have previously investigated the etiology of the skin tightening observed immediately following CO<sub>2</sub> ablative resurfacing. In this setting, the thermal reactions of the collagen helix provided an explanation, as collagen reacts in a predictable manner to heat, resulting in reconfiguration of the helical structure at specific instantaneous temperature changes 96°C in human collagen). Thermal changes beyond this point (> 70°C) resulted in denaturation of the helical structure and loss of configuration. These clinical and experimental findings with CO<sub>2</sub> laser resurfacing provided the impetus for methods that would tighten the skin laxity without ablating the epidermis. A multitude of lasers have been used in attempts to achieve this nonablative resurfacing but these systems are thought to improve skin texture and remove fine lines not via tissue tightening but by induction of minor superficial dermal wounding and subsequent regeneration of new collagen in the papillary dermis. Thus, clinical findings suggesting that a new RF device can induce skin tightening via controlled volumetric heating of the deeper cutaneous tissues are noteworthy. Questions about the exact location, timing, and mechanism of the tissue tightening remain. For example, the pain sensation at the time of treatment suggests deep-plane tightening rather than dermal layer effects; the lack of textural improvement in many patients with tightening also supports the concept of deep tightening. And while the immediate tightening noted in many patients is consistent with collagen helical

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FITZPATRICK ET AL

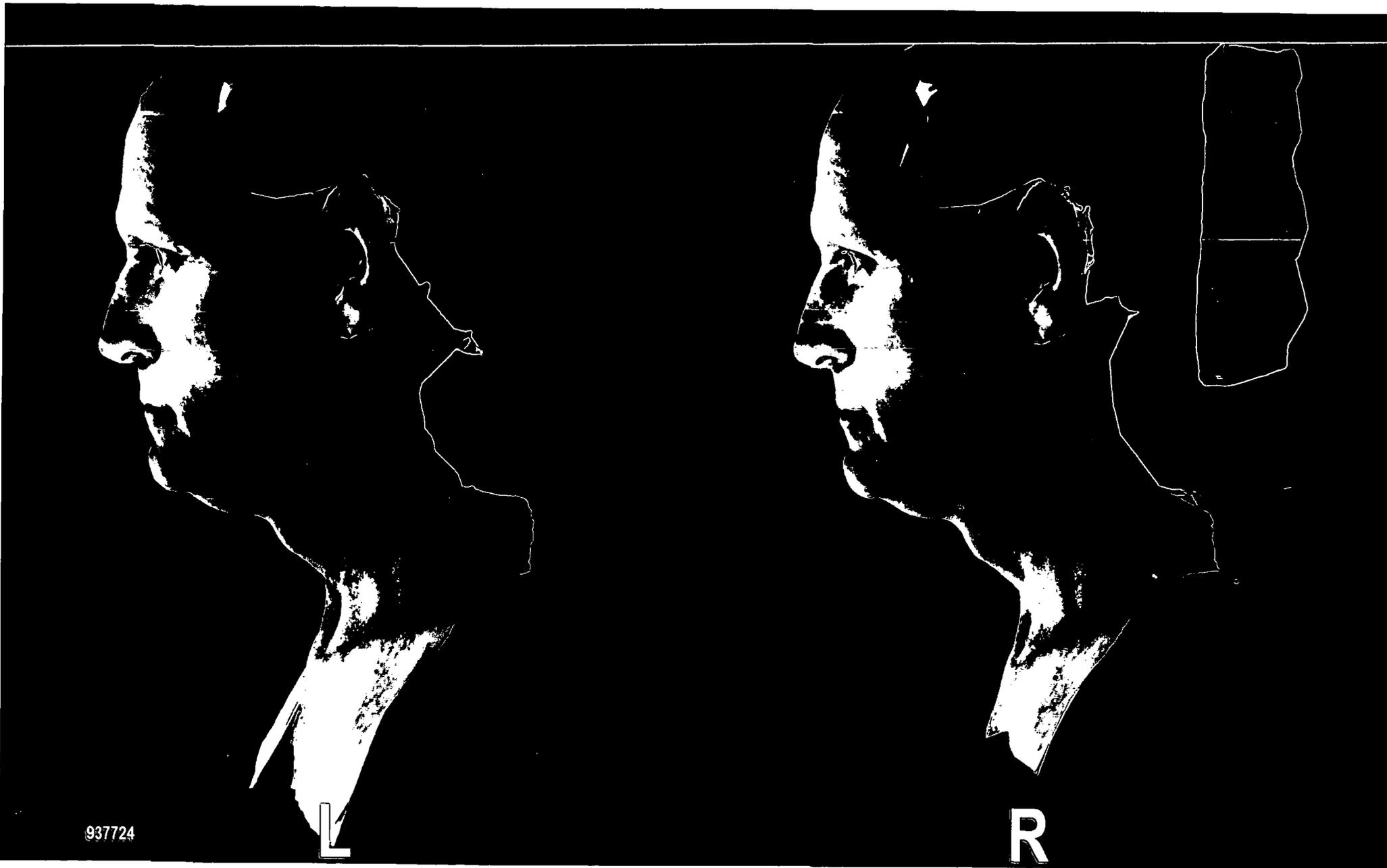
structural changes secondary to thermal change, the slower and more subtle tightening effects noted over a period of 2–6 months suggest a mechanism related to wound healing and tissue remodeling. More studies are needed to better define the depth of tissue heating and the mechanisms of tissue tightening, and to correlate these actions to clinical findings. As the novel tissue tightening effects of RF are defined, the range of clinical applications may expand. The RFTT device could potentially be useful, for example, not only on the lower face, jowls, and neck but also in other body areas (e.g., abdominal skin, arms, legs) where tissue laxity associated with aging is problematic for patients.

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**Appendix 6: Patient Photographs**

**MRN 937724 - Non- Responder (Left Pre-Treatment, Right Post-Treatment)**



**MRN 932611 - Responder (Left Post-Treatment, Right Pre-Treatment)**



932611

\* \* \* COMMUNICATION RESULT REPORT ( OCT. 5. 2012 10:08AM ) \* \* \*

FAX HEADER 1:  
FAX HEADER 2:

| TRANSMITTED/STORED<br>FILE MODE | OCT. 5. 2012 9:58AM<br>OPTION | ADDRESS      | RESULT  | PAGE |
|---------------------------------|-------------------------------|--------------|---------|------|
| 9791 MEMORY TX                  |                               | 914896194071 | E-3) 3) | 0/3  |

REASON FOR ERROR  
E-1) HANG UP OR LINE FAIL  
E-3) NO ANSWERE-2) BUSY  
E-4) NO FACSIMILE CONNECTION

## DEPARTMENT OF HEALTH &amp; HUMAN SERVICES

Public Health Service

Food and Drug Administration  
10903 New Hampshire Avenue  
Document Control Room --WO66-G609  
Silver Spring, MD 20993-0002

Ulthera, Incorporated  
% Ms. Suzon Lommel  
Vice President of Regulatory & Quality Affairs  
2150 South Country Club Drive, Suite 21  
Mesa, Arizona 85210

OCT 2 2012

Re: K121700  
Trade/Device Name: Ulthera<sup>®</sup> System  
Regulation Number: 21 CFR 878.4590  
Regulation Name: Focused ultrasound stimulator system for aesthetic use  
Regulatory Class: Class II  
Product Code: OHV  
Dated: August 1, 2012  
Received: August 3, 2012

Dear Ms. Lommel:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical



**COVER SHEET MEMORANDUM**

From: Reviewer Name Richard P. Foster  
 Subject: 510(k) Number K121700/S1  
 To: The Record

- Please list CTS decision code SE
- Refused to accept (Note: this is considered the first review cycle, See Screening Checklist [http://eroom.fda.gov/eRoomReq/Files/CDRH3/CDRHPremarketNotification510kProgram/0\\_5631/Screening%20Checklist%207%202%2007.doc](http://eroom.fda.gov/eRoomReq/Files/CDRH3/CDRHPremarketNotification510kProgram/0_5631/Screening%20Checklist%207%202%2007.doc))
  - Hold (Additional Information or Telephone Hold).
  - Final Decision (SE, SE with Limitations, NSE (select code below), Withdrawn, etc.).

Not Substantially Equivalent (NSE) Codes

- NO NSE for lack of predicate
- NI NSE for new intended use
- NQ NSE for new technology that raises new questions of safety and effectiveness
- NU NSE for new intended use AND new technology raising new questions of safety and effectiveness
- NP NSE for lack of performance data
- NS NSE no response
- NL NSE for lack of performance data AND no response
- NM NSE pre-amendment device call for PMAs (515i)
- NC NSE post-amendment device requires PMAs
- NH NSE for new molecular entity requires PMA
- TR NSE for transitional device

| Please complete the following for a final clearance decision (i.e., SE, SE with Limitations, etc.):   |                                      | YES | NO |
|---|--------------------------------------|-----|----|
| Indications for Use Page  | Attach IFU                           | X   |    |
| 510(k) Summary /510(k) Statement  | Attach Summary                       | X   |    |
| Truthful and Accurate Statement.  | Must be present for a Final Decision | X   |    |
| Is the device Class III?  |                                      |     | X  |
| If yes, does firm include Class III Summary?  | Must be present for a Final Decision |     | NA |
| Does firm reference standards?<br>(If yes, please attach form from <a href="http://www.fda.gov/opacom/morechoices/fdaforms/FDA-3654.pdf">http://www.fda.gov/opacom/morechoices/fdaforms/FDA-3654.pdf</a> )  |                                      | X   |    |
| Is this a combination product?<br>(Please specify category <u>N</u> , see <a href="http://eroom.fda.gov/eRoomReq/Files/CDRH3/CDRHPremarketNotification510kProgram/0_413b/CO-MBINATION%20PRODUCT%20ALGORITHM%20(REVISED%203-12-03).DOC">http://eroom.fda.gov/eRoomReq/Files/CDRH3/CDRHPremarketNotification510kProgram/0_413b/CO-MBINATION%20PRODUCT%20ALGORITHM%20(REVISED%203-12-03).DOC</a> ) |                                      |     | X  |
| Is this a reprocessed single use device?<br>(Guidance for Industry and FDA Staff – MDUFMA - Validation Data in 510(k)s for Reprocessed Single-Use Medical Devices, <a href="http://www.fda.gov/cdrh/ode/guidance/1216.html">http://www.fda.gov/cdrh/ode/guidance/1216.html</a> )  |                                      |     | X  |
| Is this device intended for pediatric use only?   |                                      |     | X  |
| Is this a prescription device? (If both prescription & OTC, check both boxes.)  |                                      | X   |    |
| Did the application include a completed FORM FDA 3674, Certification with Requirements of ClinicalTrials.gov Data Bank?   |                                      |     | NA |
| Is clinical data necessary to support the review of this 510(k)?  |                                      | X   |    |
| For United States-based clinical studies only: Did the application include a completed FORM FDA 3674, Certification with Requirements of ClinicalTrials.gov Data Bank? (If study was  |                                      |     | NA |

conducted in the United States, and FORM FDA 3674 was not included or incomplete, then applicant must be contacted to obtain completed form.)

Does this device include an Animal Tissue Source?

All Pediatric Patients age <= 21

Neonate/Newborn (Birth to 28 days)

Infant (29 days - < 2 years old)

Child (2 years - < 12 years old)

Adolescent (12 years - < 18 years old)

Transitional Adolescent A (18 - < 21 years old) Special considerations are being given to this group, different from adults age >= 21 (different device design or testing, different protocol procedures, etc.)

Transitional Adolescent B (18 - <= 21; No special considerations compared to adults => 21 years old)

Nanotechnology

Is this device subject to the Tracking Regulation? (Medical Device Tracking Guidance, <http://www.fda.gov/cdrh/comp/guidance/169.html>)

Contact OC.

| Regulation Number | Class* | Product Code |
|-------------------|--------|--------------|
| 877.4190          | II     | OHV          |

(\*If unclassified, see 510(k) Staff)

Additional Product Codes:

|                |               |         |
|----------------|---------------|---------|
| Review:        | GSAB          | 10/2/12 |
| (Branch Chief) | (Branch Code) | (Date)  |

|                     |         |
|---------------------|---------|
| Final Review:       | 10/2/12 |
| (Division Director) | (Date)  |



## DEPARTMENT OF HEALTH AND HUMAN SERVICES

## MEMORANDUM

Food and Drug Administration  
Office of Device Evaluation  
9200 Corporate Boulevard  
Rockville, MD 20850

**Premarket Notification [510(k)] Review  
Traditional/Abbreviated**

**K121700/S1\_\_\_\_\_**

Date: September 30, 2012

To: The Record

From: Richard P. Felten

Office: ODE

Division: DSORD

510(k) Holder: Ulthera, Inc.

Device Name: Ulthera System

Contact: Suzon Lommel

Phone: 480-649-4069

Fax: 480-619-4071

Email: s.lommel@ulthera.com

**I. Purpose and Submission Summary**

The 510(k) holder would like to introduce add a new indication for use to their already legally marketed focused ultrasound system identified as the Ulthera System.

**II. Administrative Requirements**

|   | Yes | No | N/A |
|---|-----|----|-----|
| Indications for Use page (Indicate if: Prescription or OTC) | X   |    |     |
| Truthful and Accuracy Statement                             | X   |    |     |
| 510(k) Summary or 510(k) Statement                          | X   |    |     |
| Standards Form  |     |    | X   |

**III. Device Description**

|   | Yes | No | N/A |
|---|-----|----|-----|
| Is the device life-supporting or life sustaining?         |     | X  |     |
| Is the device an implant (implanted longer than 30 days)? |     | X  |     |
| Does the device design use software?                      | X   |    |     |
| Is the device sterile?                                    |     | X  |     |
| Is the device reusable (not reprocessed single use)?      | X   |    |     |
| Are "cleaning" instructions included for the end user?    |     |    |     |

The Ulthera System is a focused ultrasound system that is designed to deliver focused ultrasound to a fixed depth to provided localized coagulation for the purpose of production of new collagen that is

intended to result in tissue tightening for the requested indications for use.

#### **IV. Indications for Use**

The Ulthera System is presently legally marketed for the indication for use of eyebrow lift. The company is now requesting marketing clearance for the indications of "lift lax submental (beneath the chin) and neck tissue" and "lift lax tissue to achieve a desired aesthetic effect for the full face and neck". The "desired aesthetic effect" indication is problematic and it is doubtful at this time whether or not ODE would grant this indication for use.

The company has addressed the issue of "desired aesthetic effect" by discussing that aging produces sagging of the brow, chin, and neck and therefore by showing their device can lift these sites they have shown that the full face is being affected. This indication is still problematic in that in order to achieve both process then the individual would seem to require an eyebrow lift and the chin and neck lift at the same time. There does not appear to be data to support this simultaneous procedure in terms of safety and adverse effects.

Following discussions within the branch and with the company on October 1, 2012, the company has decided to delete their request for the third indication for use "lift lax tissue to achieve a desired aesthetic effect for the full face and neck". The concern the Branch has with this indication for use is in terms of what other benefit does full face treatment provide and is there evidence if a full face procedure is performed would the individual show benefit for eyebrow and chin/neck or is the benefit that has been seen in the individual studies more the effect of proper patient selection for eyebrow lift versus selecting a different subject for chin and neck.

#### **V. Predicate Device Comparison**

This is the identical device granted marketing approval through a de Novo reclassification that was approved by letter dated September 11, 2009. Subsequent to this approval the company has expanded the number of transducers via documentation to file. The new transducers include a narrower version of the de Novo approved DS 7-3.0 device and two new transducers DS 10-1.5 and DS 10-1.5N which have a depth of penetration of only 1.5 mm and include the full size and narrow version. The company provided a discussion related to the new transducers in K122528 and it was decided that they could be found equivalent to the transducers previously cleared, therefore, these new transducer are now cleared devices under K122528.

#### **VI. Labeling**

The User Manual is essentially the same as was originally reviewed in K072505 except for that appears to be an expanded recommended treatment parameter table. This table includes recommendations for infraorbital treatments and includes the new versions of the ultrasound transducers. Also there are two versions of these recommendations, 5.0 and 5.0 Plus. The Plus version has slightly higher number of lines. The company will be asked to provide information to support this difference between the two versions of treatment guidelines.

The company has provided an explanation regarding the recommended treatment table. The 5.0 guidelines were inadvertently included and have not been deleted. The terms used represent the actual treatment sites treated in the original clearance for eyebrow lift and were added to be more specific regarding these sites. The 5.0 Plus guidelines represent actual use guidelines in practice today and are supported by clinical data.

Based on their decision to delete the request for the "full face aesthetic" indication the company has submitted a revised stand alone indication for use page; a revised 510(k) Summary; and corrected pages for the User manual. In order to insure that the correct manual is part of the application the company has also provided a completely new User Manual.

#### **VII. Sterilization/Shelf Life/Reuse**

The transducers are sold non-sterile.

#### **VIII. Biocompatibility**

The devices are the same as described in K072505 and the materials being used have not changed

therefore there are no biocompatibility issues.

**IX. Software**

This is unchanged from K072505.

|                                       |            |           |
|---------------------------------------|------------|-----------|
| Version:                              |            |           |
| Level of Concern:                     |            |           |
|                                       | <b>Yes</b> | <b>No</b> |
| Software description:                 |            |           |
| Device Hazard Analysis:               |            |           |
| Software Requirements Specifications: |            |           |
| Architecture Design Chart:            |            |           |
| Design Specifications:                |            |           |
| Traceability Analysis/Matrix:         |            |           |
| Development:                          |            |           |
| Verification & Validation Testing:    |            |           |
| Revision level history:               |            |           |
| Unresolved anomalies:                 |            |           |

**X. Electromagnetic Compatibility and Electrical, Mechanical and Thermal Safety**

This is unchanged from K072505.

**XI. Performance Testing – Bench**

N/A

**XII. Performance Testing – Animal**

N/A

**XIII. Performance Testing – Clinical**

The company has provided clinical data to support their request for the expansion of their indication for use to now include lift lax submental and neck tissue. The data was previously presented in K110007 and found not adequate thus this 510(k) was determined to be NSE for lack of performance data. The major problem with the data as presented in K11007 was that the method used to provide quantitative values for submental and neck lift relied on photographs. There was a relatively large loss of data since the photographic system used by the company cropped part of the photographs which prevented quantitative measurement of change. Also the data showed a number of subjects having improvement on one side but not the other. Because of small numbers of apparent success out of a relatively small number of measurable subjects it was determined that the data was not adequate to support the proposed change in indications.

The clinical data provided in this study is the same data set with a new method of measure area of change for submental and neck lift. The new method avoids the issues of photograph cropping and therefore all 70 subjects enrolled into the study can be analyzed.

The clinical data used for support is based on 70 evaluable subjects ranging in age from 35-60 years. Of the subjects enrolled into the study 57 were female and 13 were male. Enrolled patients include Fitzpatrick Skin type I-V with the majority of subjects being type II and III. The company has stated that the treatment targeted the lower face and neck with treatment exposure using up to a 25 mm line of coagulation spots with the distance between spots being 1.5 mm. Follow-ups were at 2, 3, and 6 months with photographic evaluation by blinded evaluators for efficacy being at 3 months and patient satisfaction questionnaires being completed at 3.

The company has stated that the Primary Outcome Measure for the study was improvement in overall lift and tightening of tissue determined by qualitative assessment at three months compared to baseline based on a masked reviewer assessment. The Secondary Outcome Measure was evaluation of improvement in jawline definition and submental skin laxity at three months compared to baseline based on the consensus of the three masked reviewers and patient satisfaction by scores on a patient satisfaction questionnaire at three months post-treatment.

The company has also provided quantitative values for the amount of lift occurring by comparing baseline submental areas at baseline to the same area 3 months after last treatment. The company has stated that if the amount of change between baseline and 3 months is less than 10 mm<sup>2</sup> this would be considered a failure. The company stated that this is a visibly observable change but has not provided any basis for making this statement. The company has not stated whether or not the quantitative measurement values were Primary or Secondary endpoint.

The company has also conducted a patient satisfaction questionnaire at the end of the study. The company claims greater than 60% satisfaction but has not provided the individual patient data for this endpoint.

In their response to issues raised concerning the clinical data the company has provided the following information. Ulthera has provided several sets of clinical data to support the requested expansion of their indication for use to include "lift lax submental (beneath the chin) and neck tissue". This data includes masked evaluation of before and after photographs showed 49/70 subjects (70%) improving. They also provided measured improvement using both 10 mm<sup>2</sup> and 20 mm<sup>2</sup> measured change that produced 53/70 (75.7%) successes or 51/70 (72.9%) success. Using the 10 mm<sup>2</sup> you have 83% or 44.7/70 subject who have both the measured success as well as masked evaluator success. Taken as a whole this data set does provide solid evidence that the use of the Ulthera system can improve lax chin and neck.

**XIV. Substantial Equivalence Discussion**

|  | Yes | No |                                     |
|--|-----|----|-------------------------------------|
| 1. Same Indication Statement?  |     | X  | If YES = Go To 3                    |
| 2. Do Differences Alter The Effect Or Raise New Issues of Safety Or Effectiveness? |     | X  | If YES = Stop NSE                   |
| 3. Same Technological Characteristics?   | X   |    | If YES = Go To 5                    |
| 4. Could The New Characteristics Affect Safety Or Effectiveness?                   |     |    | If YES = Go To 6                    |
| 5. Descriptive Characteristics Precise Enough?                                     |     | X  | If NO = Go To 8<br>If YES = Stop SE |
| 6. New Types Of Safety Or Effectiveness Questions?                                 |     |    | If YES = Stop NSE                   |
| 7. Accepted Scientific Methods Exist?  |     |    | If NO = Stop NSE                    |
| 8. Performance Data Available?   | X   |    | If NO = Request Data                |
| 9. Data Demonstrate Equivalence?   | X   |    | Final Decision: SE                  |

Question 1. This application was submitted to request a new indication for use for "lift lax submental (beneath the chin) and neck tissue".

Question 2. This new indication for use does not alter the fundamental technology of the Ulthera Focused Ultrasound system but only changes the location of treatment. No new safety issues are raised.

Question 3. The device used in this study is identical to the cleared predicate Ulthera Focused Ultrasound system.

Question 5. Device descriptive information is not sufficient by itself. For the new indication for use performance data is required.

Question 8. The company has provided clinical data that demonstrated 51 of 70 subjects showed at least a 20 mm<sup>2</sup> tightening of the submental area and over 80% of these same subjects were deemed improved by masked evaluators who evaluated before and after photographs of the treated area.

Question 9. Based on the clinical data provided a determination of Substantial Equivalence is recommended.

**XV. Deficiencies**

**XVI. Contact History**

The company was contacted by telephone on October 1, 2012 and a discussion was held with Mr. Randy Miller and the company's Regulatory Staff. This discussion concerned the company's request for a third indication for use for "full face laxity treatment". The company was informed that the Agency did not believe that data from two separate studies investigating use for stand alone indications for eyebrow and chin/neck was adequate for a full face generic indication for use. The company accepted this decision and has provided by electronic mail a revised stand alone indication for use page; a revised 510(k) Summary and a revised User Manual.

In addition to the indication for use changes, the company was also requested to expand the performance section of the 510(k) Summary to include additional information related to the clinical study in terms of patients enrolled into the study and the number of patients that were successfully treated.

**XVII. Recommendation SE**

Regulation Number: 21 CFR 878.4590

Regulation Name: Focused Ultrasound Stimulator System for Aesthetic Use

Regulatory Class: Class II,

Product Code: OHV

Richard P. Fetter  
Reviewer

022, 2012  
Date

Neil Ogle Encour with  
Branch Chief STC

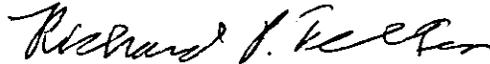
10/2/12  
Date

September 30, 2012

Review of K121700/S1

Submitted by Ulthera, Inc.

Reviewed by Richard P. Felten, DSORD, GSDB



This Supplement is the company's response to a number of issues that were identified during our review of their original submittal and were communicated to the company on July 6, 2012 to the contact person for this application Suzon Lommel. Ms. Lommel was also contacted by telephone and the issues were discussed with her.

This application was submitted by Ulthera following a previous Not Substantially Equivalent decision for the same clinical data that has been submitted in this application. The major issue with the initial application, K110007, was that the method used to provide quantitative values for submental and neck lift relied on photographs. There was a relatively large loss of data since the photographic system used by the company cropped part of the photographs which prevented quantitative measurement of change. Also the data showed a number of subjects having improvement on one side but not the other, possibly due to the photographic cropping. Because of small numbers of apparent success out of a relatively small number of measurable subjects it was determined that the data was not adequate to support the proposed change in indications.

The clinical data provided in this study is the same data set with a new method of measuring area of change for submental and neck lift. The new method avoids the issues of photograph cropping and therefore all 70 subjects enrolled into the study can be analyzed.

The clinical data used for support is based on 70 evaluable subjects ranging in age from 35-60 years. Of the subjects enrolled into the study 57 were female and 13 were male. Enrolled patients include Fitzpatrick Skin type I-V with the majority of subjects being type II and III. The company has stated that the treatment targeted the lower face and neck with treatment exposure using up to a 25 mm line of coagulation spots with the distance between spots being 1.5 mm. Follow-ups were at 2, 3, and 6 months with photographic evaluation by blinded evaluators for efficacy being at 3 months and patient satisfaction questionnaires being completed at 3.

The company has stated that the Primary Outcome Measure for the study was improvement in overall lift and tightening of tissue determined by qualitative assessment at three months compared to baseline based on a masked reviewer assessment. The Secondary Outcome Measure was evaluation of improvement in jawline definition and submental skin laxity at three months compared to baseline based on the consensus of the three masked reviewers and patient satisfaction by scores on a patient satisfaction questionnaire at three months post-treatment.

In addition to these endpoints the company has developed a method for quantifying the amount of lift or tightening produced but they did not include this data as part of the original submittal. The company did state in the original submittal that a 10 mm<sup>2</sup> was clinically meaningful.

Based on our review of the initial submittal a number of issues were identified and the company was requested to provide responses to these issues. The company's responses were:

1. In responding to our question about defining the basis for stating that a 10 mm<sup>2</sup> was clinically meaningful the company has stated that this amount of change can be observed and clearly seen by the evaluators. They have stated that this amount of change was clearly identifiable in the photographs evaluated by blinded evaluators. Based on this endpoint the company has stated that 53 of the 70 subjects enrolled into the study did meet this criteria for quantitative success. In addition 83% of these were also identified as success by the blinded photographic evaluators.
2. The company has also provided information using a slightly higher success criteria, 20 mm<sup>2</sup>, for the quantifiable endpoint. If this value is used for measurable success then the number of success becomes 51 out of 70 subjects, thus even a doubling of the success criteria only changes the success number by 2.
3. The company was asked to clarify Table 20-4 in terms of whether or not a person could be shown as a success yet have only one side of the face actually meet the quantifiable success measure. The company has responded that all subjects reported as having less than 10 mm<sup>2</sup> change had this on both sides. This does suggest that the effect is symmetrical in the patients.
4. The company was asked to discuss/justify their request for an indication for use of "lift lax tissue to achieve a desired aesthetic effect for the full face and neck". Their response discusses the normal sagging that occurs to the face, specifically the eyebrow and the chin/neck area. Their argument is that by lifting the eyebrow, the already cleared indication for this system, and lifting the chin and neck, the requested new indication you would in effect have produced a lifting of the full face and neck. This seems a reasonable argument but granting this as an indication may require some additional information in the professional use section of the application to make clear that this indication only occurs when the patient has had both the eyebrow lift and the chin/neck lift. Also this indication implies doing both eyebrow and chin/neck at the same time we do not at present have any clinical data showing that such a procedure is safe. Based on this lack of confirming clinical data the company will be asked to delete this full face indication from their indications for use.

5. The company has provided the requested revised 510(k) Summary with an expended clinical section. This will need to be discussed within the branch to determine if additional clinical data such as subject numbers and number of successes should be added. The summary should include a brief description of the number of subjects enrolled and the number successful. The best set of data for this would be the 20 mm<sup>2</sup> success which is 51 of 70 versus the 53 of 70 for the 10 mm<sup>2</sup> value. Also it would be a good idea to include a statement that the masked evaluators were successful in identifying 80% of these same individuals as improved thus having two independent endpoints showing success for the same individual.
6. In responding to our question concerning selection of 60 day follow-up photographs to be the basis for their validation process the company has explained that in order to have a valid method, the scale being used must represent the full range of possible outcomes from no detectable change, to minimal change, to good improvement. Based on literature reports on the progression of improvement for treatment of wrinkles and lax skin it can be determined that this is a gradual process that continues for several months following end of treatment, in some cases up to 6 months has been reported as the time required for complete improvement. Based on this literature information the company determined that 60 day follow-up would include the full range of possible outcomes and therefore decided to use these photographs for their validation study. This is a reasonable explanation.
7. In responding to our issue of why the quantified data was not part of their result table, the company has taken the position that this would in effect be requiring a 4 endpoint success for their study. Their position that this is not a justifiable requirement of a clinical study and is outside the bounds of requirements for clinical studies. This is a reasonable argument, however, in order to meet the suggested data requirements for aesthetic devices as discussed at the November 2008 General and Plastic Surgery Panel on Aesthetic Devices, combining the quantifiable data with blinded evaluation and patient satisfaction is considered a necessary process to support a marketing application for an aesthetic device.
8. The company has provided the requested patient satisfaction questionnaire.
9. The company has clarified the information in the User Manual related to treatment guidelines. The terms "lateral orbit"; "brow"; and "infraorbital" all relate to the actual treatment sites for the clinical study used to support the cleared indication of eyebrow lift. The company has stated that the 5.0 guideline was erroneously included in the manual and they have been deleted. A redlined copy of the manual has been provided to show these changes.

10. The company has clarified sections 20.4.2.1 and 20.4.2.2 in the use of the terms masked and unmasked. This response is adequate.

Regarding the process for masked evaluation, the individual masked evaluators were requested to identify the post treatment photograph from the baseline photograph. If they identified the post treatment photograph the subject was marked as improved; if they saw not difference between the photographs the subjects was marked no change and if the selected the wrong photograph as baseline the subject was marked incorrect. The value given to each subject was based on the majority value of the three masked evaluators and if each evaluator chose a different value then that subject was marked no change.

For the study the results of the masked evaluation were 49/70 subjects showing improvement for a 70% success rate. If the success is based on amount of tissue lift measured, using the 10 mm<sup>2</sup> you would have a success rate of 75.7% and if you use the alternative success as a 20 mm<sup>2</sup> you have a 72.9% success rate. In addition the company has stated that of the 75.7% success rate based on the 10 mm<sup>2</sup> measured change, that 83% of these were also identified as responders using the qualitative measure which would be approximately 44 of 70 subjects. The most stringent measure of success would be to determine the number of subjects who had quantified improvement plus qualitative improvement plus patient satisfaction. When this is evaluated only 33 of 70 subjects meet this level of success, however, use of patient satisfaction does come with some built in issues. If you patient satisfaction as a primary endpoint then you would have 47 of 70 subjects saying they were satisfied with the procedural effect. Of this number there were 6 subjects who were satisfied that were not marked successful by the masked evaluators but did have greater than 10 mm<sup>2</sup> quantitative change and there were 7 subjects who were satisfied who had less than a 10 mm<sup>2</sup> measured change. At the same time 10 subjects stated they were not satisfied yet they showed greater than the 10 mm<sup>2</sup> measured change and were marked as improved by the masked evaluators. Overall, the data from this study does support the claim that use of the Ulthera system according to the directions for use will result in a measurable and observable tightening or lift of the chin and neck.

This clinical data was also reviewed by Dr. Janette Alexander. A copy of her review is attached. Dr. Alexander has stated that the company's explanation for use of the 10 mm<sup>2</sup> does appear to be sufficient and does support a favorable benefit/risk ratio. Dr. Alexander does have concerns related to the company's request for the full face aesthetic indication and this does need to be addressed at the branch level.

In summary Ulthera has provided several sets of clinical data to support the requested expansion of their indication for use to include "lift lax submental (beneath the chin) and neck tissue". This data includes masked evaluation of before and after photographs showed 49/70 subjects (70%) improving. They also provided measured improvement using both 10 mm<sup>2</sup> and 20 mm<sup>2</sup> measured change that produced 53/70 (75.7%) successes or 51/70 (72.9%) success. Using the 10 mm<sup>2</sup> you have 83% or 44.7/70 subject who have both the measured success as well as masked evaluator success. Taken as a whole this data set does provide solid evidence that the use of the Ulthera system can improve lax chin and neck.

The company was contacted by telephone on October 1, 2012 and requested to delete their third indication for use, the request for full face treatment of lax skin for a desired aesthetic result. The company was informed that the Agency did not believe that the data from the two individual studies, one for eyebrow lift and one for chin/neck lift was adequate to support a generic full face lax skin lift indication. The company accepted this decision and provided by electronic mail a revised indications for use page; a revised 510(k) Summary; and a revised User Manual. The company was also requested to provide an expanded performance section for the 510(k) Summary that include additional information related to the number of subjects in the clinical study and the number of subjects successfully treated. The company has made this change.

Based on the clinical data that does demonstrate successful lax skin lift of the chin and neck based on quantitative measurements of the change in this tissue as well as correct identification of the post treatment photograph by masked evaluators, I recommend that this application be determined to be Substantially Equivalent for the new indication for use of "lift lax submental (beneath the chin) and neck tissue".

*I concur with the ~~SE~~  
Neil 10/2/12*

G120004/S1

## OFFICE OF DEVICE EVALUATION G120004/S3 CLINICAL REVIEW

---

**From:** Janette Alexander, MD  
PRSB/DSORD/ ODE

**To:** Richard Felten, Lead Reviewer  
GSDB/DSORD/ ODE

**CC:** Neil Ogden, Branch Chief GSDB  
David Krause, PhD, Branch Chief PRSB

**Subject:** **G121700/S1**  
Ulthera Neck Response to Additional Information Letter for K121700  
dated July 5, 2012

**Date:** 09/20/12

### SUMMARY

Ulthera submitted a 510(k) application (K072505) which was cleared on September 11, 2009 with the following indication for use:

The Ulthera System is indicated for:

- non-invasive dermatological treatment to produce eyebrow lift through tissue coagulation and tightening, and

Proposed indication for use:

- lift the eyebrow (current cleared indication)
- lift lax submental (beneath the chin) and neck tissue (requested expanded indication)
- lift lax tissue to achieve a desired aesthetic effect for the full face and neck (current cleared indication + requested expanded indication)

**Reviewer comment:** *This expanded indication seems to include the face (between the eyebrow and the neck) which has not been evaluated.*

### BACKGROUND INFORMATION

#### Brief Clinical Background

Current Indication for Use: Non-invasive aesthetic treatment to produce eyebrow lift

The Ulthera<sup>®</sup> System integrates high-resolution ultrasound imaging with ultrasound therapy. The Ulthera<sup>®</sup> System has been demonstrated to be safe and effective in previous clinical trials as a non-invasive treatment to produce improvement in the areas of treatment (i.e., eyebrow lift) through sub-dermal tissue coagulation and tightening, and for imaging skin and sub-dermal tissue.

#### Mechanism of Action

The Ulthera<sup>®</sup> System images and delivers focused ultrasound energy to a specific soft tissue layer under the superficial layers of epidermis. Ultrasound treatment creates a focal lesion in the skin, causing thermally

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induced contraction of tissue and a "wound-healing" response to stimulate the formation of new tissue and collagen, and to cause a skin-tightening effect.

The device is designed and configured to produce small (approximately 1 mm<sup>3</sup>) micro-thermal lesions in the mid to deep reticular layer of dermis and sub-dermis, while sparing overlying papillary dermal and epidermal layers of skin. The device also incorporates an ultrasound imaging capability to evaluate the skin tissue.

#### **Proposed Indication for Use**

The Ulthera® System is indicated for use as a non-invasive dermatological aesthetic treatment to:

- lift the eyebrow (current cleared indication)
- lift lax submental (beneath the chin) and neck tissue (requested expanded indication)
- lift lax tissue to achieve a desired aesthetic effect for the full face and neck (current cleared indication + requested expanded indication)

#### **Review of Clinical Deficiency Responses**

The following deficiencies have been identified in our review of this application:

1. You have stated that a 10 mm<sub>2</sub> is a visibly observable change and therefore those sites having less than a 10 mm<sub>2</sub> change would be considered a failure. Please provide the basis for this statement since such a small change appears not to be easily observable.

As agreed with the agency during the review of our cleared 510(k), observable changes are those which can be determined during masked assessment. Taking this definition into account, Ulthera defined 10 mm<sub>2</sub> as visibly observable change and therefore those sites having less than a 10 mm<sub>2</sub> change would be considered a failure. Visibly observable change has been determined based on changes that can be seen through masked assessment.

Based on this criteria, Ulthera identified 17 out of 70 subjects as nonresponders (<10 mm<sub>2</sub>). Therefore, 53 out of 70 subjects (75.7%) were identified as responders (≥10 mm<sub>2</sub>) by quantitative assessment. 83.0% of those subjects who were identified as responders in the quantitative assessment were also identified as responders in the qualitative masked assessment.

However, if the criteria for visibly observable change is doubled from 10mm<sub>2</sub> to 20mm<sub>2</sub>, 19 out of 70 subjects would be identified as non-responders (<20 mm<sub>2</sub>). Therefore, 51 out of 70 (72.9%) subjects would be identified as responders (≥20 mm<sub>2</sub>) by quantitative assessment. 84.3% of the subjects who would be identified as responders, based on this criteria, in the quantitative assessment were also identified as responders from the qualitative masked assessment.

**Reviewer comment: This appears to be sufficient and support a favorable benefit/risk ratio.**

2. Please clarify in the individual data table, Table 20-4, whether or not both sides of the subjects reported as having less than 10 mm<sub>2</sub> change actually had less on both sides or were marked as less based only on a single side failing.

Non-responders were identified as having < 10.0 mm<sub>2</sub> tissue lift. Each side/score was evaluated independently. For example, if the right side resulted in a 9.00 mm<sub>2</sub> lift and the left side resulted in an 11.00 mm<sub>2</sub> lift then the results would be recorded as <10.00 mm<sub>2</sub> and 11.00 mm<sub>2</sub> respectively.

Regardless of small differences between opposite sides of the face, the data for the area of tissue lift and the response rate yielded consistent results (as % responders) for both

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the right and left side of the face. All subjects that were reported as having less than 10 mm<sup>2</sup> change actually had less on both sides.

**Reviewer comment: This response is acceptable.**

3. You have requested an indication for use of "lift lax tissue to achieve a desired aesthetic effect for full face and neck". It is not clear exactly what this indication for use is measuring or how you would determine "a desired aesthetic effect". Please provide additional discussion of what this indication for use is defining and how you would determine success for this indication for use.

During the aging process the skin tissue in the face and neck develops laxity that results in tissue descent that is manifested by "sagging" of the skin in both the face and neck. The sagging is noticeable in the brow area, where there is descent of the brow, and in the lower face (chin/neck area), where there is descent of tissue in the submental and upper neck area. A full face and neck treatment will achieve lifting of the brow and the submental/neck tissue to produce an overall lifting of the full face and neck tissue. Lifting of the eyebrow is the cleared indication. Lifting of the submental/neck tissue is determined by evaluation of patient photographs. Success was determined by quantitative assessment, qualitative assessment (by masked clinician) and patient satisfaction. The combination of these two indications will result in a lifting of the face and neck.

**Reviewer comment: It does not appear that any testing has been done on the full face. Therefore the IFU that includes the full face seems to be inappropriate.**

4. Please expand the Performance section of the 510(k) Summary. According to 21 CFR 807.92(b)(2) the 510(k) Summary should include information on patient population tested; discussion of safety and effectiveness data with references to adverse effects and complications observed; and any other information that may be relevant to the substantial equivalence determination.

Please see Attachment 1 for a redlined 510(k) Summary.

**Reviewer comment:**

**The proposed indication for use includes full face, however the Summary Performance data describes "treatment with the Ulthera® System to achieve lifting of lax submental (beneath the chin) and neck tissue." The IFU should reflect the performance data.**

5. Please describe the process used in selecting the photographs used for the 2 month validation testing.

Validation of the masked clinician assessment method requires that photographs of subjects with the full range of potential responses be included in the validation study. We included photographs representing a range of clinical responses: no detectable improvement, minimal improvement and good improvement. This is similar to the approach by Kim, et. al. to validate a scale for facial lines where they included the full range of possible facial wrinkles in the validation study. Including a full range of possible clinical responses is also consistent with ICH (International Conference on Harmonization) guidelines for validation of analytical procedures. In order to obtain an adequate distribution of responses to the treatment, ranging from not detectable improvement to good improvement we used Day 60 photographs. As described in the detail, the masked reviewer will identify the pre- and post-treatment images, the endpoint from the review being, "improvement" or "no-change" for the image pair. Based on the data from the predicate device (K072505) described in the Fitzpatrick et al. publication in which there was continued improvement in clinical response from 4 months to 6 months, we believe that using Day 90 photographs for the validation study will not provide an adequate distribution of subjects at the low end of

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the response curve. Based on published studies of the Thermage device for similar claims, the Day 60 results for lower face and submental region changes fall well into the time window where the entire range of clinical outcomes are represented, namely non-responders to good responders.

The endpoint used in the validation study is the same as the endpoint intended to be used in the efficacy evaluation. The masked clinicians evaluated photographs for a detectable change in tissue lift in the lower face and neck. The only difference between the clinical response detected at Day 60 and at Day 90 is the distribution of responses.

1 Kim EJ, Reeck JB, Maas CS. A validated rating scale for hyperkinetic facial lines. Arch. Fac. Plast. Surg. 2004, Vol. 6 July/Aug., 253-256.

2 Fitzpatrick R, Geronemus R, Goldberg D, Kaminer M, Kilmer S, Ruiz-Esparza J. Multicenter study of noninvasive radiofrequency for periorbital tissue tightening. Lasers Surg Med. 2003;33(4):232-42.

**Reviewer comment:**

***This response is acceptable.***

6. The use of Quantitative analysis is not listed under either the Primary or Secondary Outcome Measure. Please indicate whether or not the Quantitative measurements are a Primary or Secondary endpoint. Please be advised that in reviewing your application the Agency will look at all endpoints as a combined effectiveness result for each individual subject.

Per FDA's feedback, the quantitative method was developed as a Primary Outcome Measure. Combining effectiveness results for un-poolable endpoints is not appropriate for this study. Each individual endpoint should be based on study patient population response for each individual endpoint.

Requiring each patient to meet four independent endpoints in order to demonstrate successful efficacy is outside the bounds of normal clinical trial design and analyses.

**Reviewer comment:**

***Per Mr. Felten, as I have not reviewed the endpoints or study design.***

7. Please provide a copy of the patient satisfaction questionnaire and the individual patients responses to the questionnaire.

As requested, please see Attachment 2 for a copy of the patient satisfaction questionnaire.

**Reviewer comment:**

***This response is complete.***

8. Please provide a table listing the individual subjects with blinded assessment; quantitative lift value; and patient satisfaction values to show if each individual subject is a success across the board.

As requested, please see Attachment 3 for a table listing the individual subjects' masked assessment, quantitative lift values and patient satisfaction values.

**Reviewer comment:**

***This response is complete.***

9. The Operator Manual has two tables of suggested Treatment Guidelines identified as 5.0 and 5.0 Plus. It is not clear what is the basis for the guidelines. The Ulthera System is presently cleared for eyebrow lift only and the new requested indication is for submental and neck lift. The charts include infraorbital and orbit treatment which do not appear to be compatible with eyebrow lift or treatment of the submental or neck tissue. Also the 5.0 Plus recommendations contain an increase in number of lines for each of the 5.0 recommendations. Please provide information explaining the basis for the recommended Guidelines including the increase in number of lines for the 5.0 Plus table.

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The anatomical sites specified in the table in Appendix A (i.e., "Lateral Orbit," "Brow," and "Infraorbital") are the same sites that were used for treatment of the subjects in the eyebrow clinical study and do not represent an expansion of recommended treatment parameters, areas, or indications related to those specific areas. The terms were changed for precise identification of the treatment sites, and to reduce any confusion for the clinician performing the treatment and do not represent an expansion of the cleared indication.

Guidelines have been provided as a safety feature since the clearance of this device. The guidelines are included in to provide the user with recommended levels of energy and lines (upper guidelines) to ensure a safe level of use. Therefore, the 5.0 guidelines were erroneously included and have been removed from the labeling. Please see Attachment 4 for the redlined IFU. The 5.0 Plus guideline is currently the upper guideline being used by physicians. The following study supporting the 5.0 Plus guideline is included in Attachment 5.

Sasaki, Gordon H., Tevez, Ana. Clinical Efficacy and Safety of Focused-Image Ultrasonography: A 2-Year Experience. Aesthetic Surgery Journal published online 23 April 2012

**Reviewer comment:**

***To a plastic surgeon, infraorbital implies below the eye - i.e. crow's feet or lower lid. If this area was not evaluated in the prior study, the nomenclature should be changed.***

10. The narrative on page 77 and 78 under section 20.4.2.1 does not seem to make sense. Page 77 appears to be describing how the unmasked evaluation will be performed but the top of page 78 begins with a statement about each blinded assessor, yet section 20.4.2.2 at the bottom of page 78 is titled Masked Assessment. Please clarify these sections.

Section 20.4.2.1 describes the unmasked qualitative assessment and the reviewers were not blinded. The use of the word "blinded" in "Section 20.4.2.1. Unmasked Qualitative Assessment" was used in error.

The statement should be updated as follows:

Each ~~blinded~~ unmasked assessor conducted their assessment independently.

Each ~~blinded~~ unmasked assessor reviewed the set of images for improvement in the submental (lower chin) and neck tissue.

Section 20.4.2.2 describes the masked qualitative assessment. The reviewers in this assessment were masked.

**Reviewer comment: This response is acceptable.**

***Janette Alexander, MD      PRSB/CDRH***

**Felten, Richard P.**

---

**From:** Alexander, Janette  
**Sent:** Wednesday, September 19, 2012 12:39 PM  
**To:** Felten, Richard P.  
**Cc:** Ogden, Neil; Krause, David  
**Subject:** G121700 JA Clin Rev0912.doc  
**Attachments:** G121700 JA Clin Rev0912.doc

Ulthera Neck review enclosed.

Janette



Ulthera® System

# Instructions for Use

Featuring

DeepSEE® Technology

for

Ultherapy®

PROPOSED DRAFT

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Various features of the Ulthera® System are covered by U.S. Patents 6,049,159 and 7,758,524, and contemplated features may be covered by one or more of the following U.S. Patents: 5,820,564; 6,036,646; 6,050,943; 6,120,452; 6,213,948; 6,440,071; 6,500,121; 6,540,679; 7,142,905; 7,229,411; 7,393,325; 7,491,171; 7,530,958; 7,571,336; 7,615,016; and 7,824,348. More than 100 other U.S. and International patents to which Ulthera has rights are issued, published, or pending.

EC REP

MedPass International Limited  
Windsor House Barnett Way  
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United Kingdom

CE

PROPOSED DRAFT

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# Ulthera® System

CAUTION: UNITED STATES FEDERAL LAW RESTRICTS THIS DEVICE TO SALE BY OR ON THE ORDER OF A PHYSICIAN.

THE ULTHERA® SYSTEM IS INTENDED FOR USE ONLY BY PROPERLY TRAINED PHYSICIANS AND PROPERLY TRAINED PERSONS UNDER THE SUPERVISION OF SUCH A TRAINED PHYSICIAN (HENCEFORTH "THE USER").

PRIOR TO OPERATING THE SYSTEM, THE USER MUST THOROUGHLY READ AND UNDERSTAND THIS INSTRUCTIONS FOR USE. IMPROPER USE OF THE SYSTEM MAY CAUSE PERSONAL INJURY AND/OR DAMAGE TO THE SYSTEM THAT MAY INVALIDATE THE WARRANTY AGREEMENT.

NOTE: THESE INSTRUCTIONS FOR USE DESCRIBES THE OPERATION OF THE ULTHERA SYSTEM ONLY. IT IS NOT A SUBSTITUTE FOR THE REQUIRED CLINICAL TRAINING ON THE PROCEDURE THAT UTILIZES THE SYSTEM.

PROPOSED DRAFT

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# 1. Introduction to Instructions for Use

## 1.1. Purpose

These Instructions for Use (IFU) provides a description of the System components, its controls and displays, instructions for its operation, and other equipment information important to the user.

**Warning:** Do NOT operate the Ulthera System before reading this IFU thoroughly AND being trained on the clinical procedure by an authorized Ulthera representative. This IFU is not a substitute for clinical treatment guidelines and training provided by the Company. For more information on training available please contact your local representative.

## 1.2. Conventions



**Note:** Notes designate information of special interest.



**Caution:** Cautions alert the user to precautionary steps necessary to properly operate the system. Failure to observe these cautions may void the warranty.



**Warning:** Warnings alert the user to information that is of the highest importance and vital to the safety of the patient and user.

All procedures are broken down by numbered steps. Steps must be completed in the sequence they are presented.

Bulleted lists indicate general information about a particular function or procedure. They do not imply a sequential procedure.

Control names are spelled as they are on the system, and they appear in **Bold** text.

---

## 2. Medical Safety

### 2.1. Indications for Use

The Ulthera System is indicated for non-invasive dermatological aesthetic treatment to:

- lift the eyebrow
- lift lax submental (beneath the chin) and neck tissue

### 2.2. Contraindications

The Ulthera System is contraindicated for use in patients with

- open facial wounds or lesions
- severe or cystic acne on the face and/or neck

### 2.3. Precautions

When not in use by trained personnel, the Ulthera System User Access Key should be removed from the system to help prevent unauthorized use. Keep the Ulthera System User Access Key in a designated place accessible only to authorized and trained personnel.

The Ulthera System has not been evaluated for use over various materials. Therefore, treatment is not recommended directly over those areas with any of the following:

- Mechanical implants
- Dermal fillers
- Implanted electrical devices
- Metal stents in the face and neck area

Treatment energy is not recommended for use directly on an existing keloid.

The Ulthera System has not been evaluated for use in patients on an anticoagulant treatment plan.

The Ulthera System has not been evaluated for use in the following patient populations:

- Pregnant or breast feeding women
- Children
- Those with the following disease states
  - A hemorrhagic disorder or haemostatic dysfunction
  - An active or local skin disease that may alter wound healing
  - Herpes Simplex
  - Autoimmune Disease
  - Diabetes
  - Epilepsy
  - Bell's Palsy

#### 2.4. Patient Safety



**Warning:** Ulthera should not be used on a patient's eyes or in a location or technique where ultrasound energy can reach the eye.



**Warning:** Use this system only if you are trained and qualified to do so.



**Warning:** If any problems occur during system operation, take immediate action(s): lift the transducer off the patient's skin, press the **See** pushbutton on handle to discontinue treatment in progress, and/or press the red emergency **Stop** button to completely halt system operation.

#### 2.5. Potential Side Effects

Side effects reported in the clinical evaluation of the Ulthera System were mild and transient in nature. These were limited to:

- Erythema (redness): The treated area may exhibit erythema immediately following treatment. This typically resolves within a few hours of treatment.

- Edema (swelling): The treated area may exhibit mild edema following treatment. This typically resolves within a few days of treatment.
- Pain: Momentary discomfort may be experienced during the procedure while energy is being deposited.
- Bruising: Mild bruising, which is caused by damage to soft tissue blood vessels, may occur occasionally and typically resolves within a few days of treatment.
- Nerve Effects:
  - Transient local muscle weakness may result after treatment due to inflammation of a motor nerve.
  - Transient numbness may result after treatment due to inflammation of a sensory nerve.

No permanent injuries to facial nerves have been reported.

- Scarring: The possibility for scar formation (which will respond to medical care) may exist if incorrect treatment technique is used.

## 2.6. Complaints and Adverse Events

No serious adverse events were observed during the clinical study evaluation of the Ulthera System.

Ulthera follows MDR (Medical Device Reporting) rules for handling complaints and adverse events. Should an adverse event be suspected or reported, contact Ulthera, Inc. at the number on the cover page of this document; for those outside the U.S., contact your local Ulthera representative.

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## 3. System Overview

### 3.1. System Description

The Ulthera System integrates the capabilities of ultrasound imaging with those of ultrasound therapy.

The imaging feature allows the user to visualize the skin and sub-dermal regions of interest before treatment. It also allows the user to assure proper skin contact in order to deliver the energy at desired depths.

The therapy feature directs acoustic waves to the treatment area. This acoustic energy heats tissue as a result of frictional losses during energy absorption, producing discrete points of coagulation.

### 3.2. System Components and Features

The Ulthera System consists of three primary components: the control unit with integrated touchscreen, the handpiece with cable, and interchangeable transducers (*see Figure 3.1*).



*Figure 3.1. Main components of the Ulthera® System: Control Unit (top), Handpiece (bottom right), Image/Treat Transducer (bottom left) that inserts into the handpiece receptacle.*

### 3.2.1. Control Unit

The control unit is the tabletop information center for the Ulthera System. It houses the touchscreen monitor and Graphical User Interface (GUI) that allows the user to interact with the device. This screen sets and displays the operating conditions, including equipment activation status, treatment parameters, system messages and prompts, and ultrasound images. Figure 3.2 illustrates the physical features of the control unit, such as the various connector ports and power controls.



Figure 3.2 Control Unit front view (left) and rear view (right). See Table 3.1 for a description of the controls and connector ports of the control unit.

Table 3.1 Control Unit connector ports and controls (See Figure 3.2)

| Item                             | Description  |
|----------------------------------|--|
| 1 Handpiece Connector Receptacle | Socket for plugging in handpiece cable   |
| 2 USB Ports (two)                | For optional USB removable storage device  |
| 3 Emergency Stop                 | Halts system operation if pressed  |
| 4 On / Off Button                | <ul style="list-style-type: none"> <li>• Momentarily press to turn system ON</li> <li>• Momentarily press to turn system OFF</li> <li>• Press and hold to force system shutdown</li> </ul> |
| 5 Rear Panel USB port            | For Ulthera System User Access key   |
| 6 Main Power Switch              | Supplies power to system. Leave ON (symbol "I" pressed in)   |
| 7 Power Cord Receptacle          | Socket for attachment of power cord  |

Below the monitor, on the front panel of the control unit is a handpiece connector receptacle that interfaces with the handpiece cable. On the front right of the panel is an **On/Off** button and an emergency **Stop** button. When turned OFF via the **On/Off** button the system goes into a very low power standby mode unless the Main Power Switch is also turned to the OFF position by pressing the 'O' symbol. The front of the control unit also has two Universal Serial Bus (USB) ports: both ports may be used for the Ulthera System User Access Key or for an optional removable storage device ("thumb drive").



**Warning:** When not in use by trained personnel, the Ulthera System User Access Key should be removed from the system to help prevent unauthorized use. Keep the Ulthera System User Access Key in a designated place accessible only to authorized and trained personnel.

The rear of the control unit has a USB port, an AC power receptacle and the main power switch. The main power switch should be left in the powered position (with the "I" pressed inward). In such a configuration, the control unit may be turned ON via the front panel **On/Off** button and can be turned OFF via either the front panel **On/Off** button or the graphical user interface.

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### 3.2.2. Handpiece

The handpiece is a handle with an integrated receptacle for insertion of a transducer on one end and an electrical cable for attachment to the control system on the other end. The handpiece has two types of buttons: one to image (**SEE**) and the other to deliver therapy (**TREAT**). Figure 3.3 provides two views of the handpiece, including one showing it connected to an Image/Treat transducer. Table 3.2 is a description of the various components and features illustrated in Figure 3.3.



Figure 3.3 Handpiece with transducer inserted, top and side views.

Table 3.2 Handpiece and Transducer Description

| Item                       | Description   |
|----------------------------|---|
| 1 <b>SEE</b> Pushbutton    | <ul style="list-style-type: none"> <li>Engages IMAGING state (if not already imaging)</li> <li>Places system in READY state (times out in 40 seconds)</li> <li>Stops TREATING if treatment in progress</li> </ul> |
| 2 <b>TREAT</b> Pushbuttons | <ul style="list-style-type: none"> <li>Engages TREATING state</li> </ul>  |
| 3 Latch                    | Locks transducer into handpiece   |
| 4 Transducer               | Image/treat transducer  |
| 5 Strain Relief / Cable    | Connects handpiece to Control Unit  |

### 3.2.3. Transducers

Figure 3.4 is an illustration of an image/treat transducer. The transducer can image and treat a region of tissue up to 25 mm long and can image a depth of up to 8 millimeters. Treatment occurs along a line less than or equal to the transducer's active length, which is indicated by guides on the sides of the transducer, as described in Table 3.3. An additional guide at the front tip of the transducer represents the center of the treatment line. In therapy mode, bursts of sound energy create a linear sequence of individual, discrete, thermal coagulation zones. A label atop the transducer provides the transducer type, expiration date, and other information.

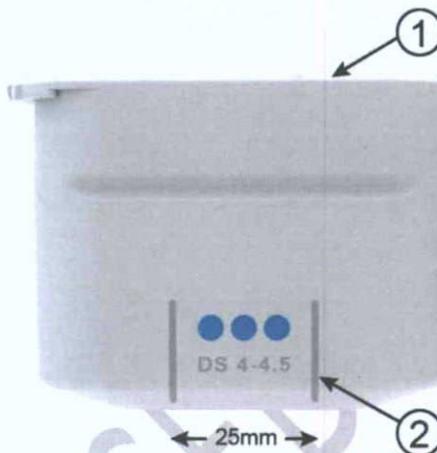


Figure 3.4 Image/Treat Transducer, separated from handpiece (see Table 3.3)

Table 3.3 Transducer Description

| Item           | Description  |
|----------------|--|
| 1 Labeling     | Transducer type and other information  |
| 2 Treat guides | Markers denoting maximum treatment line length and center of treatment line (center of transducer) |

The types of transducers reflect variations in frequencies and treatment depths as shown in Table 3.4.

Table 3.4 Transducer Types

| Transducer Type | Treat Frequency | Treat Depth | Image Depth | Scan Length |
|-----------------|-----------------|-------------|-------------|-------------|
| DS 7 – 3.0      | 7 MHz           | 3.0 mm      | 0 – 8 mm    | 25 mm       |
| DS 7 – 3.0N     | 7 MHz           | 3.0 mm      | 0 – 8 mm    | 14 mm       |
| DS 4 – 4.5      | 4 MHz           | 4.5 mm      | 0 – 8 mm    | 25 mm       |
| DS 7 – 4.5      | 7 MHz           | 4.5 mm      | 0 – 8 mm    | 25 mm       |
| DS 10 – 1.5     | 10 MHz          | 1.5 mm      | 0 – 8 mm    | 25 mm       |
| DS 10 – 1.5N    | 10 MHz          | 1.5 mm      | 0 – 8 mm    | 14 mm       |

### 3.2.4. Essential Accessories

Other essential components provided for operation of the Ulthera System are the power cord that connects the Ulthera System to an AC power outlet, and the proprietary Ulthera System User Access Key.

Ultrasound gel to facilitate transmission of the acoustic energy is also required but is not provided as part of the system.

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## 4. System Safety

The following precautions and warnings must be reviewed and observed:

### 4.1. Electrical and Fire Safety



**Warning:** To avoid risk of electric shock, always inspect the Ulthera transducer, handpiece and cable before use. Do not use a damaged cable or a transducer that has been damaged or is leaking fluid.

The Ulthera System is intended for indoor, dry location use. Avoid liquid spills and splashes. Keep coupling gel away from the handpiece-transducer connections.

The Ulthera System comes with a three-conductor AC power cord and plug. Use a properly grounded outlet and always plug the Ulthera System directly into the outlet. Never remove the ground conductor or compromise the ground conductor via any AC adapter plugs or extension cords.

Disconnect the power cord from the outlet by pulling on the plug not the cord.

AC powered USB printers or storage devices may pose a shock hazard. Do not touch the USB connectors and the patient at the same time.

Turn off the AC power switch and disconnect the AC power supply before cleaning the control unit.

Do not remove the covers on the control unit or handpiece; the control unit contains hazardous voltages. The Ulthera System contains no user-serviceable components. If the system requires service, contact Ulthera, Inc.

No modification of this equipment is allowed.

The Ulthera System should not be used near flammable gases or anesthetics. Fire or explosion can result. The Ulthera System is not AP or APG rated.

Avoid restricting ventilation under and behind the Ulthera control unit. Maintain an open space of at least 4 inches/ 10 cm around the control unit. If ventilation holes are obstructed, the system could overheat.

The Ulthera transducer and handpiece is rated as a Type B patient applied part. It may provide a connection between the patient and protective earth. This may present a hazard if the patient becomes connected to other equipment with excessive electrical current leakage.

Do not touch the handpiece electrical contacts and patient simultaneously.

To avoid a burn hazard, remove the transducer from the patient before performing HF electrosurgical procedures.

## 4.2. Equipment Use and Care



**Caution:** Failure to observe these precautions may void the warranty.

The Ulthera handpiece connectors must be kept clean and dry. Do not use the transducer if the connectors have been immersed in liquid. See the instructions for cleaning the transducer.

Every effort has been made to make the transducers as rugged as possible; however, they may be permanently damaged if dropped onto a hard surface or if the membrane is punctured. Transducers damaged in this manner are not covered by the warranty.

The Ulthera System has no user-serviceable components. Do not attempt to open the control unit enclosure or transducers. Contact Ulthera, Inc. if service is required.

When not in use by trained personnel, the Ulthera System User Access Key should be removed from the system to help prevent unauthorized use. Keep the Ulthera System User Access Key in a designated place accessible only to authorized and trained personnel.

## 4.3. Ergonomic Safety



**Warning:** Ultrasound scanning has been associated with repetitive motion injuries such as carpal tunnel syndrome. To reduce chances of such injury, maintain a balanced, comfortable posture while scanning, avoid gripping the handpiece too tightly, and keep hands and arms in a comfortable position while using.

## 4.4. Medical Ultrasound Safety



**Warning:** Use this system only if you are trained and qualified to do so.

The Ulthera System has a fixed, non-adjustable output power level for imaging, well below the limits set by FDA guidelines. However, ultrasound exposure times should be limited to the shortest amount of time needed to complete the treatment. The ALARA principle (As Low As Reasonably Achievable) can be followed by minimizing the examination time.

If the system displays unusual / inconsistent behavior, discontinue use and contact Ulthera, Inc.

Under some conditions (for example, high ambient temperature and long scanning period), the transducer surface temperature may exceed 41°C. Scanning will be automatically disabled if the internal transducer temperature reaches 43°C.

#### 4.5. Electromagnetic Compatibility and Immunity

The Ulthera System's RF emissions are very low and are not likely to cause interference in nearby electronic equipment.

Ulthera is suitable for use in all establishments other than domestic and those directly connected to the public low voltage power supply network that supplies buildings used for domestic purposes.

Mains (AC) power quality should be that of a typical commercial or hospital environment.

Floors should be wood, concrete or ceramic tile. If floors are covered with synthetic material, the relative humidity should be at least 30% to avoid excessive static electricity.



**Warning:** The Ulthera System should not be situated adjacent to, or stacked with, other electronic equipment. If the system must be installed in close proximity to other equipment, both the Ulthera System and the nearby equipment should be observed to verify normal operation in that configuration.



**Caution:** EMI (Electro-Magnetic Interference) from other electronic systems may cause degradation of the ultrasound image. Ulthera has been designed to meet the standards of IEC60601-1-2 for electromagnetic compatibility; however some computer equipment unintentionally emits strong interfering RF signals. Portable RF communication devices may also affect Ulthera. If image quality is degraded by EMI, the system may need to be relocated or reconfigured.



**Warning:** Use of accessories other than those specified, may result in increased emissions, or decreased immunity of this system.

#### 4.6. Disposal

Depleted transducers should be disposed of in accordance with federal, state, and local regulations. For expired transducers (past expiration date), please contact your local Ulthera representative.

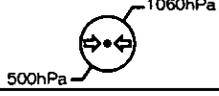
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#### 4.7. Safety Symbols

A variety of symbols appear on the transducer, handpiece, and control unit in accordance with regulatory guidance.

| SYMBOL  | DEFINITION  |
|---|---|
|    | Type B Applied Part   |
|    | CE marking indicating manufacturer's declaration of compliance with appropriate EU product directives |
|    | Canadian Standards Agency   |
|    | Consult instructions for use  |
|   | Date of Manufacture   |
| SN  | Serial Number   |
|  | Emergency Stop  |
|  | Power Standby Switch  |
|  | Indoor Use Only   |
|  | Keep electrical waste separate from municipal waste   |
|  | Recycle Packaging   |
| IPx1  | Mated handpiece and transducer protected from the effects of vertically dripping water                |

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|   |                                  |
|---|----------------------------------|
|    | Catalogue Number                 |
|    | Manufacturer                     |
|    | Storage Range                    |
|    | Keep Dry                         |
|    | Fragile Contents                 |
|    | Relative Humidity                |
|    | Use By, Expiration Date          |
|   | Lot Number                       |
|  | Atmospheric Pressure Limits      |
|  | Recycle Packaging (Polyethylene) |

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## 5. Setting Up for First-Time Use

### 5.1. Unpacking

The control unit and handpiece are shipped together in one container. Transducers are packaged and shipped separately from the control unit and handpiece, in ready-to-use, non-sterile pouches. Transducer gel is also packaged and shipped separately.

### 5.2. Physical Environment

#### 5.2.1. System Base

The System may be placed on a cart or counter with the depth to accommodate the control unit, handpiece and power cord provided. A cart is recommended to offer maximum mobility for the user when treating the patient and provide a more secure housing for the handpiece.

Space should be provided around the back, sides, bottom and top of the System for cooling. In continuous use for extended periods of time, it is normal for the System to be warm.

#### 5.2.2. Electromagnetic Environment

The System is not likely to cause interference in nearby electronic equipment; however, other electronic equipment should not be stacked or placed immediately adjacent to the System.

Flooring should be wood, concrete or ceramic tile. If covered with synthetic material, the relative humidity should be at least 30%.



**Warning:** The Ulthera System should not be situated adjacent to, or stacked with, other electronic equipment. If the system must be installed in close proximity to other equipment, both the Ulthera System and the nearby equipment should be observed to verify normal operation in that configuration.



**Caution:** EMI (Electro-Magnetic Interference) from other electronic systems may cause degradation of the ultrasound image. The Ulthera System has been designed to meet the standards of IEC60601-1-2 for electromagnetic compatibility; however, some computer equipment unintentionally emits strong interfering RF signals. Portable RF communication devices may also affect the Ulthera System. If image quality is degraded by EMI, the system may need to be relocated or reconfigured.

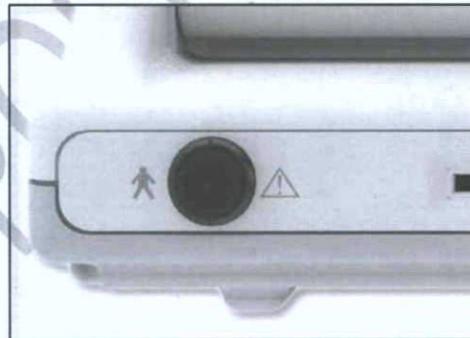
### 5.3. Electrical Requirements

The Ulthera System has an international power supply and may be used with 100-240 VAC, 50-60 Hz power systems. See Section 4.1 Electrical and Fire Safety for additional information.

### 5.4. Connecting Components

#### 5.4.1. Connecting the Handpiece

The handpiece connector receptacle is located on the left side of the control unit's front panel as shown in Figure 5.1. To attach the handpiece connector, align it with the white dot facing up and push it into the receptacle. It will latch when seated properly.



*Figure 5.1 Handpiece Connector Receptacle.*

To disconnect the handpiece, twist the coupling ring on the connector counterclockwise while pulling outwards.

### 5.4.2. Identifying and Connecting Transducers

Transducers are identified by the label on the top of the transducer which includes the name of the transducer (Ulthera DeepSEE), treatment frequency and treatment depth (DS X-X), a unique serial number, a part number, and date of manufacture.

The Treatment Guidelines on the control unit interface will display the recommended transducer to utilize based on the anatomical area you have selected to treat.

Remove the transducer indicated from its protective pouch. To connect the transducer, slide the transducer into the handpiece as shown in Figure 5.2. When the transducer is fully seated you will hear a tone indicating that it has been correctly inserted.



*Figure 5.2 Connecting a Transducer*

To disconnect the transducer, lift the latch at the tip of the handpiece and slide the transducer straight out of the handpiece.



**Caution:** Do not apply force/displacement to latching cantilever without a transducers installed in the handpiece.

When the transducer is inserted, the control unit automatically detects it and updates the graphical user interface.

### 5.4.3. Connecting Accessories

The Ulthera System User Access Key should be inserted into one of the available USB ports otherwise the message “No Key” will appear and the software will not allow user access.

An optional portable USB storage device, i.e. a “thumb drive”, can be inserted into another USB port for downloading images or treatment records.

## 6. System Operation

### 6.1. Overview of System Functions

The Ulthera System's Graphical User Interface is divided into three general functions (tabs): Settings, Patient Info, and DeepSEE. The **Settings** function allows you to recall patient treatment information and to change general system settings.

The **Patient Info** function contains the controls and information instrumental in planning a treatment. This function allows you to build patient treatment information when starting a new treatment or to drive selecting regions during a treatment in progress.

The **DeepSEE** function contains the controls and information needed for imaging soft tissue and for treating pertinent soft tissue. An overview of this screen is seen in Figure 6.1

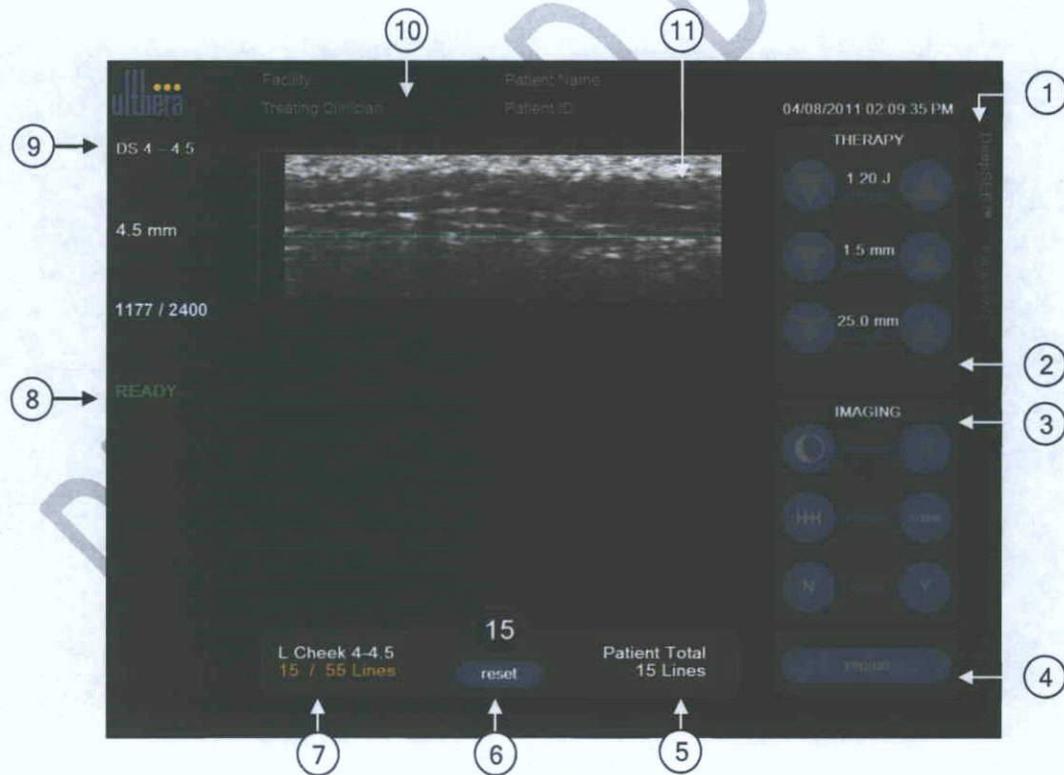


Figure 6.1 Imaging/Therapy Screen (DeepSEE Tab) in READY (to treat) state. See Table 6.1. for description

Table 6.1 Imaging/Therapy Screen Description

| Item |                          | Description   |   |                              |
|------|--------------------------|---|---|------------------------------|
| 1    | System Function Tabs     | DeepSEE   | Imaging/Therapy screen (described in this table)  |                              |
|      |                          | Settings (not scanning)   | Patient and Facility information, Treatment Records and Images, Help, Volume, and System Shutdown controls and dialogs                                      |                              |
|      |                          | Patient Info  | Allows entering of patient information, selection of treatment guidelines and selecting regions during treatments, which automatically set therapy controls |                              |
| 2    | Therapy Controls         | Energy  | Sets acoustic energy level  |                              |
|      |                          | Spacing   | Sets distance between thermal coagulation points  |                              |
|      |                          | Length  | Sets the length of the treatment line   |                              |
| 3    | Imaging Controls         | Marker (not scanning)   | Distance Icon   | Activates distance calipers  |
|      |                          |   | Text  | Activates text annotation    |
|      |                          | Display (scanning)  | Sun icon  | Increases display brightness |
|      |                          |   | Moon icon   | Decreases display brightness |
|      |                          | Image   | Treat ruler icon  | Toggles treat ruler ON/OFF   |
|      |                          |   | Save  | Saves image                  |
|      |                          | Scan  | Y   | Starts scanning (IMAGING)    |
| N    | Stops scanning (IMAGING) |   |   |                              |
| 4    | Region Control           | Launches dialog below image to select tissue region   |   |                              |
| 5    | Patient Total Line Count | Cumulative number of treatment lines delivered  |   |                              |
| 6    | Reset Counter            | Line counter that is reset to "0" by pressing the reset button or by changing regions   |   |                              |
| 7    | Treat Region-Line Count  | <ul style="list-style-type: none"> <li>• Treat region selected (e.g. forehead, submental, etc.)</li> <li>• Lines delivered to region / (vs.) recommended lines per guidelines</li> </ul>                            |   |                              |
| 8    | System Status            | READY or TREATING   |   |                              |
| 9    | Probe Information Area   | <ul style="list-style-type: none"> <li>• Name of attached transducer</li> <li>• Treat depth of transducer</li> <li>• Number of treatment lines spent / (vs.) Total treatment line capacity of transducer</li> </ul> |   |                              |
| 10   | Header Information       | <ul style="list-style-type: none"> <li>• Ulthera logo</li> <li>• Facility, Clinician, Patient Name and Patient ID (if entered)</li> <li>• Date and Time</li> </ul>  |   |                              |

|    |                    |  |
|----|--------------------|--|
| 11 | Image/Treat Region | <ul style="list-style-type: none"> <li>• Ultrasound image</li> <li>• Horizontal and vertical (depth) rulers with 1 mm tick marks</li> <li>• Treat ruler indicating spacing, length and depth of treatment</li> </ul> |
|----|--------------------|--|

## 6.2. Activating the Control Unit

**Step 1** Ensure the power cord on the back of the system is plugged into the wall socket.

**Step 2** Ensure the main power switch on the back of the control unit is in the ON position.

 **Note:** This switch may be left in the ON position even when the system is not in use.

 **Warning:** While running, this switch should not be used to shut down the system.

**Step 3** Insert the Ulthera System User Access Key into the USB port on the back of the control unit.

 **Note:** The Ulthera System must be used only with the authorized Ulthera System User Access Key.

**Step 4** Press the green On/Off button on the front of the control unit.

- The system will perform a brief self-test. After passing the self-test, a "NO KEY" message will be displayed if the Ulthera System User Access Key has not yet been inserted; otherwise the starting screen will be displayed.

 **Warning:** If the self-test screen displays any information messages, turn the system OFF and follow the instructions in Section 7.

### 6.3. Setting Up a Treatment Record

The screenshot shows the Ulthera Patient Info - Treatment Setup Screen. At the top, there are fields for Facility, Treating Clinician, Patient Name, and Patient ID. The date and time are 03/10/2010 12:31:47 PM. Below these fields, there are input fields for Patient Name, Patient ID, and Treating Clinician. A dropdown menu for Treatment Guideline is open, showing 'Ultherapy - Full Face Guideline (4.9)'. Below the dropdown, there are buttons for 'new guideline', 'edit guideline', and 'delete guideline'. At the bottom of the screen, there is a numeric keypad with letters and symbols.

Figure 6.2. Patient Info – Treatment Setup Screen



**Note:** The Patient Info screen is the startup screen.

**Step 1** Enter the patient name, patient ID and the clinician performing the treatment, using the touch pad at the bottom of the screen.



**Note:** A patient name or patient ID along with the selection of a treatment guideline is necessary to start a treatment.



**Note:** Unwanted clinician names stored in the dropdown menu may be deleted by:

- 1) selecting the name to be deleted from the dropdown menu
- 2) pressing the +/- key
- 3) pressing the **del** key followed by the **enter** key

**Step 2** Select the desired Treatment Guideline

- An overview of the various regions within the treatment guideline is visible at the bottom of the screen

**Step 3** Tap the Start Treatment button



**Note:** Once the **Start Treatment** button has been pressed the treatment guideline, patient name and patient ID may not be changed until the treatment is ended.

## 6.4. Selecting a Transducer



**Note:** The Treatment Guideline displays an overview of the various treatment regions with recommended treatment parameters for each, as shown in Appendix A. These treatment parameters are based on results from clinical trials conducted by Ulthera that demonstrated a safe and effective treatment for the treatment region selected.



**Caution:** It is the responsibility of the physician to fully understand the indications for use and safety considerations associated with the Ulthera System.



**Note:** An alternative way to access the treatment region menu is to tap the **Region** button on the **DeepSEE** screen. This approach bypasses the **Patient Info Tab** with the regions listed.

**Step 1** Decide which region you will be treating, and obtain the necessary transducer for that region as depicted on the Patient Info screen.

- The DS 10 – 1.5 transducer has a lower level of energy and a 1.5 mm focal depth.
- The DS 10 – 1.5N transducer has a lower level of energy, 1.5mm focal depth and a narrower patient contact footprint than the DS 10 – 1.5. The DS 7 – 3.0 transducer has a lower level of energy and a 3.0 mm focal depth.
- The DS 7 – 3.0N transducer has a lower level of energy, a 3.0 mm focal depth and a narrower patient contact footprint than the DS 7 – 3.0.
- The DS 7 – 4.5 transducer has an intermediate level of energy and a 4.5 mm focal depth.
- The DS 4 – 4.5 transducer has a higher level of energy and a 4.5 mm focal depth.

**Step 2** After checking the expiration date on the transducer package, open the sealed pouch and connect the transducer by pushing the handpiece latch up and sliding the transducer into the handpiece. When the transducer is fully seated, push the handpiece latch down to lock the transducer into place. You will hear a tone indicating that the transducer has been correctly inserted.



**Caution:** If a “Transducer Not Connected” or any **Warning** or **Caution** screen appears when a transducer is attached, there could be a problem with the

transducer or system. Try disconnecting then reconnecting the transducer. If the problem persists, contact your local representative.

- Step 3** On the **Patient Info** screen, the regions available for treatment with the inserted transducer will be displayed in white under “Treatment Guidelines”. Tap the region to be treated from the available regions displayed. This will take you automatically to the **DeepSEE** screen.
- The Therapy settings on the right-hand side of the screen (i.e., energy, spacing and length) are automatically set to the appropriate levels for the treatment region selected, based on the treatment guideline.

## 6.5. Imaging and Treating

The **DeepSEE** screen displays as shown in Figure 6.3.

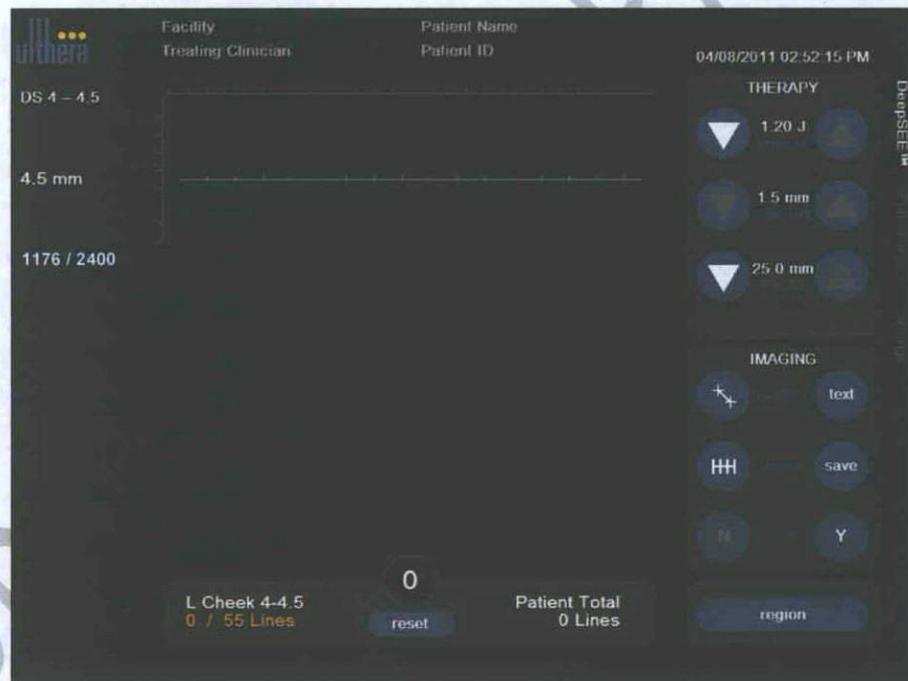


Figure 6.3. DeepSEE screen with treatment region selected (Cheek).

The region you selected from the treatment region menu will be displayed in white on the bottom left/center of the **DeepSEE** screen. The number of recommended treatment lines for the region is displayed underneath as the denominator in yellow, and the cumulative number of treatment lines delivered in that region is displayed as the numerator, in yellow. When the recommended number of treatment lines for the region have been delivered, these numbers will change color to white to signify completion for that region.

A counter for the total number of treatment lines for the patient visit is displayed on the bottom right/center of the screen.

In addition, the appropriate energy level is preset, based on treatment guidelines (see Appendix A – Treatment Guidelines) and can be adjusted down as needed to manage the patient's comfort level.



**Warning:** In the event of damage to any part of the system, as in the handpiece or transducers being dropped, broken, or leaking fluids, the equipment should be disconnected from the power source outlet prior to touching any part of the equipment. Before reconnecting the equipment it should be thoroughly inspected for external damage. Do not use damaged transducers or handpiece on a patient.

### 6.5.1. Treatment Steps

- Step 1** Ensure the face and neck have been cleansed thoroughly.
- Step 2** Carefully apply a thin layer of ultrasound gel to the transducer window. Too much or too little gel will result in poor skin contact. (Use aqueous ultrasound gel only, as other lubricants or lotions can damage the transducers and cables).
- Step 3** Place the transducer treatment window flush with the patient's skin and press the See button on the handpiece to activate the IMAGING state.

An image of the patient's soft tissue appears. The green "treat ruler" that is overlaid upon the image shows the depth that coagulative points will be formed. Green tick marks along the treat ruler show the lateral positions where the coagulative points will be placed along the horizontal plane. For example, with Length set to 25 mm, and Spacing set to 1.5 mm (center to center), a total of 17 coagulative zones would be produced in a treatment line. Verify sufficient coupling between the transducer and the skin by ensuring there are no dark, vertical artifact bars on the image.



**Note:** If the transducer is jostled, dropped or shaken while scanning, it may momentarily pause in order to recalibrate position. It should then resume normal scanning.

- Step 4** Press the See button on the handpiece while in the IMAGING state to activate the READY (to treat) state.



**Note:** The Treat buttons on the handpiece will become lit and a tone is emitted momentarily when the system enters (or exits) the READY state.

The "READY" state turns off after 40 seconds if the **Treat** button is not pressed, but can be reactivated by pressing the **See** button again.

If you would like to freeze the image, tap the Scan N (No) button in the Imaging section on the right hand side of the screen. To resume scanning, press the Scan Y (yes) button (or press the See button again).

To control the image brightness, use the Display buttons to decrease/increase the overall display brightness. These user controls appear only while the system is actively scanning (i.e. in the IMAGING state). When not in the imaging state the controls become distance measurement calipers and text annotation markers (described in Section 6.7) that can be applied to static (frozen) images.

To save a displayed image, next to Image tap Save. The image will be stored on the system and can be recalled, viewed or transferred to an external USB storage device via Images on the Settings Tab.

**Step 5** Verify sufficient coupling between the transducer and the skin by ensuring there are no dark, vertical artifact bars, as indicative of air pockets between the face of the transducer and patient. A properly coupled image should look similar to that in Figure 6.4. Reapply gel as needed to afford ample coupling. A poorly coupled image looks similar to that in Figure 6.5.

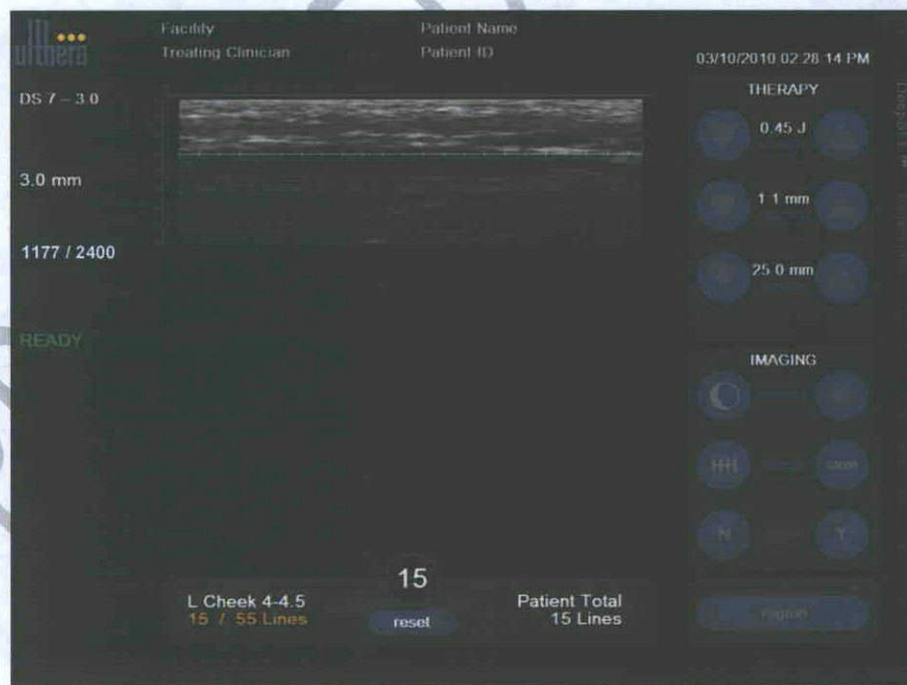


Figure 6.4. Sample image of transducer well-coupled. No vertical dark lines appear.

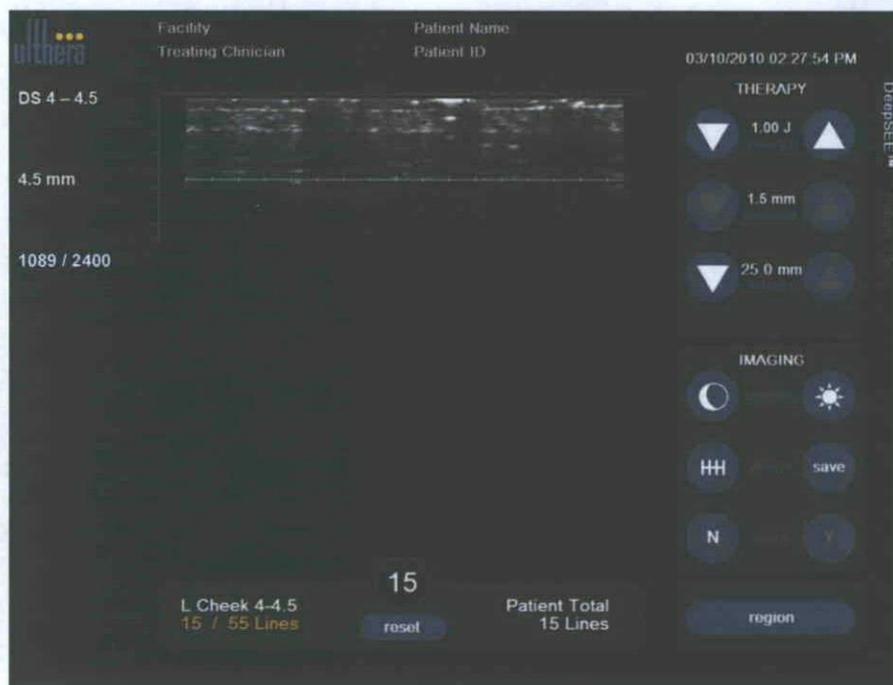


Figure 6.5. Sample Image of Transducer with Poor Coupling on the Cheeks. Large, vertical dark bars are present.

**Step 6** Press a Treat button on the handpiece to activate the TREATING state and deliver the energy between the Treat Guides. Take care that the hand remains still and the handpiece remains in place while the energy is being delivered. In addition a light constant pressure should be maintained between the transducer and the patient's skin. The Treat button's lighting will turn off and the See button will light up momentarily to indicate the system is in the TREATING state. As the energy is delivered a tone is sounded for each coagulation point being created and the green treat ruler will change to a yellow color momentarily. This is shown in Figure 6.6.

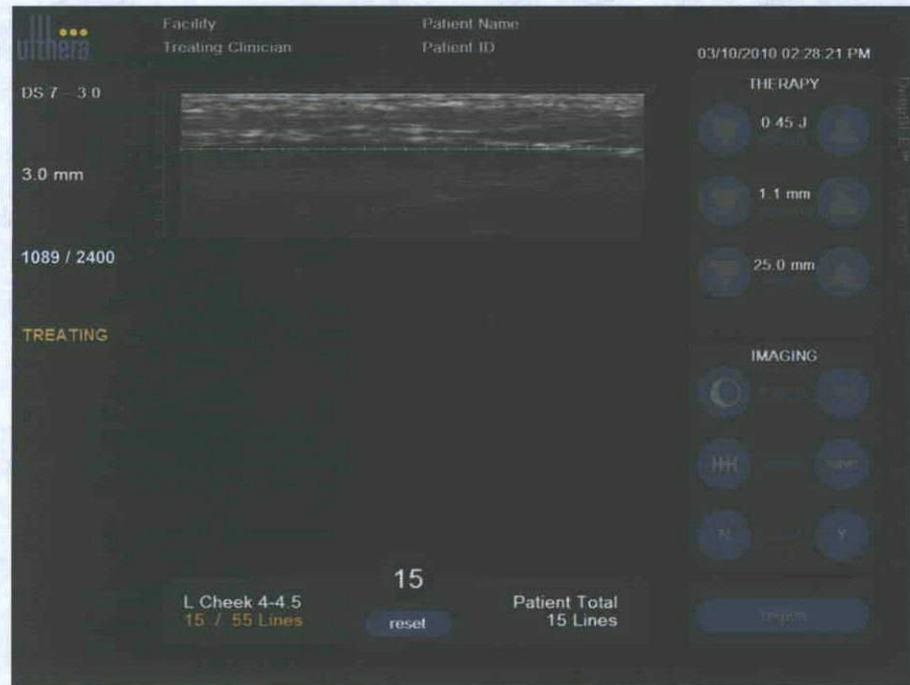


Figure 6.6. TREATING state. A yellow treat progress line is superimposed over the green treat ruler.



**Warning:** If desired, therapy may be cancelled at any time by pressing the **See** button on the handpiece, or the system can be halted by pressing the red Emergency Stop button on the front panel of the control unit. Also, the transducer can be simply lifted off the patient's skin quickly.



**Note:** If an adjustment in the volume of the audio signals is desired, tap the **Settings** tab and use the **Volume** up/down arrows as needed.



**Note:** The settings tab is not available while in the imaging mode.

**Step 7** To deliver the next treatment line of energy within the same treatment region, advance the transducer 2-3 mm to adjacent tissue and press a **Treat** button. If 40 seconds have elapsed since delivering the last treatment line of energy, press the **See** button on the handpiece to restore the READY state, then press a **Treat** button to deliver an additional line of therapy.

**Step 8** After 5 treatment lines are delivered, do a visual check of the transducer window to ascertain if gel needs to be reapplied such that a small bead of gel covers the window.

**Step 9** Continue in this fashion until the recommended number of treatment lines for the region (as shown on the bottom/left of the screen) has been delivered. When the correct number of treatment lines is delivered, the treatment line count color turns from yellow to white.

**Step 10** To continue treatment in another region, tap the **Region** button on the lower right hand of the **DeepSEE** screen. This will prompt the menu of treatment regions and appropriate treatment line counts to be displayed.

 **Note:** If the next treatment region desired is grayed out, change the transducer to the one depicted on the guideline.

 **Note:** If the Treatment Guidelines indicate that the transducer is to be changed in order to treat another section, turn scanning off by pressing the "N" (No) button on the main screen prior to switching transducers.

**Step 11.** Tap the region you will be treating next and proceed as outlined above in Steps 1 through 9.

**Step 12** When all targeted regions have been treated, tap the **End Treatment** button. If all desired treatment lines have been delivered, tap the **Confirm End** button to end the treatment session and to save the treatment record to the system. If further treatment lines are still necessary, you may tap the **Resume Treatment** button to return.

 **Warning:** The **End Treatment** button *must* be tapped at the end of each patient procedure in order to reset the treatment line counters and maintain an accurate count of treatment lines delivered to any one patient or treatment region.

 **Note:** A treatment record is automatically generated during the procedure, which is ended via the **End Treatment** button. Accessing this Record, or any saved images, is described in Section 6.8 Record Keeping.

**Step 13** The system places you back to the starting screen, **Patient Info**, where you may begin another treatment with a new patient. If treatments are finished or if you desire to review or print records from previous treatments tap the **Settings** tab. From this screen you may review records, images or tap **Shutdown** to turn OFF the system.

**Step 14** Follow cleaning and maintenance instructions in Section 8.0.

## 6.6. Adjunctive Functions

### 6.6.1. Distance Measurements

The Ulthera System allows you to make distance measurements on ultrasound images when the system is not in the active IMAGING state. Tap **Scan N** to stop scanning if necessary.

- Step 1** While you are on the DeepSEE Screen, tap the distance icon, + — + button, in the IMAGING section. A starting point marker will appear near the center of the image.
- Step 2** Touch the screen and the marker will drag along above your finger. Once you have placed the starting point marker where you want then lift your finger off of the screen. At that point an ending point marker will appear, along with a line between the two points.
- Step 3** Touch the screen again to move the ending point marker where you wish to. When you lift your finger the straight line distance between the points will be displayed.
- Step 4** To place a second distance measurement on the screen tap the distance measurement button + — + again, and repeat the above steps.

**i** **Note:** To clear the first distance measurement off of the screen tap the distance measurement button again, and then a second time if desired to delete the second distance measurement. In fact, tapping the distance measurement button cycles through distance measurements D1 and D2 in the order: *D1 (add), D2 (add), D1 (delete), D2 (delete), and then repeats.*

**i** **Note:** When imaging is restarted by pressing the **See** button or **Scan Y** all distance measurements are deleted from the image.

### 6.6.2. Text Annotations

The Ulthera System allows you to add information such as comments atop ultrasound images when the system is not in the active IMAGING state. Tap **Scan N** to stop scanning if necessary.

- Step 1** While you are on the DeepSEE Screen, tap the **TEXT** button in the IMAGING section. A text box will appear near the center of the image and a keyboard will appear below the image.
- Step 2** Type any comments and/or move the text box where desired by tapping the screen – the box will track your finger.

**Step 3** Hit Enter on the keyboard when finished entering the desired comments and when the text box is in the desired position.



**Note:** Tapping the **Text** button cycles through text annotations Text1 and Text2 in the order: *Text1 (add), Text2 (add), Text1 (delete), Text2 (delete), and then repeats.*

## 6.7. Record Keeping

The Ulthera System uses a proprietary Ulthera Database for storing a limited number of images and treatment record information. These images are readily accessible to browse, or export to another storage device.

It is strongly recommended that you properly maintain the database by regularly exporting and/or deleting unused or old images and treatment records. Excessive numbers of records and images become difficult to search and maintain on a system primarily dedicated to patient treatment, and thereby reduce productivity and system performance.

The number of images and/or treatment records that can be stored is limited to 200. At startup, if more than that are stored, the user is asked to optionally delete some of them. If not, additional storage is disabled. However, if a procedure is already in progress as the system reaches its 200 mark additional records may be stored, the user will simply be asked to reduce the number of images and/or treatment records in the database the next time the system is started.



**Note:** All image compression methods used by Ulthera System are lossless. This produces small image file size without losing any image resolution or creating any image artifacts.

### 6.7.1. Saving Records in the Database

**Step 1** To save images in the database use the Save button on the DeepSEE tab to save the current display as a single image. Treatment records will automatically be saved assuming it has been set up as stated in Section 6.3 Setting Up a Treatment Record. For accessing images and/or treatment records at a later date see 6.8.3 and 6.8.4 respectively.

### 6.7.2. Browsing the Database

**Step 1** Tap the **Settings** tab then tap on either **Records** (to view stored treatment data) or **Images** (to view scans). From here you can browse the data on screen, save to a USB thumb drive, or delete items.

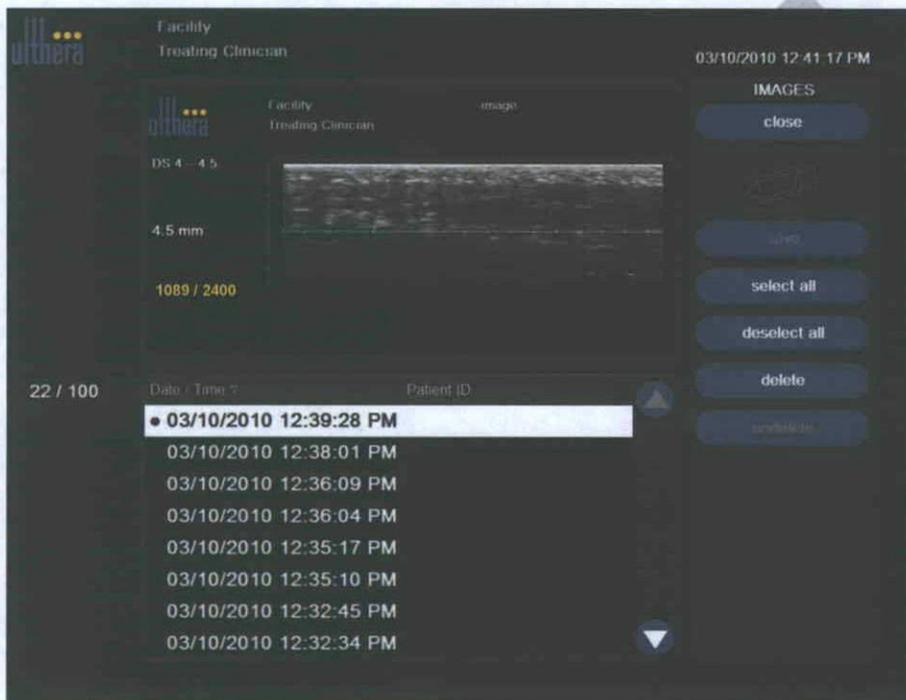


**Note:** It is advisable to store records on an accessory device before deleting.

### 6.7.3. Exporting Images

**Step 1** On the **Settings** screen, tap **Images** to view the menu of treated patients. A screen similar to Figure 6.8. will appear.

**Step 2** Tap a specific **Patient ID** to call up the image stored for that patient or tap **Select All** to call up all stored images.



*Figure 6.8. Image Export screen. Stored images are listed in the bottom dialog box and the most recently user-selected image is displayed above it. If an external storage device is attached then SAVE is enabled.*



**Note:** If you inadvertently selected an item or items, tap that item again or tap **Deselect All** to clear the selection(s).

**Step 3** Connect the generic USB storage device (as described in Section 5.4.3 Connecting Accessories).

- The icon for this appears on the right hand side of the screen; it will be grayed out if the accessory is disabled and will be displayed in white if enabled.

**Step 4** Tap **Save** to export image(s) to USB thumb drive

## 6.7.4. Exporting Records

**Step 1** On the **Settings** screen, tap **Records** to view the menu of treated patients. A screen similar to Figure 6.9. will appear.

**Step 2** Tap a specific **Patient ID** to call up the records stored for that patient or tap **Select All** to call up all stored records.



**Note:** If you inadvertently selected an item or items, tap that item again or tap **Deselect All** to clear the selection(s).

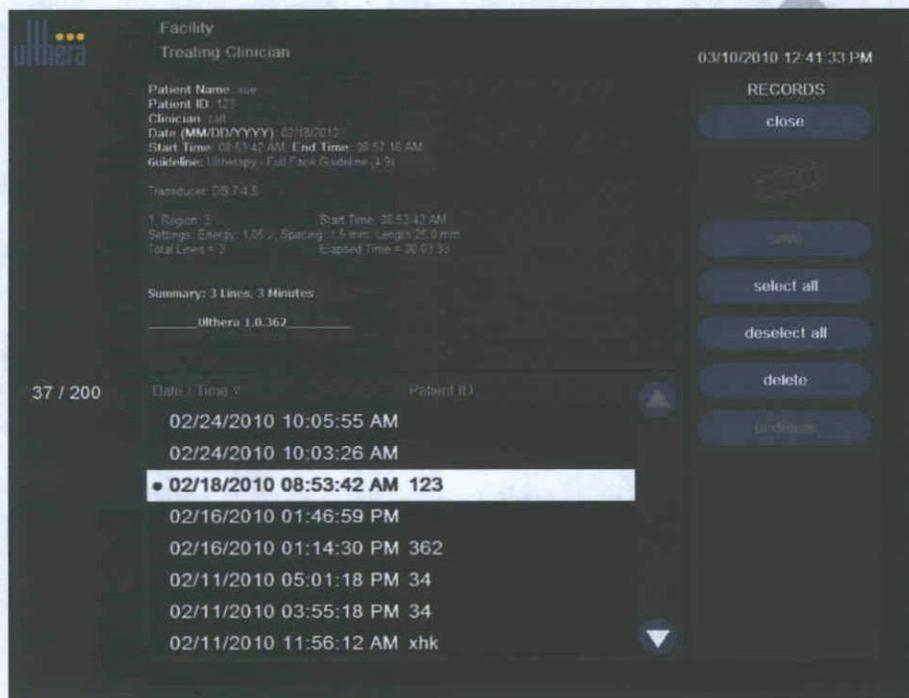


Figure 6.9 Treatment Records screen.

**Step 3** Connect the generic USB storage device (as described in Section 5.4.3 Connecting Accessories).

- The icon for this appears on the upper right hand side of the screen; it will be grayed out if the accessory is disabled and will be displayed in white if enabled.

**Step 4** Tap **Save** to export record(s) to USB thumb drive.

**Step 5** For the information to remain on the System after exporting the desired information tap **Close** to return to the Settings screen. To delete the information from the System after exporting it, see the next Section, 6.8.5.

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### 6.7.5. Deleting Records from the Database

 **Note:** It is advisable to store records on an accessory device before deleting information.

**Step 1** To remove one or more item(s) from the database, select the item(s) and tap **Delete**; to remove *all* items from the database, tap **Select All** and then tap **Delete All**.

 **Note:** If you inadvertently delete an item or items, tap **Undelete** to restore the item(s).

Records in the **Undelete** dialogue may be permanently erased by selecting the items to be permanently erased and then tapping the **Erase** button.

**Step 2** Tap **Close** to return to the **Settings** screen.

### 6.7.6. Recovering Deleted Records/Images from the Database

 **Note:** Only the 50 previously deleted records or images may be recovered.

**Step 1** To recover one or more of the 50 previously deleted records or images tap **Undelete**.

**Step 2** Select the images or records that you would like to undelete and tap **Undelete** once more.

The records or images will have now returned to the current database.

## 6.8. Troubleshooting

### 6.8.1. Ulthera System Warning and Caution Dialogs

 **Warning:** These dialogs indicate that a problem was detected. See System Messages section for more details.

An example of a system warning appears in Figure 6.10. In such cases the user is given instructions on how to resolve the issue. Please follow the guidance to help solve the problem as quickly as possible and to provide proper information in case Technical Support is needed.



Figure 6.10 Example of System Caution Dialog.

### 6.8.2. Unsatisfactory Image Quality

#### Action Required:

- Check that the display brightness is set appropriately for the transducer that is connected and the area being imaged via the **Display controls**.
- Check that enough gel is applied to the transducer.
- If the problem is not resolved, contact Ulthera, Inc. or your country representative for assistance.

### 6.9. Shutting Down the System

**Step 1** Stop any imaging and/or treatment in progress prior to shutting down the system.

**Step 2** On the **Settings** screen, tap **Shutdown**

**Step 3** Remove the Ulthera System User Access Key to prevent unauthorized usage.



**Note:** The main power switch on the rear panel of the control unit should be left in the ON position; however, it may be switched off when moving the system between rooms or for storage or cleaning.

## 7. System Messages

The Ulthera System is designed with internal checks to ensure that all aspects of the device are functioning appropriately. In the event that an information message presents itself during use, please follow the instructions on the screen or refer to the information listed below.

These messages are classified as INFORMATION SIGNALS per IEC 60601-1-8.

| Info Code | Message Displayed   | Description  |
|-----------|---|--|
| <b>B</b>  | <p>Code B</p> <p> Internal handpiece temperature is too high</p> <p>If the problem persists please see the User's Manual for further information or contact Ulthera Support.</p>   | The internal handpiece temperature is above its limit. Allow the handpiece to cool down.   |
| <b>C</b>  | <p>Code C</p> <p> Hardware halted</p> <p>Please restart the system.</p> <p>If the problem persists please see the User's Manual for further information or contact Ulthera Support.</p>                                  | Hardware was halted due to an event detected in the control unit.  |
| <b>E</b>  | <p>Code E</p> <p> Communication halted</p> <p>Please restart the system.</p> <p>If the problem persists please see the User's Manual for further information or contact Ulthera Support.</p>                           | Communication was halted due to an initialization event detected in the control unit.  |
| <b>G</b>  | <p>Code G</p> <p> Hardware halted</p> <p>Please restart the system.</p> <p>If the problem persists please see the User's Manual for further information or contact Ulthera Support.</p>                                | Hardware was halted due to an event detected in the control unit.  |
| <b>H</b>  | <p>Code H</p> <p> Transducer motion not detected</p> <p>Please remove and reinsert the transducer.</p> <p>If the problem persists please see the User's Manual for further information or contact Ulthera Support.</p> | Transducer motion was not detected. Ensure that the transducer is properly mounted in the handpiece. Please be sure to always hit Scan N before removing transducer. Remove and reinsert the transducer. |
| <b>I</b>  | <p>Code I</p> <p> Communication halted</p> <p>Please restart the system.</p> <p>If the problem persists please see the User's Manual for further information or contact Ulthera Support.</p>                           | Communication halted due to an event detected in the control unit.   |

| Info Code | Message Displayed   | Description  |
|-----------|---|--|
| J         | <p>Code J</p> <p> Handpiece communication halted<br/>Please restart the system.</p> <p>If the problem persists please see the User's Manual for further information or contact Ulthera Support.</p>          | Communication halted due to an event detected in the control unit.   |
| K         | <p>Code K</p> <p> Software halted<br/>Please restart the system.</p> <p>If the problem persists please see the User's Manual for further information or contact Ulthera Support.</p>                         | Software was halted due to an event detected in the control unit.  |
| L         | <p>Code L</p> <p> Transducer out of lines<br/>Please replace transducer and continue.</p> <p>See User's Manual for further information.</p>  | The Transducer's remaining line count is zero. Remove and replace the Transducer.  |
| M         | <p>Code M</p> <p> Handpiece motion halted</p> <p>If the problem persists please see the User's Manual for further information or contact Ulthera Support.</p>  | Inspect handpiece. Ensure that the transducer is properly mounted and latched in the handpiece.  |
| N         | <p>Code N</p> <p> USB flash memory connectivity<br/>Please check flash drive and continue.</p> <p>See User's Manual for further information.</p>   | A problem was detected with the attached USB flash memory drive. Make sure the drive is properly formatted and has enough free space. Do not remove the drive while the system is communicating with it. |
| P         | <p>Code P</p> <p> Hardware halted<br/>Please restart the system.</p> <p>If the problem persists please see the User's Manual for further information or contact Ulthera Support.</p>                       | Hardware was halted due to an event detected in the control unit.  |
| S         | <p>Code S</p> <p> The red STOP button has been pressed.<br/>Please restart the system.</p> <p>If the problem persists please see the User's Manual for further information or contact Ulthera Support.</p> | The red Stop button was pressed.   |
| T         | <p>Code T</p> <p> Internal transducer temperature is too high</p> <p>If the problem persists please see the User's Manual for further information or contact Ulthera Support.</p>                          | The internal transducer temperature is above its limit. Allow the transducer to cool down or use another transducer.   |
| U         | <p>Code U</p> <p> Control unit temperature too high</p> <p>If the problem persists please see the User's Manual for further information or contact Ulthera Support.</p>                                    | The internal control unit temperature is above its limit. Allow the control unit to cool down. Provide proper ventilation.   |

| Info Code | Message Displayed  | Description   |
|-----------|--|---|
| V         | <p>Code V</p> <p> Transducer energy delivery halted</p> <p>Tap Scan Y to resume scanning</p> <p>If the problem persists please see the User's Manual for further information or contact Ulthera Support.</p>      | <p>Excessive reflected power has been detected. If the problem persists, please try another transducer and contact Ulthera Support. Use Transducer only as instructed. Tap Scan Y to resume scanning.</p> |
| W         | <p>Code W</p> <p> Unauthorized transducer.</p> <p>Please replace the transducer and continue.</p> <p>Please contact your local representative for further assistance.</p>   | <p>The transducer connected is not an authorized transducer. Contact your local representative for further assistance.</p>  |
| X         | <p>Code X</p> <p> Transducer cannot be read</p> <p>Please remove and reinsert the transducer.</p> <p>If the problem persists please see the User's Manual for further information or contact Ulthera Support.</p> | <p>The transducer cannot be read. Remove and reinsert the transducer. Check that the transducer contact area is clean.</p>  |

PROPOSED DRAFT

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## 8. Cleaning and Care

### 8.1. Cleaning the Transducer and Handpiece



**Note:** Transducers are packaged and shipped non-sterile and ready to use.

Because the transducer will come in contact with the skin of a patient, the standard practice for cleaning and low level disinfection of transducers between patients is to gently but thoroughly wipe the transducers with a standard 70% isopropyl alcohol prep pad. One may also use a standard 70% isopropyl alcohol prep pad to gently wipe the handpiece and cable. Neither the transducers nor the handpiece should be submerged in liquid. Place the transducer back into its original packaging between uses.



**Warning:** Use only this procedure for cleaning. Do not use acetone or other solvents as this can damage the transducer.

### 8.2. General Care of the System

To get the best possible performance, treat the equipment carefully by adhering to the following guidelines:

1. Inspect the handpiece and connectors regularly for any problems.
2. Turn scanning off before changing transducers to ensure proper identification of transducers and to prolong the life of the system.
3. Do not drop the handpiece or transducers on the floor or other hard surfaces. This can cause permanent damage.
4. Do not twist or pull the transducer cables. This could cause damage to internal wires and connections.
5. Use aqueous ultrasound gel only. Other lubricants or lotions, particularly mineral oil, could eventually damage transducers or cables.
6. Do not use acoustic standoff pads or any objects between the transducer and patient.
7. Apply ultrasound gel only to the window of the transducer and wipe it from the transducer after completing a treatment. Avoid getting the gel on the handpiece or control unit.
8. Transducers should be cleaned between procedures. See cleaning procedure information immediately preceding this subsection.
9. Keep new transducers in sealed pouches until ready for use.

10. Place transducers back into original pouch and reseal for storage between procedures.
11. Do not hold the handpiece in a manner that can damage the chord or strain relief while removing or inserting transducers.



**Caution:** Always check the expiration date on the transducer before using.

PROPOSED DRAFT

## 9. Re-order Information

Please contact Ulthera, Inc. or your country representative to order transducers, accessories, or other items for your system.

| Description                               | Catalog/<br>Reorder Number |
|---|----------------------------|
| Ulthera Control Unit                      | UC-1                       |
| Ulthera® DeepSEE® Handpiece               | UH-2                       |
| Ulthera® DeepSEE® Transducer DS 7-3.0     | UT-1                       |
| Ulthera® DeepSEE® Transducer DS 7-3.0N    | UT-1N                      |
| Ulthera® DeepSEE® Transducer DS 4-4.5     | UT-2                       |
| Ulthera® DeepSEE® Transducer DS 7-4.5     | UT-3                       |
| Ulthera® DeepSEE® Transducer DS 10-1.5    | UT-4                       |
| Ulthera® DeepSEE® Transducer DS 10-1.5N   | UT-4N                      |
| Ulthera System Cart                       | UR-1                       |
| (Optional) Ulthera System Case            | US-1                       |
| (Optional) Ulthera System User Access Key | UK-1                       |
| (Optional) USB Storage Device             | UD-1                       |

PROPOSED

## 10. Safety Standards and Regulatory Classifications

|   |
|---|
| FDA Product Classification 878.4590   |
| UL60601-1, IEC60601-1 Medical Electrical Equipment, Part 1: General Requirements for Safety.                    |
| Class I device, type B applied part, non AP/APG rated.  |
| Ingress protection: IPx0 ("Ordinary Equipment") for Control Unit; IPx1 for mated transducer and handpiece.      |
| Mode of operation: Continuous.  |
| IEC60601-1-2, Electromagnetic Compatibility, CISPR 11 class A, Group 1.   |
| IEC60601-1-4, Programmable electrical medical systems   |
| IEC60601-2-37, Particular requirements for the safety of ultrasonic medical diagnostic and monitoring equipment |
| Patient-contacting materials comply with ISO 10993-1  |
| NRTE Certification: Canadian Standards Association (CSA)  |
| ISO 13485 Quality Assurance Standard  |

# Appendix A – Treatment Guidelines

As displayed on the user interface and as notated in Table A.1., guidelines are set forth for the levels of energy, available transducer and the number of treatment lines to be delivered for each treatable region.

Table A.1. Treatment Guideline (5.0 PLUS)

| Ultherapy – Guideline (5.0 PLUS) |                     |             |                   |      |      |      |       |  |
|----------------------------------|---------------------|-------------|-------------------|------|------|------|-------|--|
| Area                             | Region              | Transducer  | Energy Levels [J] |      |      |      | Lines |  |
| Medial Neck                      | Medial Neck 4-4.5   | DS 4 - 4.5  | 1.20              | 1.00 | 0.90 | 0.75 | 18    |  |
|                                  | R Neck 4-4.5        | DS 4 - 4.5  | 1.20              | 1.00 | 0.90 | 0.75 | 26    |  |
| Right Side<br>4.5                | R Cheek 4-4.5       | DS 4-4.5    | 1.20              | 1.00 | 0.90 | 0.75 | 77    |  |
|                                  | R Brow 7-4.5        | DS 7-4.5    | 1.05              | 0.90 | 0.75 | 0.66 | 10    |  |
|                                  | R Orbit 7-4.5       | DS 7-4.5    | 1.05              | 0.90 | 0.75 | 0.66 | 10    |  |
| Medial Neck                      | Medial Neck 7-3.0   | DS 7 - 3.0  | 0.45              | 0.35 | 0.30 | 0.25 | 18    |  |
|                                  | R Neck 7-3.0        | DS 7 - 3.0  | 0.45              | 0.35 | 0.30 | 0.25 | 26    |  |
| Right Side<br>3.0                | R Cheek 7-3.0       | DS 7 - 3.0  | 0.45              | 0.35 | 0.30 | 0.25 | 56    |  |
|                                  | R Brow 7-3.0        | DS 7 - 3.0  | 0.45              | 0.35 | 0.30 | 0.25 | 10    |  |
|                                  | R Orbit 7-3.0       | DS 7 - 3.0  | 0.45              | 0.35 | 0.30 | 0.25 | 10    |  |
|                                  | R Infraorbital 3.0N | DS 7 - 3.0N | 0.45              | 0.35 | 0.30 | 0.25 | 9     |  |
| Left Side<br>4.5                 | L Neck 4-4.5        | DS 4 - 4.5  | 1.20              | 1.00 | 0.90 | 0.75 | 26    |  |
|                                  | L Cheek 4-4.5       | DS 4-4.5    | 1.20              | 1.00 | 0.90 | 0.75 | 77    |  |
|                                  | L Brow 7-4.5        | DS 7-4.5    | 1.05              | 0.90 | 0.75 | 0.66 | 10    |  |
|                                  | L Orbit 7-4.5       | DS 7-4.5    | 1.05              | 0.90 | 0.75 | 0.66 | 10    |  |
| Left Side<br>3.0                 | L Neck 7-3.0        | DS 7 - 3.0  | 0.45              | 0.35 | 0.30 | 0.25 | 26    |  |
|                                  | L Cheek 7-3.0       | DS 7 - 3.0  | 0.45              | 0.35 | 0.30 | 0.25 | 56    |  |
|                                  | L Brow 7-3.0        | DS 7 - 3.0  | 0.45              | 0.35 | 0.30 | 0.25 | 10    |  |
|                                  | L Orbit 7-3.0       | DS 7 - 3.0  | 0.45              | 0.35 | 0.30 | 0.25 | 10    |  |
|                                  | L Infraorbital 3.0N | DS 7 - 3.0N | 0.45              | 0.35 | 0.30 | 0.25 | 9     |  |
| Right Side<br>1.5                | R Cheek             | DS 10-1.5   | 0.25              | 0.20 | 0.18 | 0.15 | 75    |  |
|                                  | R Brow              | DS 10-1.5   | 0.25              | 0.20 | 0.18 | 0.15 | 15    |  |
|                                  | R Orbit 10-1.5      | DS 10-1.5   | 0.25              | 0.20 | 0.18 | 0.15 | 15    |  |
|                                  | R Infraorbital 1.5  | DS 10-1.5   | 0.25              | 0.20 | 0.18 | 0.15 | 15    |  |
|                                  | R Infraorbital 1.5N | DS 10-1.5N  | 0.25              | 0.20 | 0.18 | 0.15 | 15    |  |
|                                  | R Oral 1.5          | DS 10-1.5   | 0.25              | 0.20 | 0.18 | 0.15 | 25    |  |
|                                  | R Oral 1.5N         | DS 10-1.5N  | 0.25              | 0.20 | 0.18 | 0.15 | 25    |  |
| Left Side                        | L Cheek             | DS 10-1.5   | 0.25              | 0.20 | 0.18 | 0.15 | 75    |  |

|                      |                     |             |      |      |      |      |    |
|----------------------|---------------------|-------------|------|------|------|------|----|
| <b>1.5</b>           | L Brow              | DS 10-1.5   | 0.25 | 0.20 | 0.18 | 0.15 | 15 |
|                      | L Orbit 10-1.5      | DS 10-1.5   | 0.25 | 0.20 | 0.18 | 0.15 | 15 |
|                      | L Infraorbital 1.5  | DS 10-1.5   | 0.25 | 0.20 | 0.18 | 0.15 | 15 |
|                      | L Infraorbital 1.5N | DS 10-1.5N  | 0.25 | 0.20 | 0.18 | 0.15 | 15 |
|                      | L Oral 1.5          | DS 10-1.5   | 0.25 | 0.20 | 0.18 | 0.15 | 25 |
|                      | L Oral 1.5N         | DS 10-1.5N  | 0.25 | 0.20 | 0.18 | 0.15 | 25 |
| <b>Medial Option</b> | Medial Neck 7-4.5   | DS 7-4.5    | 1.05 | 0.90 | 0.75 | 0.66 | 18 |
| <b>Right Option</b>  | R Neck 7-4.5        | DS 7-4.5    | 1.05 | 0.90 | 0.75 | 0.66 | 26 |
|                      | R Cheek 7-4.5       | DS 7-4.5    | 1.05 | 0.90 | 0.75 | 0.66 | 77 |
|                      | R Brow 7-3.0N       | DS 7 - 3.0N | 0.45 | 0.35 | 0.30 | 0.25 | 10 |
|                      | R Orbit 7-3.0N      | DS 7 - 3.0N | 0.45 | 0.35 | 0.30 | 0.25 | 10 |
|                      | R Infraorbital 3.0  | DS 7 - 3.0  | 0.45 | 0.35 | 0.30 | 0.25 | 9  |
| <b>Left Option</b>   | L Neck 7-4.5        | DS 7-4.5    | 1.05 | 0.90 | 0.75 | 0.66 | 26 |
|                      | L Cheek 7-4.5       | DS 7-4.5    | 1.05 | 0.90 | 0.75 | 0.66 | 77 |
|                      | L Brow 7-3.0N       | DS 7 - 3.0N | 0.45 | 0.35 | 0.30 | 0.25 | 10 |
|                      | L Orbit 7-3.0N      | DS 7 - 3.0N | 0.45 | 0.35 | 0.30 | 0.25 | 10 |
|                      | L Infraorbital 3.0  | DS 7 - 3.0  | 0.45 | 0.35 | 0.30 | 0.25 | 9  |

PROPOSED

K121760

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## 510(k) Summary

This 510(k) Summary for the Ulthera® System is submitted in accordance with the requirements of the Safe Medical Device Act (SMDA) of 1990 and follows the Office of Device Evaluation (ODE) guidance concerning the organization and content of a 510(k) summary.

**Applicant:** Ulthera, Inc.

**Address:** 2150 South Country Club Drive, Suite 21  
Mesa, AZ 85210

**Contact Person:** Suzon Lommel, VP of Regulatory & Quality Affairs

**Telephone:** 480-649-4069

**Fax:** 480-619-4071

**Submission Date:** June 7, 2012

**Device Trade Name:** Ulthera® System

**Common Name:** Focused Ultrasound Stimulator Use System for Aesthetic Use

**Classification:** Regulatory Class II

**Classification Name:** Focused Ultrasound Stimulator Use System for Aesthetic Use

**Product Code:** OHV

**Legally Marketed Name:** Ulthera® System

**Predicates:** 510(k): #K072505

**Applicable Guidance:** *The Class II Special Controls Guidance Document: Focused Ultrasound Stimulator System for Aesthetic Use* was developed in response to Ulthera's DeNovo submission and 510(k) clearance K072505 for the Ulthera System.



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K121700 2/2

**Device Description:** The Ulthera® System consists of the following components:

- Ulthera® Control Unit
- Handpiece
- Transducers

**Indications for Use:** The Ulthera® System is indicated for use as a non-invasive dermatological aesthetic treatment to:

- lift the eyebrow (current cleared indication)
- lift lax submental (beneath the chin) and neck tissue (requested expanded indication)

**Performance Data:** To support the expanded indication, the Ulthera® System was evaluated in an open-label clinical trial investigating the clinical response following treatment with the Ulthera® System to achieve lifting of lax submental (beneath the chin) and neck tissue. Improvement was evaluated through quantitative assessment, qualitative assessment and patient satisfaction questionnaires. There were 51/70 patients that had an improvement of  $\geq 20$  mm<sup>2</sup> in lift, of these patients 84.3% were identified as showing improvement by masked evaluators. The adverse events resulting from treatment with the Ulthera® System during this study were mild, short-lived in duration, and resolved without incident. There were no serious adverse events (SAEs) or unanticipated adverse device effects (UADEs) related to treatment with the Ulthera® System.

**Conclusion:** Based on the design, materials, principle of operation, and intended use, the Ulthera® System is substantially equivalent to the legally marketed predicate device.



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## Indications for Use Statement

**510(k) Number:** K121700

**Device Name:** Ulthera® System

**Indications for Use:**

The Ulthera® System is indicated for use as a non-invasive dermatological aesthetic treatment to:

- lift the eyebrow
- lift lax submental (beneath the chin) and neck tissue

Prescription Use  AND/OR Over-The-Counter Use   
(Part 21 CFR 801 Subpart D) (21 CFR 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

---

Concurrence of CDRH, Office of Device Evaluation (ODE)



**Felten, Richard P.**

---

**From:** Ashley Fickett [a.fickett@ulthera.com]  
**Sent:** Monday, October 01, 2012 1:39 PM  
**To:** Felten, Richard P.  
**Cc:** Randy Miller; Suzon Lommel  
**Subject:** K121700 - Ulthera  
**Attachments:** Attachment 1 - Section 5 510(k) Summary.pdf; Indications for Use Statement.pdf

Hello Richard,

Thank you for your time today.

1. Per your request, the indications for use have been updated to remove the full face indication (see redlines below):

**Indications for Use:**

The Ulthera® System is indicated for use as a non-invasive dermatological aesthetic treatment to:

- lift the eyebrow
- lift lax submental (beneath the chin) and neck tissue
- ~~lift lax tissue to achieve a desired aesthetic effect for the full face and neck~~

The indications for use have been updated in the 510(k) Summary and Indications for Use Statement (see attached).

2. In addition, the performance data section in the 510(k) Summary has been updated to include the requested information regarding number of patients and results (see below):

*There were 51/70 patients that had an improvement of  $\geq 20$  mm<sup>2</sup> in lift, of these patients 84.3% were identified as showing improvement by masked evaluators.*

Please let me know if you have any additional questions or concerns. We look forward to hearing from you later today on the revised Indications for Use Statement and 510(k) Summary.

Best regards,  
Ashley

**Ashley Fickett**  
Regulatory Affairs Associate  
Ulthera, Inc.  
phone: 480-619-4069  
email: [a.fickett@ulthera.com](mailto:a.fickett@ulthera.com)



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10/1/2012

Questions? Contact FDA/CDRH/OCE/DID at [CDRH-FOISTATUS@fda.hhs.gov](mailto:CDRH-FOISTATUS@fda.hhs.gov) or 301-796-8118

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## 2. Medical Safety

### 2.1. Indications for Use

The Ulthera System is indicated for non-invasive dermatological aesthetic treatment to:

- lift the eyebrow
- lift lax submental (beneath the chin) and neck tissue

### 2.2. Contraindications

The Ulthera System is contraindicated for use in patients with

- open facial wounds or lesions
- severe or cystic acne on the face and/or neck

### 2.3. Precautions

When not in use by trained personnel, the Ulthera System User Access Key should be removed from the system to help prevent unauthorized use. Keep the Ulthera System User Access Key in a designated place accessible only to authorized and trained personnel.

The Ulthera System has not been evaluated for use over various materials. Therefore, treatment is not recommended directly over those areas with any of the following:

- Mechanical implants
- Dermal fillers
- Implanted electrical devices
- Metal stents in the face and neck area

Treatment energy is not recommended for use directly on an existing keloid.

The Ulthera System has not been evaluated for use in patients on an anticoagulant treatment plan.

The Ulthera System has not been evaluated for use in the following patient populations:

- Pregnant or breast feeding women
- Children
- Those with the following disease states
  - A hemorrhagic disorder or haemostatic dysfunction
  - An active or local skin disease that may alter wound healing
  - Herpes Simplex
  - Autoimmune Disease
  - Diabetes
  - Epilepsy
  - Bell's Palsy

#### 2.4. Patient Safety



**Warning:** Ulthera should not be used on a patient's eyes or in a location or technique where ultrasound energy can reach the eye.



**Warning:** Use this system only if you are trained and qualified to do so.



**Warning:** If any problems occur during system operation, take immediate action(s): lift the transducer off the patient's skin, press the **See** pushbutton on handle to discontinue treatment in progress, and/or press the red emergency **Stop** button to completely halt system operation.

#### 2.5. Potential Side Effects

Side effects reported in the clinical evaluation of the Ulthera System were mild and transient in nature. These were limited to:

- Erythema (redness): The treated area may exhibit erythema immediately following treatment. This typically resolves within a few hours of treatment.

- **Edema (swelling):** The treated area may exhibit mild edema following treatment. This typically resolves within a few days of treatment.
- **Pain:** Momentary discomfort may be experienced during the procedure while energy is being deposited.
- **Bruising:** Mild bruising, which is caused by damage to soft tissue blood vessels, may occur occasionally and typically resolves within a few days of treatment.
- **Nerve Effects:**
  - Transient local muscle weakness may result after treatment due to inflammation of a motor nerve.
  - Transient numbness may result after treatment due to inflammation of a sensory nerve.

No permanent injuries to facial nerves have been reported.

- **Scarring:** The possibility for scar formation (which will respond to medical care) may exist if incorrect treatment technique is used.

## 2.6. Complaints and Adverse Events

No serious adverse events were observed during the clinical study evaluation of the Ulthera System.

Ulthera follows MDR (Medical Device Reporting) rules for handling complaints and adverse events. Should an adverse event be suspected or reported, contact Ulthera, Inc. at the number on the cover page of this document; for those outside the U.S., contact your local Ulthera representative.

**Felten, Richard P.**

---

**From:** Ashley Fickett [a.fickett@ulthera.com]  
**Sent:** Monday, October 01, 2012 2:40 PM  
**To:** Felten, Richard P.  
**Cc:** Randy Miller; Suzon Lommel  
**Subject:** RE: K121700 - Ulthera  
**Attachments:** 1001085IFU IFU, Ulthera System Lower Face IFU - Section 2 Medical Safety Only.pdf;  
1001085IFU IFU, Ulthera System Lower Face IFU.pdf

Hello Richard,

Per your request, the indications for use have been updated in the proposed Instructions for Use (IFU) in Section 2: Medical Safety. Please see attached for the updated Section 2: Medical Safety.

For your reference, I also attached the complete IFU which includes the updated indications for use (see page 8 of 1001085IFU IFU, Ulthera System Lower Face IFU).

Please let me know if you have any questions or concerns.

Best regards,  
Ashley

**Ashley Fickett**  
Regulatory Affairs Associate  
Ulthera, Inc.  
phone: 480-619-4069  
email: [a.fickett@ulthera.com](mailto:a.fickett@ulthera.com)



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---

**From:** Ashley Fickett  
**Sent:** Monday, October 01, 2012 10:39 AM  
**To:** Richard.Felten@fda.hhs.gov  
**Cc:** Randy Miller; Suzon Lommel  
**Subject:** K121700 - Ulthera

Hello Richard,

Thank you for your time today.

1. Per your request, the indications for use have been updated to remove the full face indication (see redlines below):

**Indications for Use:**

10/1/2012

Questions? Contact FDA/CDRH/OCE/DID at [CDRH-FOISTATUS@fda.hhs.gov](mailto:CDRH-FOISTATUS@fda.hhs.gov) or 301-796-8118

The Ulthera® System is indicated for use as a non-invasive dermatological aesthetic treatment to:

- lift the eyebrow
- lift lax submental (beneath the chin) and neck tissue
- ~~lift lax tissue to achieve a desired aesthetic effect for the full face and neck~~

The indications for use have been updated in the 510(k) Summary and Indications for Use Statement (see attached).

2. In addition, the performance data section in the 510(k) Summary has been updated to include the requested information regarding number of patients and results (see below):

*There were 51/70 patients that had an improvement of  $\geq 20$  mm<sup>2</sup> in lift, of these patients 84.3% were identified as showing improvement by masked evaluators.*

Please let me know if you have any additional questions or concerns. We look forward to hearing from you later today on the revised Indications for Use Statement and 510(k) Summary.

Best regards,  
Ashley

**Ashley Fickett**  
Regulatory Affairs Associate  
Ulthera, Inc.  
phone: 480-619-4069  
email: [a.fickett@ulthera.com](mailto:a.fickett@ulthera.com)



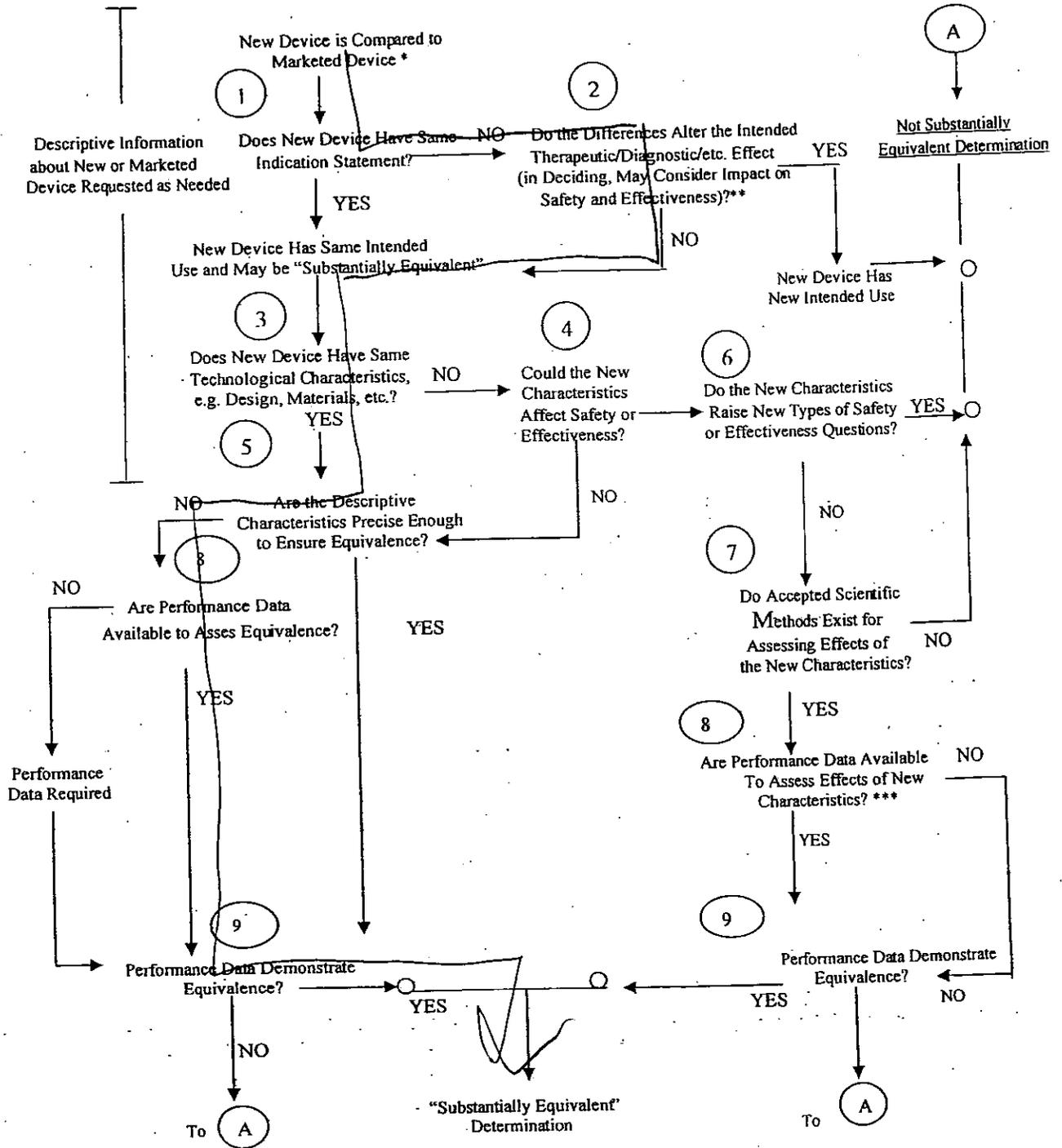
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10/1/2012

Questions? Contact FDA/CDRH/OCE/DID at [CDRH-FOISTATUS@fda.hhs.gov](mailto:CDRH-FOISTATUS@fda.hhs.gov) or 301-796-8118

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### 510(k) "SUBSTANTIAL EQUIVALENCE" DECISION-MAKING PROCESS



\* 510(k) Submissions compare new devices to marketed devices. FDA requests additional information if the relationship between marketed and "predicate" (pre-Amendments or reclassified post-Amendments) devices is unclear.

\*\* This decision is normally based on descriptive information alone, but limited testing information is sometimes required.

\*\*\* Data maybe in the 510(k), other 510(k)s, the Center's classification files, or the literature.

K121700/S1  
SU/ASORO



August 1, 2012

U.S. Food and Drug Administration  
Center for Devices and Radiological Health  
Document Mail Center – WO66-G609  
10903 New Hampshire Avenue  
Silver Spring, MD 20993-0002

FDA/CDRH/DCC

AUG 3 2012

RECEIVED

K121

Re: Response to Additional Information Letter for K121700 dated July 5, 2012

Dear Sir or Madam:

The information provided in this submission is a response to agency request for additional information for the Ulthera 510(k) submission K121700.

The device name is: Ulthera® System.

The Ulthera® System is indicated for use as a non-invasive dermatological aesthetic treatment to:

- lift the eyebrow (current cleared indication)
- lift lax submental (beneath the chin) and neck tissue (requested expanded indication)
- lift lax tissue to achieve a desired aesthetic effect for the full face and neck (current cleared indication + requested expanded indication)

Sponsor contact information:

Ulthera, Inc.  
2150 S. Country Club Drive, Suite 21  
Mesa, AZ 85210-6809  
Contact: Suzon Lommel  
Phone: 480-649-4399  
FAX: 480-649-1605  
Email: [s.lommel@ulthera.com](mailto:s.lommel@ulthera.com)

An exact duplicate of all documentation provide in hard copy is also provided in electronic format in the form of a CD provided with each copy of the response.

**Agency queries and company responses:**

The following deficiencies have been identified in our review of this application:

1. You have stated that a 10 mm<sup>2</sup> is a visibly observable change and therefore those sites having less than a 10 mm<sup>2</sup> change would be considered a failure. Please provide the basis for this statement since such a small change appears not to be easily observable.

As agreed with the agency during the review of our cleared 510(k), observable changes are those which can be determined during masked assessment. Taking this definition into account, Ulthera defined 10 mm<sup>2</sup> as visibly observable change and therefore those sides having less than a 10 mm<sup>2</sup> change would be considered a failure. Visibly observable change has been determined based on changes that can be seen through masked assessment.

Based on this criteria, Ulthera identified 17 out of 70 subjects as non-responders (<10 mm<sup>2</sup>). Therefore, 53 out of 70 subjects (75.7%) were identified as responders (≥10 mm<sup>2</sup>) by quantitative assessment. 83.0% of those subjects who were identified as responders in the quantitative assessment were also identified as responders in the qualitative masked assessment.

However, if the criteria for visibly observable change is doubled from 10mm<sup>2</sup> to 20mm<sup>2</sup>, 19 out of 70 subjects would be identified as non-responders (<20 mm<sup>2</sup>). Therefore, 51 out of 70 (72.9%) subjects would be identified as responders (≥20 mm<sup>2</sup>) by quantitative assessment. 84.3% of the subjects who would be identified as responders, based on this criteria, in the quantitative assessment were also identified as responders from the qualitative masked assessment.

2. Please clarify in the individual data table, Table 20-4, whether or not both sides of the subjects reported as having less than 10 mm<sup>2</sup> change actually had less on both sides or were marked as less based only on a single side failing.

Non-responders were identified as having < 10.0 mm<sup>2</sup> tissue lift. Each side/score was evaluated independently. For example, if the right side resulted in a 9.00 mm<sup>2</sup> lift and the left side resulted in an 11.00 mm<sup>2</sup> lift then the results would be recorded as <10.00 mm<sup>2</sup> and 11.00 mm<sup>2</sup> respectively. Regardless of small differences between opposite sides of the face, the data for the area of tissue lift and the response rate yielded consistent results (as % responders) for both the right and left side of the face. All subjects that were reported as having less than 10 mm<sup>2</sup> change actually had less on both sides.

3. You have requested an indication for use of "lift lax tissue to achieve a desired aesthetic effect for full face and neck". It is not clear exactly what this indication for use is measuring or how you would determine "a desired aesthetic effect". Please provide additional discussion of what this indication

for use is defining and how you would determine success for this indication for use.

During the aging process the skin tissue in the face and neck develops laxity that results in tissue descent that is manifested by “sagging” of the skin in both the face and neck. The sagging is noticeable in the brow area, where there is descent of the brow, and in the lower face (chin/neck area), where there is descent of tissue in the submental and upper neck area. A full face and neck treatment will achieve lifting of the brow and the submental/neck tissue to produce an overall lifting of the full face and neck tissue. Lifting of the eyebrow is the cleared indication. Lifting of the submental/neck tissue is determined by evaluation of patient photographs. Success was determined by quantitative assessment, qualitative assessment (by masked clinician) and patient satisfaction. The combination of these two indications will result in a lifting of the face and neck.

4. Please expand the Performance section of the 510(k) Summary. According to 21 CFR 807.92(b)(2) the 519(k) Summary should include information on patient population tested; discussion of safety and effectiveness data with references to adverse effects and complications observed; and any other information that may be relevant to the substantial equivalence determination.

Please see Attachment 1 for a redlined 510(k) Summary.

5. Please describe the process used in selecting the photographs used for the 2 month validation testing.

Validation of the masked clinician assessment method requires that photographs of subjects with the full range of potential responses be included in the validation study. We included photographs representing a range of clinical responses: no detectable improvement, minimal improvement and good improvement. This is similar to the approach by Kim, et. al.<sup>1</sup> to validate a scale for facial lines where they included the full range of possible facial wrinkles in the validation study. Including a full range of possible clinical responses is also consistent with ICH (International Conference on Harmonization) guidelines for validation of analytical procedures. In order to obtain an adequate distribution of responses to the treatment, ranging from not detectable improvement to good improvement we used Day 60 photographs. As described in the detail, the masked reviewer will identify the pre- and post-treatment images, the endpoint from the review being, “improvement” or “no-change” for the image pair. Based on the data from the predicate device (K072505) described in the Fitzpatrick et al.<sup>2</sup> publication in which there was continued improvement in clinical response from 4 months to 6 months, we believe that using Day 90 photographs for the validation study will not provide an adequate distribution of subjects at the low end of the response curve. Based on published studies of the Thermage device for similar claims, the Day 60 results for lower face and submental region changes fall well into the time window where the entire range of clinical outcomes are represented, namely non-responders to good responders.

The endpoint used in the validation study is the same as the endpoint intended to be used in the efficacy evaluation. The masked clinicians evaluated photographs for a detectable change in tissue lift in the lower face and neck. The only difference between the clinical response detected at Day 60 and at Day 90 is the distribution of responses.

<sup>1</sup>Kim EJ, Reeck JB, Maas CS. A validated rating scale for hyperkinetic facial lines. Arch. Fac. Plast. Surg. 2004, Vol. 6 July/Aug., 253-256.

<sup>2</sup>Fitzpatrick R, Geronemus R, Goldberg D, Kaminer M, Kilmer S, Ruiz-Esparza J. Multicenter study of noninvasive radiofrequency for periorbital tissue tightening. Lasers Surg Med. 2003;33(4):232-42.

6. The use of Quantitative analysis is not listed under either the Primary or Secondary Outcome Measure. Please indicate whether or not the Quantitative measurements are a Primary or Secondary endpoint. Please be advised that in reviewing your application the Agency will look at all endpoints as a combined effectiveness result for each individual subject.

Per FDA's feedback, the quantitative method was developed as a Primary Outcome Measure. Combining effectiveness results for un-poolable endpoints is not appropriate for this study. Each individual endpoint should be based on study patient population response for each individual endpoint. Requiring each patient to meet four independent endpoints in order to demonstrate successful efficacy is outside the bounds of normal clinical trial design and analyses.

7. Please provide a copy of the patient satisfaction questionnaire and the individual patients responses to the questionnaire.

As requested, please see Attachment 2 for a copy of the patient satisfaction questionnaire.

8. Please provide a table listing the individual subjects with blinded assessment; quantitative lift value; and patient satisfaction values to show if each individual subject is a success across the board.

As requested, please see Attachment 3 for a table listing the individual subjects' masked assessment, quantitative lift values and patient satisfaction values.

9. The Operator Manual has two tables of suggested Treatment Guidelines identified as 5.0 and 5.0 Plus. It is not clear what is the basis for the guidelines. The Ulthera System is presently cleared for eyebrow lift only and the new requested indication is for submental and neck lift. The charts include infraorbital and orbit treatment which do not appear to be compatible with eyebrow lift or treatment of the submental or neck tissue. Also the 5.0 Plus recommendations contain an increase in number of lines for each of the 5.0 recommendations. Please provide information explaining the basis for the recommended Guidelines including the increase in number of lines for the 5.0 Plus table.

The anatomical sites specified in the table in Appendix A (i.e., "Lateral Orbit," "Brow," and "Infraorbital") are the same sites that were used for treatment of the subjects in the eyebrow clinical study and do not represent an expansion



of recommended treatment parameters, areas, or indications related to those specific areas. The terms were changed for precise identification of the treatment sites, and to reduce any confusion for the clinician performing the treatment and do not represent an expansion of the cleared indication.

Guidelines have been provided as a safety feature since the clearance of this device. The guidelines are included in to provide the user with recommended levels of energy and lines (upper guidelines) to ensure a safe level of use. Therefore, the 5.0 guidelines were erroneously included and have been removed from the labeling. Please see Attachment 4 for the redlined IFU. The 5.0 Plus guideline is currently the upper guideline being used by physicians. The following study supporting the 5.0 Plus guideline is included in Attachment 5.

Sasaki, Gordon H., Tevez, Ana. Clinical Efficacy and Safety of Focused-Image Ultrasonography: A 2-Year Experience. Aesthetic Surgery Journal published online 23 April 2012

10. The narrative on page 77 and 78 under section 20.4.2.1 does not seem to make sense. Page 77 appears to be describing how the unmasked evaluation will be performed but the top of page 78 begins with a statement about each blinded assessor, yet section 20.4.2.2 at the bottom of page 78 is titled Masked Assessment. Please clarify these sections.

Section 20.4.2.1 describes the unmasked qualitative assessment and the reviewers were not blinded. The use of the word "blinded" in "Section 20.4.2.1. Unmasked Qualitative Assessment" was used in error.

The statement should be updated as follows:

Each ~~blinded~~ unmasked assessor conducted their assessment independently. Each ~~blinded~~ unmasked assessor reviewed the set of images for improvement in the submental (lower chin) and neck tissue.

Section 20.4.2.2 describes the masked qualitative assessment. The reviewers in this assessment were masked.

We look forward to Agency response.

Best regards,



**Suzon Lommel**  
Vice President, Regulatory and Quality Affairs  
Ulthera, Inc.  
phone: 480-619-4069  
mobile: 408-910-1222  
email: [s.lommel@ulthera.com](mailto:s.lommel@ulthera.com)



August 1, 2012

U.S. Food and Drug Administration  
Center for Devices and Radiological Health  
Document Mail Center – WO66-G609  
10903 New Hampshire Avenue  
Silver Spring, MD 20993-0002

Re: Response to Additional Information Letter for K121700 dated July 5, 2012

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- lift lax submental (beneath the chin) and neck tissue (requested expanded indication)
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Sponsor contact information: Ulthera, Inc.  
2150 S. Country Club Drive, Suite 21  
Mesa, AZ 85210-6809  
Contact: Suzon Lommel  
Phone: 480-649-4399  
FAX: 480-649-1605  
Email: [s.lommel@ulthera.com](mailto:s.lommel@ulthera.com)

An exact duplicate of all documentation provide in hard copy is also provided in electronic format in the form of a CD provided with each copy of the response.

## Agency queries and company responses:

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3. You have requested an indication for use of “lift lax tissue to achieve a desired aesthetic effect for full face and neck”. It is not clear exactly what this indication for use is measuring or how you would determine “a desired aesthetic effect”. Please provide additional discussion of what this indication

for use is defining and how you would determine success for this indication for use.

During the aging process the skin tissue in the face and neck develops laxity that results in tissue descent that is manifested by “sagging” of the skin in both the face and neck. The sagging is noticeable in the brow area, where there is descent of the brow, and in the lower face (chin/neck area), where there is descent of tissue in the submental and upper neck area. A full face and neck treatment will achieve lifting of the brow and the submental/neck tissue to produce an overall lifting of the full face and neck tissue. Lifting of the eyebrow is the cleared indication. Lifting of the submental/neck tissue is determined by evaluation of patient photographs. Success was determined by quantitative assessment, qualitative assessment (by masked clinician) and patient satisfaction. The combination of these two indications will result in a lifting of the face and neck.

4. Please expand the Performance section of the 510(k) Summary. According to 21 CFR 807.92(b)(2) the 519(k) Summary should include information on patient population tested; discussion of safety and effectiveness data with references to adverse effects and complications observed; and any other information that may be relevant to the substantial equivalence determination.

Please see Attachment 1 for a redlined 510(k) Summary.

5. Please describe the process used in selecting the photographs used for the 2 month validation testing.

Validation of the masked clinician assessment method requires that photographs of subjects with the full range of potential responses be included in the validation study. We included photographs representing a range of clinical responses: no detectable improvement, minimal improvement and good improvement. This is similar to the approach by Kim, et. al.<sup>1</sup> to validate a scale for facial lines where they included the full range of possible facial wrinkles in the validation study. Including a full range of possible clinical responses is also consistent with ICH (International Conference on Harmonization) guidelines for validation of analytical procedures. In order to obtain an adequate distribution of responses to the treatment, ranging from not detectable improvement to good improvement we used Day 60 photographs. As described in the detail, the masked reviewer will identify the pre- and post-treatment images, the endpoint from the review being, "improvement" or "no-change" for the image pair. Based on the data from the predicate device (K072505) described in the Fitzpatrick et al.<sup>2</sup> publication in which there was continued improvement in clinical response from 4 months to 6 months, we believe that using Day 90 photographs for the validation study will not provide an adequate distribution of subjects at the low end of the response curve. Based on published studies of the Thermage device for similar claims, the Day 60 results for lower face and submental region changes fall well into the time window where the entire range of clinical outcomes are represented, namely non-responders to good responders.

The endpoint used in the validation study is the same as the endpoint intended to be used in the efficacy evaluation. The masked clinicians evaluated photographs for a detectable change in tissue lift in the lower face and neck. The only difference between the clinical response detected at Day 60 and at Day 90 is the distribution of responses.

<sup>1</sup>Kim EJ, Reeck JB, Maas CS. A validated rating scale for hyperkinetic facial lines. Arch. Fac. Plast. Surg. 2004, Vol. 6 July/Aug., 253-256.

<sup>2</sup>Fitzpatrick R, Geronemus R, Goldberg D, Kaminer M, Kilmer S, Ruiz-Esparza J. Multicenter study of noninvasive radiofrequency for periorbital tissue tightening. Lasers Surg Med. 2003;33(4):232-42.

6. The use of Quantitative analysis is not listed under either the Primary or Secondary Outcome Measure. Please indicate whether or not the Quantitative measurements are a Primary or Secondary endpoint. Please be advised that in reviewing your application the Agency will look at all endpoints as a combined effectiveness result for each individual subject.

Per FDA's feedback, the quantitative method was developed as a Primary Outcome Measure. Combining effectiveness results for un-poolable endpoints is not appropriate for this study. Each individual endpoint should be based on study patient population response for each individual endpoint. Requiring each patient to meet four independent endpoints in order to demonstrate successful efficacy is outside the bounds of normal clinical trial design and analyses.

7. Please provide a copy of the patient satisfaction questionnaire and the individual patients responses to the questionnaire.

As requested, please see Attachment 2 for a copy of the patient satisfaction questionnaire.

8. Please provide a table listing the individual subjects with blinded assessment; quantitative lift value; and patient satisfaction values to show if each individual subject is a success across the board.

As requested, please see Attachment 3 for a table listing the individual subjects' masked assessment, quantitative lift values and patient satisfaction values.

9. The Operator Manual has two tables of suggested Treatment Guidelines identified as 5.0 and 5.0 Plus. It is not clear what is the basis for the guidelines. The Ulthera System is presently cleared for eyebrow lift only and the new requested indication is for submental and neck lift. The charts include infraorbital and orbit treatment which do not appear to be compatible with eyebrow lift or treatment of the submental or neck tissue. Also the 5.0 Plus recommendations contain an increase in number of lines for each of the 5.0 recommendations. Please provide information explaining the basis for the recommended Guidelines including the increase in number of lines for the 5.0 Plus table.

The anatomical sites specified in the table in Appendix A (i.e., "Lateral Orbit," "Brow," and "Infraorbital") are the same sites that were used for treatment of the subjects in the eyebrow clinical study and do not represent an expansion

of recommended treatment parameters, areas, or indications related to those specific areas. The terms were changed for precise identification of the treatment sites, and to reduce any confusion for the clinician performing the treatment and do not represent an expansion of the cleared indication.

Guidelines have been provided as a safety feature since the clearance of this device. The guidelines are included in to provide the user with recommended levels of energy and lines (upper guidelines) to ensure a safe level of use. Therefore, the 5.0 guidelines were erroneously included and have been removed from the labeling. Please see Attachment 4 for the redlined IFU. The 5.0 Plus guideline is currently the upper guideline being used by physicians. The following study supporting the 5.0 Plus guideline is included in Attachment 5.

Sasaki, Gordon H., Tevez, Ana. Clinical Efficacy and Safety of Focused-Image Ultrasonography: A 2-Year Experience. Aesthetic Surgery Journal published online 23 April 2012

10. The narrative on page 77 and 78 under section 20.4.2.1 does not seem to make sense. Page 77 appears to be describing how the unmasked evaluation will be performed but the top of page 78 begins with a statement about each blinded assessor, yet section 20.4.2.2 at the bottom of page 78 is titled Masked Assessment. Please clarify these sections.

Section 20.4.2.1 describes the unmasked qualitative assessment and the reviewers were not blinded. The use of the word “blinded” in “Section 20.4.2.1. Unmasked Qualitative Assessment” was used in error.

The statement should be updated as follows:

Each ~~blinded unmasked~~ assessor conducted their assessment independently. Each ~~blinded unmasked~~ assessor reviewed the set of images for improvement in the submental (lower chin) and neck tissue.

Section 20.4.2.2 describes the masked qualitative assessment. The reviewers in this assessment were masked.

We look forward to Agency response.

Best regards,

## Suzon Lommel

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Ulthera, Inc.

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## 510(k) Summary

This 510(k) Summary for the Ulthera® System is submitted in accordance with the requirements of the Safe Medical Device Act (SMDA) of 1990 and follows the Office of Device Evaluation (ODE) guidance concerning the organization and content of a 510(k) summary.

**Applicant:** Ulthera, Inc.

**Address:** 2150 South Country Club Drive, Suite 21  
Mesa, AZ 85210

**Contact Person:** Suzon Lommel, VP of Regulatory & Quality Affairs

**Telephone:** 480-649-4069

**Fax:** 480-619-4071

**Submission Date:** June 7, 2012

**Device Trade Name:** Ulthera® System

**Common Name:** Focused Ultrasound Stimulator Use System for Aesthetic Use

**Classification:** Regulatory Class II

**Classification Name:** Focused Ultrasound Stimulator Use System for Aesthetic Use

**Product Code:** OHV

**Legally Marketed** Name: Ulthera® System

**Predicates:** 510(k): #K072505

**Applicable Guidance:** *The Class II Special Controls Guidance Document: Focused Ultrasound Stimulator System for Aesthetic Use* was developed in response to Ulthera's DeNovo submission and 510(k) clearance K0272505 for the Ulthera System.

**Device Description:** The Ulthera® System consists of the following components:

- Ulthera® Control Unit
- Handpiece
- Transducers

**Indications for Use:** The Ulthera® System is indicated for use as a non-invasive dermatological aesthetic treatment to:

- lift the eyebrow (current cleared indication)
- lift lax submental (beneath the chin) and neck tissue (requested expanded indication)
- lift lax tissue to achieve a desired aesthetic effect for the full face and neck (current cleared indication + requested expanded indication)

**Performance Data:** To support the expanded indication, the Ulthera® System was evaluated in an open-label clinical trial investigating the clinical response following treatment with the Ulthera® System to achieve lifting of lax submental (beneath the chin) and neck tissue. Improvement was evaluated through quantitative assessment, qualitative assessment and patient satisfaction questionnaires. The adverse events resulting from treatment with the Ulthera® System during this study were mild, short-lived in duration, and resolved without incident. There were no serious adverse events (SAEs) or unanticipated adverse device effects (UADEs) related to treatment with the Ulthera® System.

**Conclusion:** Based on the design, materials, principle of operation, and intended use, the Ulthera® System is substantially equivalent to the legally marketed predicate device.

|                   |   |
|-------------------|---|
| Study Site: _____ | Subject ID: _____   |
| Clinician: _____  | Follow-up Visit: <input type="checkbox"/> 90 Days <input type="checkbox"/> 180 Days |

**ULTHERAPY™ PATIENT SATISFACTION QUESTIONNAIRE  
LOWER FACE ONLY**

**PLEASE HAVE PATIENT PHOTOS AVAILABLE FOR VIEWING BEFORE COMPLETING THIS QUESTIONNAIRE WITH THE PATIENT**

1. Before Ultherapy™, had you ever had any type of aesthetic procedure such as Botox, laser skin rejuvenation, laser hair removal, microdermabrasion, cosmetic surgery or the like?

YES

- Botox       Laser Skin Rejuvenation       Laser Hair Removal  
 Microdermabrasion       Cosmetic Surgery  
 Other \_\_\_\_\_

NO

2. What specific areas were you most hoping to improve with Ultherapy?

- Wrinkles →  Forehead       Eyes       Mouth       Cheeks       Neck  
 Sagging →  Eyelids       Mouth       Cheeks       Jawline       Neck  
 More even skin tone (color)  
 Smoother skin texture (decreased pore size/crepe-paper effect)  
 Other (specify) \_\_\_\_\_



**WITH YOUR PHOTOS, LOOKING AT THE BOTTOM HALF OF YOUR FACE AND YOUR NECK**  
**(The cheeks, jawline, upper neck/under the chin)**

3. Have you noticed any improvement in how your skin looks on the lower half of your face/neck?

YES →

- Improvement in lines/wrinkles on the cheeks, neck, or around the mouth  
 Less sagging on the cheeks or jawline       More even skin tone (color)  
 Tighter/lifted under the chin       Smoother skin texture  
 Other: \_\_\_\_\_

NO

|                   |   |
|-------------------|---|
| Study Site: _____ | Subject ID: _____   |
| Clinician: _____  | Follow-up Visit: <input type="checkbox"/> 90 Days <input type="checkbox"/> 180 Days |

4. Compared to before treatment, does your skin ***feel*** better or about the same?

- Better →  
  Tighter  
  Firmer  
  Smoother  
  Makeup application/shaving easier  
 Same

5. For the bottom half of your face in particular, how would you characterize your satisfaction with the treatment?

- Very Satisfied  
  Satisfied  
  Neutral  
  Dissatisfied

6. Would you be interested in receiving treatments in the future?

- YES  
 NO

| Subject ID | Amount of Tissue Lift - Left (mm <sup>2</sup> ) | Amount of Tissue Lift - Right (mm <sup>2</sup> ) | Three Masked Reviewer | Improvement Noticed in Lower Half Face PSQ |
|------------|---|--|-----------------------|--|
| 002Y       | 71.13   | 70.79  | Improved              | No   |
| 005Y       | 60.89   | 60.16  | Improved              | Yes  |
| 006Y       | 58.87   | 61.13  | Improved              | Yes  |
| 007Y       | 39.34   | 34.69  | No Change             | Yes  |
| 009Y       | 30.06   | 30.17  | Improved              | Yes  |
| 011Y       | 77.82   | 81.54  | Improved              | Yes  |
| 013Y       | 106.78  | 96.33  | Improved              | No   |
| 016Y       | 25.84   | 23.56  | No change             | Yes  |
| 017Y       | 30.06   | 30.23  | Improved              | Yes  |
| 018Y       | 64.03   | 66.32  | Improved              | Yes  |
| 019Y       | 164.88  | 161.6  | Improved              | Yes  |
| 021Y       | 98.27   | 96.11  | Improved              | Yes  |
| 023Y       | 79.92   | 77.48  | Improved              | Yes  |
| 024Y       | 51.1  | 51.33  | Improved              | No   |
| 027Y       | <10.00  | <10.00   | Incorrect             | No   |
| 029Y       | 33.78   | 34.02  | No Change             | No   |
| 030Y       | 43.67   | 45.12  | Improved              | No   |
| 035Y       | 17.36   | 18.92  | No Change             | Yes  |
| 037Y       | 182.44  | 180.89   | Improved              | Yes  |
| 039Y       | <10.00  | <10.00   | No Change             | No   |
| 040Y       | 120.87  | 119.06   | Improved              | Yes  |
| 041Y       | 92.01   | 91.59  | No Change             | Yes  |
| 044Y       | 28.64   | 28.8   | Improved              | Yes  |
| 045Y       | 40.61   | 42.36  | Improved              | No   |
| 046Y       | 29.65   | 29.04  | No Change             | Yes  |
| 048Y       | <10.00  | <10.00   | Incorrect             | No   |
| 049Y       | <10.00  | <10.00   | Incorrect             | No   |
| 050Y       | 19.56   | 18.42  | Improved              | Yes  |
| 051Y       | 69.05   | 69.66  | Improved              | Yes  |
| 052Y       | <10.00  | <10.00   | No Change             | No   |
| 055Y       | <10.00  | <10.00   | Incorrect             | No   |
| 057Y       | <10.00  | <10.00   | Improved              | No   |
| 060Y       | 53.99   | 51.66  | Improved              | Yes  |
| 062Y       | 78.57   | 78.35  | Improved              | Yes  |
| 064Y       | <10.00  | <10.00   | Incorrect             | Yes  |
| 065Y       | 217.66  | 218.5  | Improved              | Yes  |

| Subject ID | Amount of Tissue Lift - Left (mm <sup>2</sup> ) | Amount of Tissue Lift - Right (mm <sup>2</sup> ) | Three Masked Reviewer | Improvement Noticed in Lower Half Face PSQ |
|------------|---|--|-----------------------|--|
| 066Y       | <10.00  | <10.00   | No Change             | Yes  |
| 067Y       | <10.00  | <10.00   | Improved              | Yes  |
| 068Y       | 39.06   | 38.46  | Incorrect             | No   |
| 069Y       | 181.4   | 178.47   | Improved              | Yes  |
| 070Y       | 43.98   | 43.76  | Improved              | Yes  |
| 071Y       | 106.75  | 107.4  | Improved              | Yes  |
| 072Y       | 56.37   | 57.53  | Improved              | No   |
| 074Y       | 38.88   | 37.58  | Improved              | Yes  |
| 075Y       | 79.3  | 80.34  | Improved              | No   |
| 077Y       | 74.92   | 74.81  | Improved              | No   |
| 079Y       | 94.69   | 109.46   | Improved              | Yes  |
| 080Y       | 131.73  | 136.76   | Improved              | Yes  |
| 081Y       | 28.76   | 30.01  | Improved              | Yes  |
| 083Y       | <10.00  | <10.00   | Incorrect             | No   |
| 084Y       | 36.84   | 35.85  | Improved              | Yes  |
| 085Y       | 131.37  | 131.08   | Improved              | Yes  |
| 087Y       | <10.00  | <10.00   | Incorrect             | No   |
| 091Y       | <10.00  | <10.00   | Incorrect             | Yes  |
| 093Y       | 31.87   | 28.14  | Improved              | Yes  |
| 095Y       | <10.00  | <10.00   | Incorrect             | Yes  |
| 097Y       | 38.74   | 38.36  | Improved              | Yes  |
| 098Y       | 28.12   | 26.91  | Improved              | Yes  |
| 099Y       | <10.00  | <10.00   | Improved              | Yes  |
| 100Y       | 65.61   | 64.07  | Improved              | No   |
| 105Y       | 46.51   | 46.43  | Improved              | Yes  |
| 106Y       | <10.00  | <10.00   | Improved              | No   |
| 107Y       | 135.77  | 130.2  | Improved              | Yes  |
| 108Y       | 45.4  | 42.68  | No Change             | Yes  |
| 109Y       | 73.36   | 76.43  | Improved              | No   |
| 110Y       | 50.01   | 48.46  | Improved              | Yes  |
| 111Y       | <10.00  | <10.00   | Incorrect             | Yes  |
| 112Y       | 93.37   | 95.21  | Improved              | Yes  |
| 115Y       | 22.41   | 21.78  | Improved              | No   |
| 116Y       | 45.21   | 45.67  | No Change             | Yes  |



Ulthera® System

# Instructions for Use

Featuring

DeepSEE® Technology  
for  
Ultherapy®

**Ulthera, Inc.**

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Mesa, AZ 85210 USA

Phone: (480) 619-4069

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For U.S. Customers contact Ulthera Customer Relations toll-free at (877) 858-4372 (877-ULATHERA). For customers outside of the U.S. contact your local Ulthera representative.

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Revision X~~32~~

~~June-August~~ 2012

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Various features of the Ulthera® System are covered by U.S. Patents 6,049,159 and 7,758,524, and contemplated features may be covered by one or more of the following U.S. Patents: 5,820,564; 6,036,646; 6,050,943; 6,120,452; 6,213,948; 6,440,071; 6,500,121; 6,540,679; 7,142,905; 7,229,411; 7,393,325; 7,491,171; 7,530,958; 7,571,336; 7,615,016; and 7,824,348. More than 100 other U.S. and International patents to which Ulthera has rights are issued, published, or pending.

EC REP

MedPass International Limited  
Windsor House Barnett Way  
Barnwood Gloucester GL4 3RT  
United Kingdom

CE

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# Ulthera® System

**CAUTION: UNITED STATES FEDERAL LAW RESTRICTS THIS DEVICE TO SALE BY OR ON THE ORDER OF A PHYSICIAN.**

THE ULTHERA® SYSTEM IS INTENDED FOR USE ONLY BY PROPERLY TRAINED PHYSICIANS AND PROPERLY TRAINED PERSONS UNDER THE SUPERVISION OF SUCH A TRAINED PHYSICIAN (HENCEFORTH “THE USER”).

PRIOR TO OPERATING THE SYSTEM, THE USER MUST THOROUGHLY READ AND UNDERSTAND THIS INSTRUCTIONS FOR USE. IMPROPER USE OF THE SYSTEM MAY CAUSE PERSONAL INJURY AND/OR DAMAGE TO THE SYSTEM THAT MAY INVALIDATE THE WARRANTY AGREEMENT.

NOTE: THESE INSTRUCTIONS FOR USE DESCRIBES THE OPERATION OF THE ULTHERA SYSTEM ONLY. IT IS NOT A SUBSTITUTE FOR THE REQUIRED CLINICAL TRAINING ON THE PROCEDURE THAT UTILIZES THE SYSTEM.

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PROPOSED DRAFT

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# 1. Introduction to Instructions for Use

## 1.1. Purpose

These Instructions for Use (IFU) provides a description of the System components, its controls and displays, instructions for its operation, and other equipment information important to the user.

**Warning:** Do NOT operate the Ulthera System before reading this IFU thoroughly AND being trained on the clinical procedure by an authorized Ulthera representative. This IFU is not a substitute for clinical treatment guidelines and training provided by the Company. For more information on training available please contact your local representative.

## 1.2. Conventions



**Note:** Notes designate information of special interest.



**Caution:** Cautions alert the user to precautionary steps necessary to properly operate the system. Failure to observe these cautions may void the warranty.



**Warning:** Warnings alert the user to information that is of the highest importance and vital to the safety of the patient and user.

All procedures are broken down by numbered steps. Steps must be completed in the sequence they are presented.

Bulleted lists indicate general information about a particular function or procedure. They do not imply a sequential procedure.

Control names are spelled as they are on the system, and they appear in **Bold** text.

---

## 2. Medical Safety

### 2.1. Indications for Use

The Ulthera System is indicated for non-invasive dermatological aesthetic treatment to:

- lift the eyebrow
- lift lax submental (beneath the chin) and neck tissue
- lift lax tissue to achieve a desired aesthetic effect for the full face and neck

### 2.2. Contraindications

The Ulthera System is contraindicated for use in patients with

- open facial wounds or lesions
- severe or cystic acne on the face and/or neck

### 2.3. Precautions

When not in use by trained personnel, the Ulthera System User Access Key should be removed from the system to help prevent unauthorized use. Keep the Ulthera System User Access Key in a designated place accessible only to authorized and trained personnel.

The Ulthera System has not been evaluated for use over various materials. Therefore, treatment is not recommended directly over those areas with any of the following:

- Mechanical implants
- Dermal fillers
- Implanted electrical devices
- Metal stents in the face and neck area

Treatment energy is not recommended for use directly on an existing keloid.

The Ulthera System has not been evaluated for use in patients on an anticoagulant treatment plan.

The Ulthera System has not been evaluated for use in the following patient populations:

- Pregnant or breast feeding women
- Children
- Those with the following disease states
  - A hemorrhagic disorder or haemostatic dysfunction
  - An active or local skin disease that may alter wound healing
  - Herpes Simplex
  - Autoimmune Disease
  - Diabetes
  - Epilepsy
  - Bell's Palsy

## 2.4. Patient Safety



**Warning:** Ulthera should not be used on a patient's eyes or in a location or technique where ultrasound energy can reach the eye.



**Warning:** Use this system only if you are trained and qualified to do so.



**Warning:** If any problems occur during system operation, take immediate action(s): lift the transducer off the patient's skin, press the **See** pushbutton on handle to discontinue treatment in progress, and/or press the red emergency **Stop** button to completely halt system operation.

## 2.5. Potential Side Effects

Side effects reported in the clinical evaluation of the Ulthera System were mild and transient in nature. These were limited to:

- Erythema (redness): The treated area may exhibit erythema immediately following treatment. This typically resolves within a few hours of treatment.

- Edema (swelling): The treated area may exhibit mild edema following treatment. This typically resolves within a few days of treatment.
- Pain: Momentary discomfort may be experienced during the procedure while energy is being deposited.
- Bruising: Mild bruising, which is caused by damage to soft tissue blood vessels, may occur occasionally and typically resolves within a few days of treatment.
- Nerve Effects:
  - Transient local muscle weakness may result after treatment due to inflammation of a motor nerve.
  - Transient numbness may result after treatment due to inflammation of a sensory nerve.

No permanent injuries to facial nerves have been reported.

- Scarring: The possibility for scar formation (which will respond to medical care) may exist if incorrect treatment technique is used.

## 2.6. Complaints and Adverse Events

No serious adverse events were observed during the clinical study evaluation of the Ulthera System.

Ulthera follows MDR (Medical Device Reporting) rules for handling complaints and adverse events. Should an adverse event be suspected or reported, contact Ulthera, Inc. at the number on the cover page of this document; for those outside the U.S., contact your local Ulthera representative.

---

## 3. System Overview

### 3.1. System Description

The Ulthera System integrates the capabilities of ultrasound imaging with those of ultrasound therapy.

The imaging feature allows the user to visualize the skin and sub-dermal regions of interest before treatment. It also allows the user to assure proper skin contact in order to deliver the energy at desired depths.

The therapy feature directs acoustic waves to the treatment area. This acoustic energy heats tissue as a result of frictional losses during energy absorption, producing discrete points of coagulation.

### 3.2. System Components and Features

The Ulthera System consists of three primary components: the control unit with integrated touchscreen, the handpiece with cable, and interchangeable transducers (see *Figure 3.1*).



*Figure 3.1. Main components of the Ulthera® System: Control Unit (top), Handpiece (bottom right), Image/Treat Transducer (bottom left) that inserts into the handpiece receptacle.*

### 3.2.1. Control Unit

The control unit is the tabletop information center for the Ulthera System. It houses the touchscreen monitor and Graphical User Interface (GUI) that allows the user to interact with the device. This screen sets and displays the operating conditions, including equipment activation status, treatment parameters, system messages and prompts, and ultrasound images. Figure 3.2 illustrates the physical features of the control unit, such as the various connector ports and power controls.



Figure 3.2 Control Unit front view (left) and rear view (right). See Table 3.1 for a description of the controls and connector ports of the control unit.

Table 3.1 Control Unit connector ports and controls (See Figure 3.2)

| Item                             | Description  |
|----------------------------------|--|
| 1 Handpiece Connector Receptacle | Socket for plugging in handpiece cable   |
| 2 USB Ports (two)                | For optional USB removable storage device  |
| 3 Emergency Stop                 | Halts system operation if pressed  |
| 4 On / Off Button                | <ul style="list-style-type: none"> <li>• Momentarily press to turn system ON</li> <li>• Momentarily press to turn system OFF</li> <li>• Press and hold to force system shutdown</li> </ul> |
| 5 Rear Panel USB port            | For Ulthera System User Access key   |
| 6 Main Power Switch              | Supplies power to system. Leave ON (symbol “ ” pressed in)   |
| 7 Power Cord Receptacle          | Socket for attachment of power cord  |

Below the monitor, on the front panel of the control unit is a handpiece connector receptacle that interfaces with the handpiece cable. On the front right of the panel is an **On/Off** button and an emergency **Stop** button. When turned OFF via the **On/Off** button the system goes into a very low power standby mode unless the Main Power Switch is also turned to the OFF position by pressing the 'O' symbol. The front of the control unit also has two Universal Serial Bus (USB) ports: both ports may be used for the Ulthera System User Access Key or for an optional removable storage device ("thumb drive").



**Warning:** When not in use by trained personnel, the Ulthera System User Access Key should be removed from the system to help prevent unauthorized use. Keep the Ulthera System User Access Key in a designated place accessible only to authorized and trained personnel.

The rear of the control unit has a USB port, an AC power receptacle and the main power switch. The main power switch should be left in the powered position (with the "I" pressed inward). In such a configuration, the control unit may be turned ON via the front panel **On/Off** button and can be turned OFF via either the front panel **On/Off** button or the graphical user interface.

### 3.2.2. Handpiece

The handpiece is a handle with an integrated receptacle for insertion of a transducer on one end and an electrical cable for attachment to the control system on the other end. The handpiece has two types of buttons: one to image (**SEE**) and the other to deliver therapy (**TREAT**). Figure 3.3 provides two views of the handpiece, including one showing it connected to an Image/Treat transducer. Table 3.2 is a description of the various components and features illustrated in Figure 3.3.

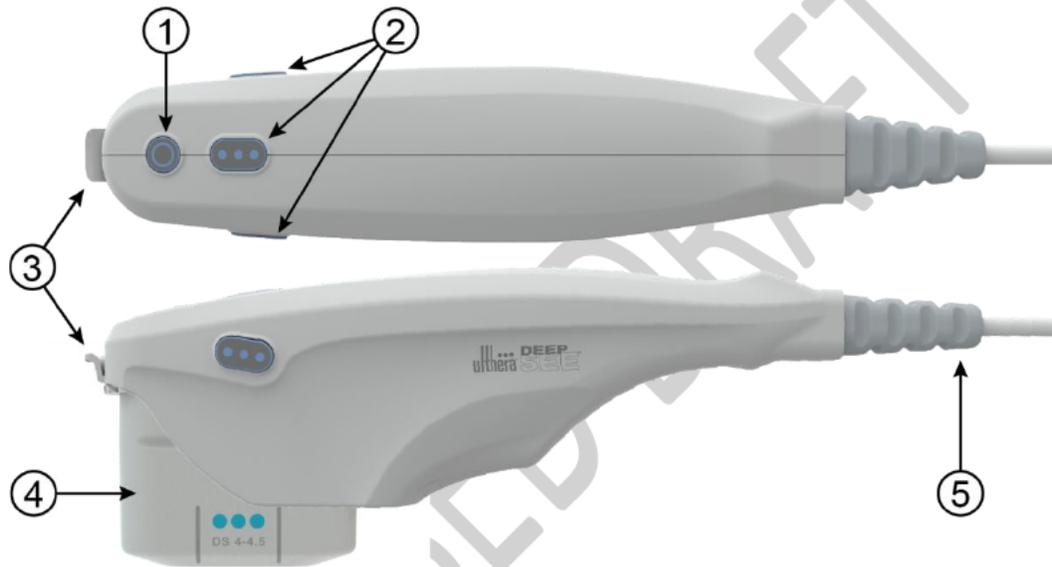


Figure 3.3 Handpiece with transducer inserted, top and side views.

Table 3.2 Handpiece and Transducer Description

| Item                    | Description   |
|-------------------------|---|
| 1 SEE Pushbutton        | <ul style="list-style-type: none"> <li>Engages IMAGING state (if not already imaging)</li> <li>Places system in READY state (times out in 40 seconds)</li> <li>Stops TREATING if treatment in progress</li> </ul> |
| 2 TREAT Pushbuttons     | <ul style="list-style-type: none"> <li>Engages TREATING state</li> </ul>  |
| 3 Latch                 | Locks transducer into handpiece   |
| 4 Transducer            | Image/treat transducer  |
| 5 Strain Relief / Cable | Connects handpiece to Control Unit  |

### 3.2.3. Transducers

Figure 3.4 is an illustration of an image/treat transducer. The transducer can image and treat a region of tissue up to 25 mm long and can image a depth of up to 8 millimeters. Treatment occurs along a line less than or equal to the transducer's active length, which is indicated by guides on the sides of the transducer, as described in Table 3.3. An additional guide at the front tip of the transducer represents the center of the treatment line. In therapy mode, bursts of sound energy create a linear sequence of individual, discrete, thermal coagulation zones. A label atop the transducer provides the transducer type, expiration date, and other information.



Figure 3.4 Image/Treat Transducer, separated from handpiece (see Table 3.3)

Table 3.3 Transducer Description

| Item           | Description  |
|----------------|--|
| 1 Labeling     | Transducer type and other information  |
| 2 Treat guides | Markers denoting maximum treatment line length and center of treatment line (center of transducer) |

The types of transducers reflect variations in frequencies and treatment depths as shown in Table 3.4.

Table 3.4 Transducer Types

| <b>Transducer Type</b> | <b>Treat Frequency</b> | <b>Treat Depth</b> | <b>Image Depth</b> | <b>Scan Length</b> |
|------------------------|------------------------|--------------------|--------------------|--------------------|
| DS 7 – 3.0             | 7 MHz                  | 3.0 mm             | 0 – 8 mm           | 25 mm              |
| DS 7 – 3.0N            | 7 MHz                  | 3.0 mm             | 0 – 8 mm           | 14 mm              |
| DS 4 – 4.5             | 4 MHz                  | 4.5 mm             | 0 – 8 mm           | 25 mm              |
| DS 7 – 4.5             | 7 MHz                  | 4.5 mm             | 0 – 8 mm           | 25 mm              |
| DS 10 – 1.5            | 10 MHz                 | 1.5 mm             | 0 – 8 mm           | 25 mm              |
| DS 10 – 1.5N           | 10 MHz                 | 1.5 mm             | 0 – 8 mm           | 14 mm              |

### 3.2.4. Essential Accessories

Other essential components provided for operation of the Ulthera System are the power cord that connects the Ulthera System to an AC power outlet, and the proprietary Ulthera System User Access Key.

Ultrasound gel to facilitate transmission of the acoustic energy is also required but is not provided as part of the system.

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## 4. System Safety

The following precautions and warnings must be reviewed and observed:

### 4.1. Electrical and Fire Safety



**Warning:** To avoid risk of electric shock, always inspect the Ulthera transducer, handpiece and cable before use. Do not use a damaged cable or a transducer that has been damaged or is leaking fluid.

The Ulthera System is intended for indoor, dry location use. Avoid liquid spills and splashes. Keep coupling gel away from the handpiece-transducer connections.

The Ulthera System comes with a three-conductor AC power cord and plug. Use a properly grounded outlet and always plug the Ulthera System directly into the outlet. Never remove the ground conductor or compromise the ground conductor via any AC adapter plugs or extension cords.

Disconnect the power cord from the outlet by pulling on the plug not the cord.

AC powered USB printers or storage devices may pose a shock hazard. Do not touch the USB connectors and the patient at the same time.

Turn off the AC power switch and disconnect the AC power supply before cleaning the control unit.

Do not remove the covers on the control unit or handpiece; the control unit contains hazardous voltages. The Ulthera System contains no user-serviceable components. If the system requires service, contact Ulthera, Inc.

No modification of this equipment is allowed.

The Ulthera System should not be used near flammable gases or anesthetics. Fire or explosion can result. The Ulthera System is not AP or APG rated.

Avoid restricting ventilation under and behind the Ulthera control unit. Maintain an open space of at least 4 inches/ 10 cm around the control unit. If ventilation holes are obstructed, the system could overheat.

The Ulthera transducer and handpiece is rated as a Type B patient applied part. It may provide a connection between the patient and protective earth. This may present a hazard if the patient becomes connected to other equipment with excessive electrical current leakage.

Do not touch the handpiece electrical contacts and patient simultaneously.

To avoid a burn hazard, remove the transducer from the patient before performing HF electrosurgical procedures.

## 4.2. Equipment Use and Care



**Caution:** Failure to observe these precautions may void the warranty.

The Ulthera handpiece connectors must be kept clean and dry. Do not use the transducer if the connectors have been immersed in liquid. See the instructions for cleaning the transducer.

Every effort has been made to make the transducers as rugged as possible; however, they may be permanently damaged if dropped onto a hard surface or if the membrane is punctured. Transducers damaged in this manner are not covered by the warranty.

The Ulthera System has no user-serviceable components. Do not attempt to open the control unit enclosure or transducers. Contact Ulthera, Inc. if service is required.

When not in use by trained personnel, the Ulthera System User Access Key should be removed from the system to help prevent unauthorized use. Keep the Ulthera System User Access Key in a designated place accessible only to authorized and trained personnel.

## 4.3. Ergonomic Safety



**Warning:** Ultrasound scanning has been associated with repetitive motion injuries such as carpal tunnel syndrome. To reduce chances of such injury, maintain a balanced, comfortable posture while scanning, avoid gripping the handpiece too tightly, and keep hands and arms in a comfortable position while using.

## 4.4. Medical Ultrasound Safety



**Warning:** Use this system only if you are trained and qualified to do so.

The Ulthera System has a fixed, non-adjustable output power level for imaging, well below the limits set by FDA guidelines. However, ultrasound exposure times should be limited to the shortest amount of time needed to complete the treatment. The ALARA principle (As Low As Reasonably Achievable) can be followed by minimizing the examination time.

If the system displays unusual / inconsistent behavior, discontinue use and contact Ulthera, Inc.

Under some conditions (for example, high ambient temperature and long scanning period), the transducer surface temperature may exceed 41°C. Scanning will be automatically disabled if the internal transducer temperature reaches 43°C.

## 4.5. Electromagnetic Compatibility and Immunity

The Ulthera System's RF emissions are very low and are not likely to cause interference in nearby electronic equipment.

Ulthera is suitable for use in all establishments other than domestic and those directly connected to the public low voltage power supply network that supplies buildings used for domestic purposes.

Mains (AC) power quality should be that of a typical commercial or hospital environment.

Floors should be wood, concrete or ceramic tile. If floors are covered with synthetic material, the relative humidity should be at least 30% to avoid excessive static electricity.



**Warning:** The Ulthera System should not be situated adjacent to, or stacked with, other electronic equipment. If the system must be installed in close proximity to other equipment, both the Ulthera System and the nearby equipment should be observed to verify normal operation in that configuration.



**Caution:** EMI (Electro-Magnetic Interference) from other electronic systems may cause degradation of the ultrasound image. Ulthera has been designed to meet the standards of IEC60601-1-2 for electromagnetic compatibility; however some computer equipment unintentionally emits strong interfering RF signals. Portable RF communication devices may also affect Ulthera. If image quality is degraded by EMI, the system may need to be relocated or reconfigured.



**Warning:** Use of accessories other than those specified, may result in increased emissions, or decreased immunity of this system.

## 4.6. Disposal

Depleted transducers should be disposed of in accordance with federal, state, and local regulations. For expired transducers (past expiration date), please contact your local Ulthera representative.

## 4.7. Safety Symbols

A variety of symbols appear on the transducer, handpiece, and control unit in accordance with regulatory guidance.

| SYMBOL  | DEFINITION  |
|---|---|
|    | Type B Applied Part   |
|    | CE marking indicating manufacturer's declaration of compliance with appropriate EU product directives |
|    | Canadian Standards Agency   |
|    | Consult instructions for use  |
|    | Date of Manufacture   |
| <b>SN</b>   | Serial Number   |
|  | Emergency Stop  |
|  | Power Standby Switch  |
|  | Indoor Use Only   |
|  | Keep electrical waste separate from municipal waste   |
|  | Recycle Packaging   |
| <b>IPx1</b>   | Mated handpiece and transducer protected from the effects of vertically dripping water                |

|   |   |
|---|---|
|    | <b>Catalogue Number</b>                 |
|    | <b>Manufacturer</b>                     |
|    | <b>Storage Range</b>                    |
|    | <b>Keep Dry</b>                         |
|    | <b>Fragile Contents</b>                 |
|    | <b>Relative Humidity</b>                |
|    | <b>Use By, Expiration Date</b>          |
|    | <b>Lot Number</b>                       |
|  | <b>Atmospheric Pressure Limits</b>      |
|  | <b>Recycle Packaging (Polyethylene)</b> |

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## 5. Setting Up for First-Time Use

### 5.1. Unpacking

The control unit and handpiece are shipped together in one container. Transducers are packaged and shipped separately from the control unit and handpiece, in ready-to-use, non-sterile pouches. Transducer gel is also packaged and shipped separately.

### 5.2. Physical Environment

#### 5.2.1. System Base

The System may be placed on a cart or counter with the depth to accommodate the control unit, handpiece and power cord provided. A cart is recommended to offer maximum mobility for the user when treating the patient and provide a more secure housing for the handpiece.

Space should be provided around the back, sides, bottom and top of the System for cooling. In continuous use for extended periods of time, it is normal for the System to be warm.

#### 5.2.2. Electromagnetic Environment

The System is not likely to cause interference in nearby electronic equipment; however, other electronic equipment should not be stacked or placed immediately adjacent to the System.

Flooring should be wood, concrete or ceramic tile. If covered with synthetic material, the relative humidity should be at least 30%.



**Warning:** The Ulthera System should not be situated adjacent to, or stacked with, other electronic equipment. If the system must be installed in close proximity to other equipment, both the Ulthera System and the nearby equipment should be observed to verify normal operation in that configuration.



**Caution:** EMI (Electro-Magnetic Interference) from other electronic systems may cause degradation of the ultrasound image. The Ulthera System has been designed to meet the standards of IEC60601-1-2 for electromagnetic compatibility; however, some computer equipment unintentionally emits strong interfering RF signals. Portable RF communication devices may also affect the Ulthera System. If image quality is degraded by EMI, the system may need to be relocated or reconfigured.

### 5.3. Electrical Requirements

The Ulthera System has an international power supply and may be used with 100-240 VAC, 50-60 Hz power systems. See Section 4.1 Electrical and Fire Safety for additional information.

### 5.4. Connecting Components

#### 5.4.1. Connecting the Handpiece

The handpiece connector receptacle is located on the left side of the control unit's front panel as shown in Figure 5.1. To attach the handpiece connector, align it with the white dot facing up and push it into the receptacle. It will latch when seated properly.



*Figure 5.1 Handpiece Connector Receptacle.*

To disconnect the handpiece, twist the coupling ring on the connector counterclockwise while pulling outwards.

### 5.4.2. Identifying and Connecting Transducers

Transducers are identified by the label on the top of the transducer which includes the name of the transducer (Ulthera DeepSEE), treatment frequency and treatment depth (DS X-X), a unique serial number, a part number, and date of manufacture.

The Treatment Guidelines on the control unit interface will display the recommended transducer to utilize based on the anatomical area you have selected to treat.

Remove the transducer indicated from its protective pouch. To connect the transducer, slide the transducer into the handpiece as shown in Figure 5.2. When the transducer is fully seated you will hear a tone indicating that it has been correctly inserted.



*Figure 5.2 Connecting a Transducer*

To disconnect the transducer, lift the latch at the tip of the handpiece and slide the transducer straight out of the handpiece.



**Caution:** Do not apply force/displacement to latching cantilever without a transducers installed in the handpiece.

When the transducer is inserted, the control unit automatically detects it and updates the graphical user interface.

### 5.4.3. Connecting Accessories

The Ulthera System User Access Key should be inserted into one of the available USB ports otherwise the message “No Key” will appear and the software will not allow user access.

An optional portable USB storage device, i.e. a “thumb drive”, can be inserted into another USB port for downloading images or treatment records.

## 6. System Operation

### 6.1. Overview of System Functions

The Ulthera System's Graphical User Interface is divided into three general functions (tabs): Settings, Patient Info, and DeepSEE. The **Settings** function allows you to recall patient treatment information and to change general system settings.

The **Patient Info** function contains the controls and information instrumental in planning a treatment. This function allows you to build patient treatment information when starting a new treatment or to drive selecting regions during a treatment in progress.

The **DeepSEE** function contains the controls and information needed for imaging soft tissue and for treating pertinent soft tissue. An overview of this screen is seen in Figure 6.1

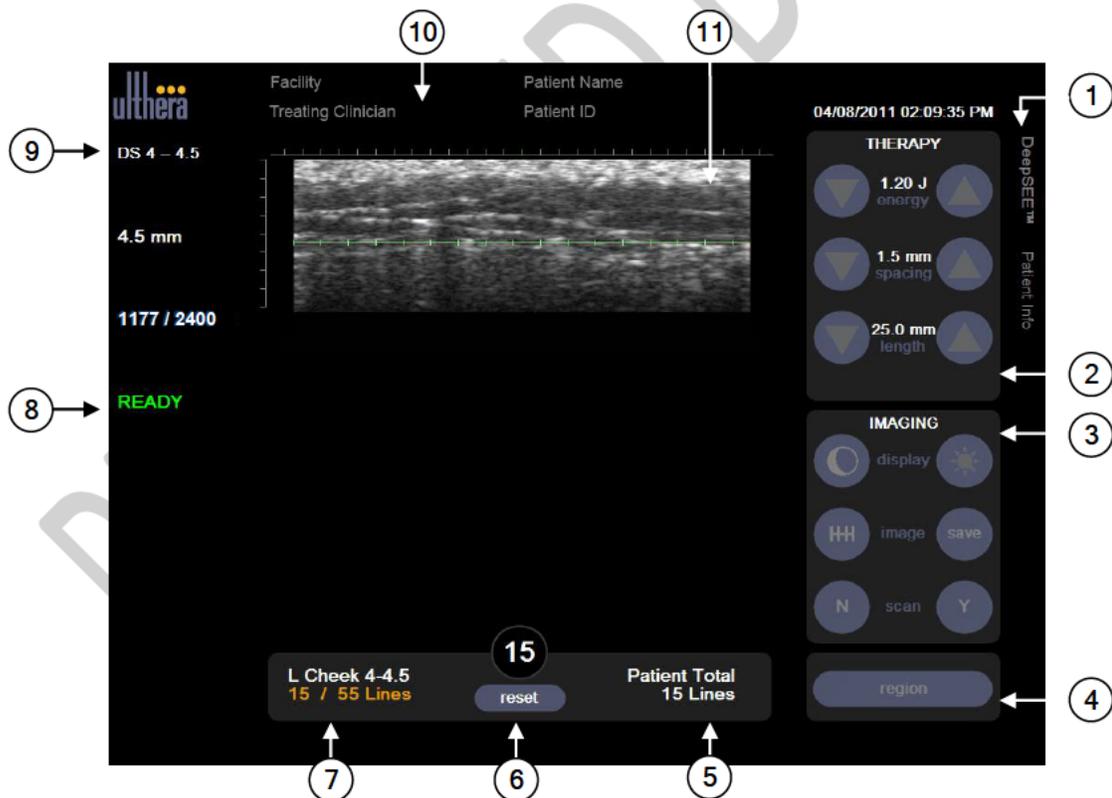


Figure 6.1 Imaging/Therapy Screen (DeepSEE Tab) in READY (to treat) state. See Table 6.1. for description

Table 6.1 Imaging/Therapy Screen Description

| Item |                          | Description   |   |                              |
|------|--------------------------|---|---|------------------------------|
| 1    | System Function Tabs     | DeepSEE   | Imaging/Therapy screen (described in this table)  |                              |
|      |                          | Settings (not scanning)   | Patient and Facility information, Treatment Records and Images, Help, Volume, and System Shutdown controls and dialogs                                      |                              |
|      |                          | Patient Info  | Allows entering of patient information, selection of treatment guidelines and selecting regions during treatments, which automatically set therapy controls |                              |
| 2    | Therapy Controls         | Energy  | Sets acoustic energy level  |                              |
|      |                          | Spacing   | Sets distance between thermal coagulation points  |                              |
|      |                          | Length  | Sets the length of the treatment line   |                              |
| 3    | Imaging Controls         | Marker (not scanning)   | Distance Icon   | Activates distance calipers  |
|      |                          |   | Text  | Activates text annotation    |
|      |                          | Display (scanning)  | Sun icon  | Increases display brightness |
|      |                          |   | Moon icon   | Decreases display brightness |
|      |                          | Image   | Treat ruler icon  | Toggles treat ruler ON/OFF   |
|      |                          |   | Save  | Saves image                  |
|      |                          | Scan  | Y   | Starts scanning (IMAGING)    |
| N    | Stops scanning (IMAGING) |   |   |                              |
| 4    | Region Control           | Launches dialog below image to select tissue region   |   |                              |
| 5    | Patient Total Line Count | Cumulative number of treatment lines delivered  |   |                              |
| 6    | Reset Counter            | Line counter that is reset to "0" by pressing the <b>reset</b> button or by changing regions  |   |                              |
| 7    | Treat Region Line Count  | <ul style="list-style-type: none"> <li>• Treat region selected (e.g. forehead, submental, etc.)</li> <li>• Lines delivered to region / (vs.) recommended lines per guidelines</li> </ul>                            |   |                              |
| 8    | System Status            | READY or TREATING   |   |                              |
| 9    | Probe Information Area   | <ul style="list-style-type: none"> <li>• Name of attached transducer</li> <li>• Treat depth of transducer</li> <li>• Number of treatment lines spent / (vs.) Total treatment line capacity of transducer</li> </ul> |   |                              |
| 10   | Header Information       | <ul style="list-style-type: none"> <li>• Ulthera logo</li> <li>• Facility, Clinician, Patient Name and Patient ID (if entered)</li> <li>• Date and Time</li> </ul>  |   |                              |

|    |                    |  |
|----|--------------------|--|
| 11 | Image/Treat Region | <ul style="list-style-type: none"> <li>• Ultrasound image</li> <li>• Horizontal and vertical (depth) rulers with 1 mm tick marks</li> <li>• Treat ruler indicating spacing, length and depth of treatment</li> </ul> |
|----|--------------------|--|

## 6.2. Activating the Control Unit

**Step 1** Ensure the power cord on the back of the system is plugged into the wall socket.

**Step 2** Ensure the main power switch on the back of the control unit is in the ON position.



**Note:** This switch may be left in the ON position even when the system is not in use.



**Warning:** While running, this switch should not be used to shut down the system.

**Step 3** Insert the Ulthera System User Access Key into the USB port on the back of the control unit.



**Note:** The Ulthera System must be used only with the authorized Ulthera System User Access Key.

**Step 4** Press the green On/Off button on the front of the control unit.

- The system will perform a brief self-test. After passing the self-test, a “NO KEY” message will be displayed if the Ulthera System User Access Key has not yet been inserted; otherwise the starting screen will be displayed.



**Warning:** If the self-test screen displays any information messages, turn the system OFF and follow the instructions in Section 7.

### 6.3. Setting Up a Treatment Record

Figure 6.2. Patient Info – Treatment Setup Screen



**Note:** The Patient Info screen is the startup screen.

- Step 1** Enter the patient name, patient ID and the clinician performing the treatment, using the touch pad at the bottom of the screen.



**Note:** A patient name or patient ID along with the selection of a treatment guideline is necessary to start a treatment.



**Note:** Unwanted clinician names stored in the dropdown menu may be deleted by:

- 1) selecting the name to be deleted from the dropdown menu
- 2) pressing the +/- key
- 3) pressing the del key followed by the enter key

- Step 2** Select the desired Treatment Guideline
- An overview of the various regions within the treatment guideline is visible at the bottom of the screen
- Step 3** Tap the Start Treatment button



**Note:** Once the **Start Treatment** button has been pressed the treatment guideline, patient name and patient ID may not be changed until the treatment is ended.

## 6.4. Selecting a Transducer



**Note:** The Treatment Guideline displays an overview of the various treatment regions with recommended treatment parameters for each, as shown in Appendix A. These treatment parameters are based on results from clinical trials conducted by Ulthera that demonstrated a safe and effective treatment for the treatment region selected.



**Caution:** It is the responsibility of the physician to fully understand the indications for use and safety considerations associated with the Ulthera System.



**Note:** An alternative way to access the treatment region menu is to tap the **Region** button on the **DeepSEE** screen. This approach bypasses the **Patient Info Tab** with the regions listed.

**Step 1** Decide which region you will be treating, and obtain the necessary transducer for that region as depicted on the Patient Info screen.

- The DS 10 – 1.5 transducer has a lower level of energy and a 1.5 mm focal depth.
- The DS 10 – 1.5N transducer has a lower level of energy, 1.5mm focal depth and a narrower patient contact footprint than the DS 10 – 1.5. The DS 7 – 3.0 transducer has a lower level of energy and a 3.0 mm focal depth.
- The DS 7 – 3.0N transducer has a lower level of energy, a 3.0 mm focal depth and a narrower patient contact footprint than the DS 7 – 3.0.
- The DS 7 – 4.5 transducer has an intermediate level of energy and a 4.5 mm focal depth.
- The DS 4 – 4.5 transducer has a higher level of energy and a 4.5 mm focal depth.

**Step 2** After checking the expiration date on the transducer package, open the sealed pouch and connect the transducer by pushing the handpiece latch up and sliding the transducer into the handpiece. When the transducer is fully seated, push the handpiece latch down to lock the transducer into place. You will hear a tone indicating that the transducer has been correctly inserted.



**Caution:** If a “Transducer Not Connected” or any **Warning** or **Caution** screen appears when a transducer is attached, there could be a problem with the

transducer or system. Try disconnecting then reconnecting the transducer. If the problem persists, contact your local representative.

- Step 3** On the **Patient Info** screen, the regions available for treatment with the inserted transducer will be displayed in white under “Treatment Guidelines”. Tap the region to be treated from the available regions displayed. This will take you automatically to the **DeepSEE** screen.
- The Therapy settings on the right-hand side of the screen (i.e., energy, spacing and length) are automatically set to the appropriate levels for the treatment region selected, based on the treatment guideline.

## 6.5. Imaging and Treating

The **DeepSEE** screen displays as shown in Figure 6.3.



Figure 6.3. DeepSEE screen with treatment region selected (Cheek).

The region you selected from the treatment region menu will be displayed in white on the bottom left/center of the **DeepSEE** screen. The number of recommended treatment lines for the region is displayed underneath as the denominator in yellow, and the cumulative number of treatment lines delivered in that region is displayed as the numerator, in yellow. When the recommended number of treatment lines for the region have been delivered, these numbers will change color to white to signify completion for that region.

A counter for the total number of treatment lines for the patient visit is displayed on the bottom right/center of the screen.

In addition, the appropriate energy level is preset, based on treatment guidelines (see Appendix A – Treatment Guidelines) and can be adjusted down as needed to manage the patient’s comfort level.



**Warning:** In the event of damage to any part of the system, as in the handpiece or transducers being dropped, broken, or leaking fluids, the equipment should be disconnected from the power source outlet prior to touching any part of the equipment. Before reconnecting the equipment it should be thoroughly inspected for external damage. Do not use damaged transducers or handpiece on a patient.

### 6.5.1. Treatment Steps

**Step 1** Ensure the face and neck have been cleansed thoroughly.

**Step 2** Carefully apply a thin layer of ultrasound gel to the transducer window. Too much or too little gel will result in poor skin contact. (Use aqueous ultrasound gel only, as other lubricants or lotions can damage the transducers and cables).

**Step 3** Place the transducer treatment window flush with the patient’s skin and press the See button on the handpiece to activate the IMAGING state.

An image of the patient’s soft tissue appears. The green “treat ruler” that is overlaid upon the image shows the depth that coagulative points will be formed. Green tick marks along the treat ruler show the lateral positions where the coagulative points will be placed along the horizontal plane. For example, with Length set to 25 mm, and Spacing set to 1.5 mm (center to center), a total of 17 coagulative zones would be produced in a treatment line. Verify sufficient coupling between the transducer and the skin by ensuring there are no dark, vertical artifact bars on the image.



**Note:** If the transducer is jostled, dropped or shaken while scanning, it may momentarily pause in order to recalibrate position. It should then resume normal scanning.

**Step 4** Press the See button on the handpiece while in the IMAGING state to activate the READY (to treat) state.



**Note:** The **Treat** buttons on the handpiece will become lit and a tone is emitted momentarily when the system enters (or exits) the READY state.

The “READY” state turns off after 40 seconds if the **Treat** button is not pressed, but can be reactivated by pressing the **See** button again.

If you would like to freeze the image, tap the Scan N (No) button in the Imaging section on the right hand side of the screen. To resume scanning, press the Scan Y (yes) button (or press the See button again).

To control the image brightness, use the Display buttons to decrease/increase the overall display brightness. These user controls appear only while the system is actively scanning (i.e. in the IMAGING state). When not in the imaging state the controls become distance measurement calipers and text annotation markers (described in Section 6.7) that can be applied to static (frozen) images.

To save a displayed image, next to Image tap Save. The image will be stored on the system and can be recalled, viewed or transferred to an external USB storage device via Images on the Settings Tab.

- Step 5** Verify sufficient coupling between the transducer and the skin by ensuring there are no dark, vertical artifact bars, as indicative of air pockets between the face of the transducer and patient. A properly coupled image should look similar to that in Figure 6.4. Reapply gel as needed to afford ample coupling. A poorly coupled image looks similar to that in Figure 6.5.

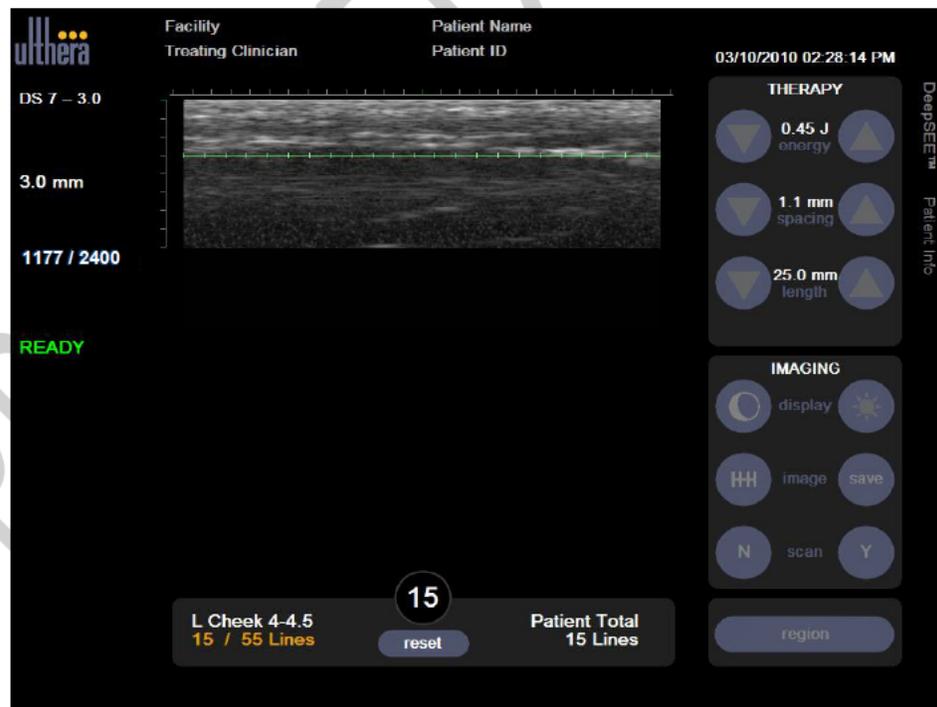


Figure 6.4. Sample image of transducer well-coupled. No vertical dark lines appear.

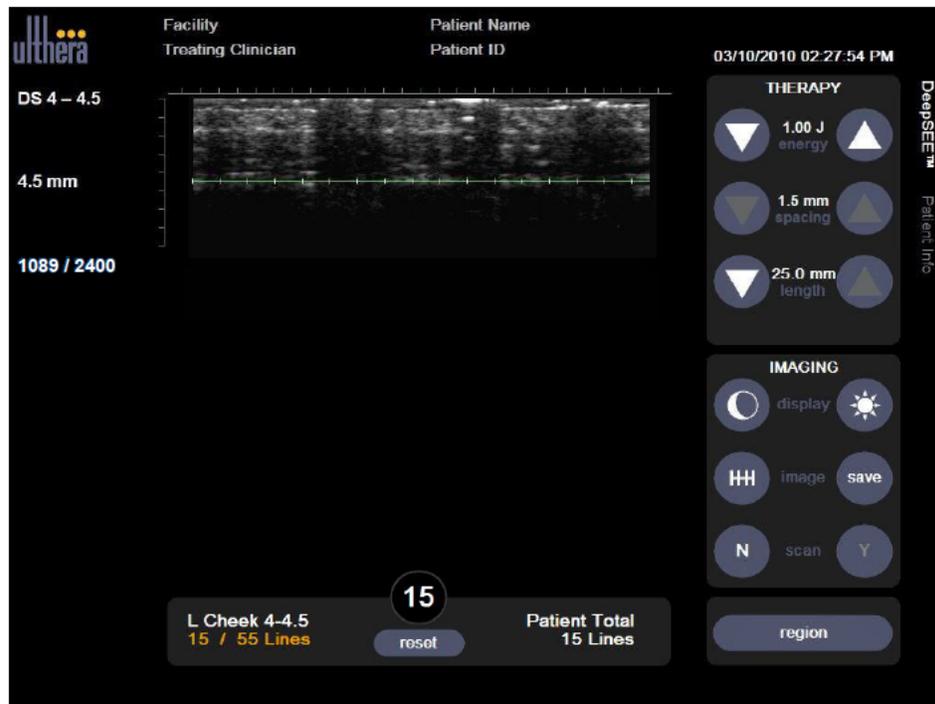


Figure 6.5. Sample Image of Transducer with Poor Coupling on the Cheeks. Large, vertical dark bars are present.

- Step 6** Press a Treat button on the handpiece to activate the TREATING state and deliver the energy between the Treat Guides. Take care that the hand remains still and the handpiece remains in place while the energy is being delivered. In addition a light constant pressure should be maintained between the transducer and the patient's skin. The **Treat** button's lighting will turn off and the **See** button will light up momentarily to indicate the system is in the TREATING state. As the energy is delivered a tone is sounded for each coagulation point being created and the green treat ruler will change to a yellow color momentarily. This is shown in Figure 6.6.

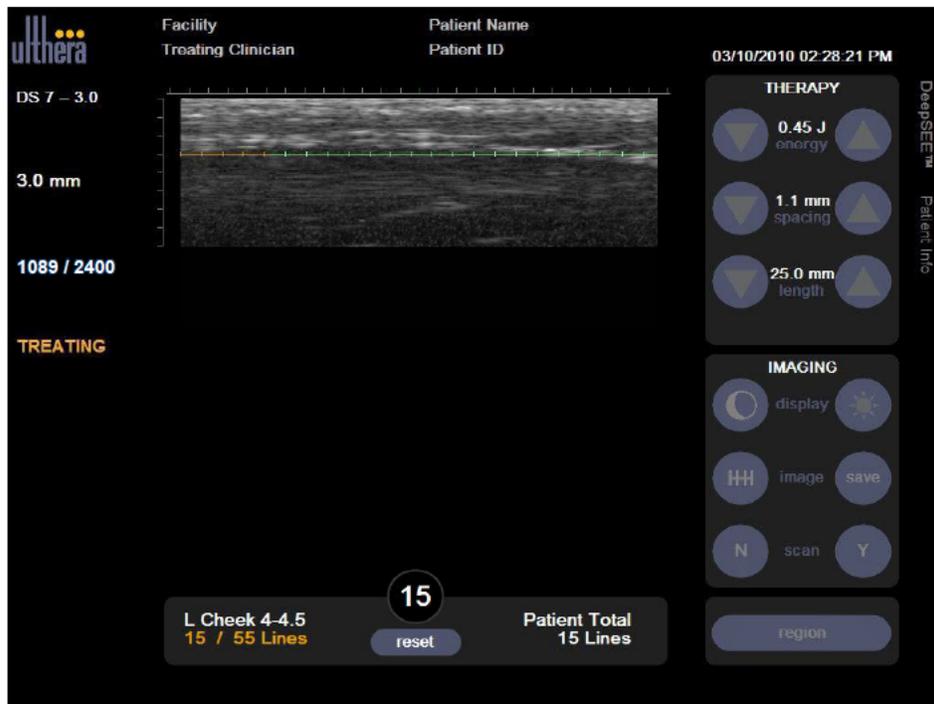


Figure 6.6. TREATING state. A yellow treat progress line is superimposed over the green treat ruler.



**Warning:** If desired, therapy may be cancelled at any time by pressing the **See** button on the handpiece, or the system can be halted by pressing the red Emergency Stop button on the front panel of the control unit. Also, the transducer can be simply lifted off the patient's skin quickly.



**Note:** If an adjustment in the volume of the audio signals is desired, tap the **Settings** tab and use the **Volume** up/down arrows as needed.



**Note:** The settings tab is not available while in the imaging mode.

**Step 7** To deliver the next treatment line of energy within the same treatment region, advance the transducer 2-3 mm to adjacent tissue and press a **Treat** button. If 40 seconds have elapsed since delivering the last treatment line of energy, press the **See** button on the handpiece to restore the READY state, then press a **Treat** button to deliver an additional line of therapy.

**Step 8** After 5 treatment lines are delivered, do a visual check of the transducer window to ascertain if gel needs to be reapplied such that a small bead of gel covers the window.

**Step 9** Continue in this fashion until the recommended number of treatment lines for the region (as shown on the bottom/left of the screen) has been delivered. When the correct number of treatment lines is delivered, the treatment line count color turns from yellow to white.

**Step 10** To continue treatment in another region, tap the **Region** button on the lower right hand of the **DeepSEE** screen. This will prompt the menu of treatment regions and appropriate treatment line counts to be displayed.



**Note:** If the next treatment region desired is grayed out, change the transducer to the one depicted on the guideline.



**Note:** If the Treatment Guidelines indicate that the transducer is to be changed in order to treat another section, turn scanning off by pressing the "N" (No) button on the main screen prior to switching transducers.

**Step 11.** Tap the region you will be treating next and proceed as outlined above in Steps 1 through 9.

**Step 12** When all targeted regions have been treated, tap the **End Treatment** button. If all desired treatment lines have been delivered, tap the **Confirm End** button to end the treatment session and to save the treatment record to the system. If further treatment lines are still necessary you may tap the **Resume Treatment** button to return.



**Warning:** The **End Treatment** button *must* be tapped at the end of each patient procedure in order to reset the treatment line counters and maintain an accurate count of treatment lines delivered to any one patient or treatment region.



**Note:** A treatment record is automatically generated during the procedure, which is ended via the **End Treatment** button. Accessing this Record, or any saved images, is described in Section 6.8 Record Keeping.

**Step 13** The system places you back to the starting screen, **Patient Info**, where you may begin another treatment with a new patient. If treatments are finished or if you desire to review or print records from previous treatments tap the **Settings** tab. From this screen you may review records, images or tap **Shutdown** to turn OFF the system.

**Step 14** Follow cleaning and maintenance instructions in Section 8.0.

## 6.6. Adjunctive Functions

### 6.6.1. Distance Measurements

The Ulthera System allows you to make distance measurements on ultrasound images when the system is not in the active IMAGING state. Tap **Scan N** to stop scanning if necessary.

- Step 1** While you are on the DeepSEE Screen, tap the distance icon, + — + button, in the IMAGING section. A starting point marker will appear near the center of the image.
- Step 2** Touch the screen and the marker will drag along above your finger. Once you have placed the starting point marker where you want then lift your finger off of the screen. At that point an ending point marker will appear, along with a line between the two points.
- Step 3** Touch the screen again to move the ending point marker where you wish to. When you lift your finger the straight line distance between the points will be displayed.
- Step 4** To place a second distance measurement on the screen tap the distance measurement button + — + again, and repeat the above steps.



**Note:** To clear the first distance measurement off of the screen tap the distance measurement button again, and then a second time if desired to delete the second distance measurement. In fact, tapping the distance measurement button cycles through distance measurements D1 and D2 in the order: *D1 (add), D2 (add), D1 (delete), D2 (delete), and then repeats.*



**Note:** When imaging is restarted by pressing the **See** button or **Scan Y** all distance measurements are deleted from the image.

### 6.6.2. Text Annotations

The Ulthera System allows you to add information such as comments atop ultrasound images when the system is not in the active IMAGING state. Tap **Scan N** to stop scanning if necessary.

- Step 1** While you are on the DeepSEE Screen, tap the TEXT button in the IMAGING section. A text box will appear near the center of the image and a keyboard will appear below the image.
- Step 2** Type any comments and/or move the text box where desired by tapping the screen – the box will track your finger.

**Step 3** Hit Enter on the keyboard when finished entering the desired comments and when the text box is in the desired position.



**Note:** Tapping the **Text** button cycles through text annotations Text1 and Text2 in the order: *Text1 (add), Text2 (add), Text1 (delete), Text2 (delete), and then repeats.*

## 6.7. Record Keeping

The Ulthera System uses a proprietary Ulthera Database for storing a limited number of images and treatment record information. These images are readily accessible to browse, or export to another storage device.

It is strongly recommended that you properly maintain the database by regularly exporting and/or deleting unused or old images and treatment records. Excessive numbers of records and images become difficult to search and maintain on a system primarily dedicated to patient treatment, and thereby reduce productivity and system performance.

The number of images and/or treatment records that can be stored is limited to 200. At startup, if more than that are stored, the user is asked to optionally delete some of them. If not, additional storage is disabled. However, if a procedure is already in progress as the system reaches its 200 mark additional records may be stored – the user will simply be asked to reduce the number of images and/or treatment records in the database the next time the system is started.



**Note:** All image compression methods used by Ulthera System are lossless. This produces small image file size without losing any image resolution or creating any image artifacts.

### 6.7.1. Saving Records in the Database

**Step 1** To save images in the database use the Save button on the DeepSEE tab to save the current display as a single image. Treatment records will automatically be saved assuming it has been set up as stated in Section 6.3 Setting Up a Treatment Record. For accessing images and/or treatment records at a later date see 6.8.3 and 6.8.4 respectively.

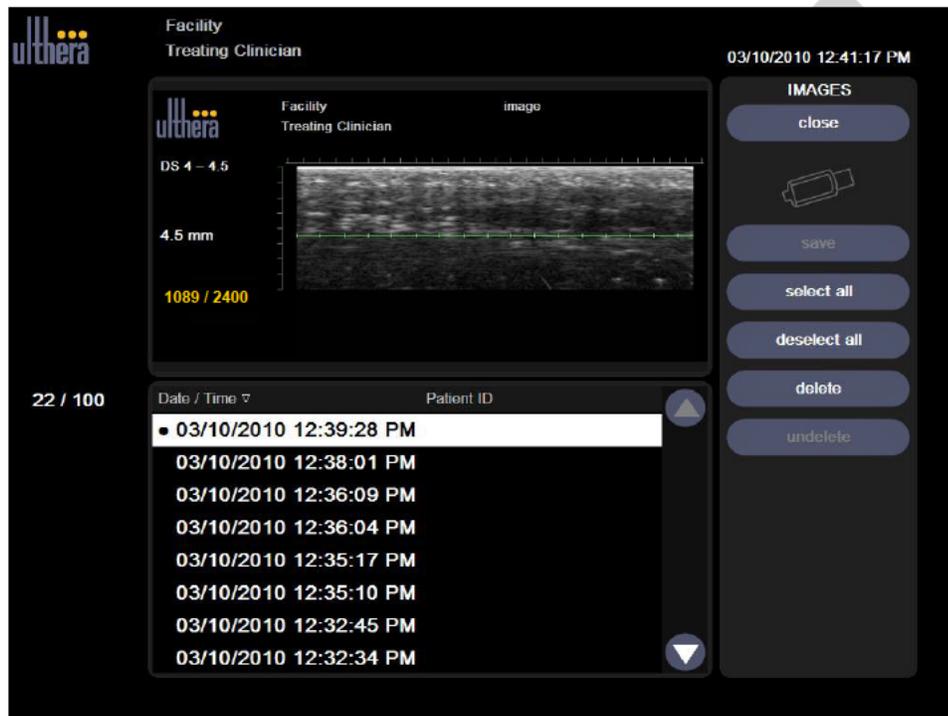
### 6.7.2. Browsing the Database

**Step 1** Tap the **Settings** tab then tap on either **Records** (to view stored treatment data) or **Images** (to view scans). From here you can browse the data on screen, save to a USB thumb drive, or delete items.

**Note:** It is advisable to store records on an accessory device before deleting.

### 6.7.3. Exporting Images

- Step 1** On the **Settings** screen, tap **Images** to view the menu of treated patients. A screen similar to Figure 6.8. will appear.
- Step 2** Tap a specific **Patient ID** to call up the image stored for that patient or tap **Select All** to call up all stored images.



*Figure 6.8. Image Export screen. Stored images are listed in the bottom dialog box and the most recently user-selected image is displayed above it. If an external storage device is attached then SAVE is enabled.*



**Note:** If you inadvertently selected an item or items, tap that item again or tap **Deselect All** to clear the selection(s).

- Step 3** Connect the generic USB storage device (as described in Section 5.4.3 Connecting Accessories).
- The icon for this appears on the right hand side of the screen; it will be grayed out if the accessory is disabled and will be displayed in white if enabled.
- Step 4** Tap **Save** to export image(s) to USB thumb drive

## 6.7.4. Exporting Records

**Step 1** On the **Settings** screen, tap **Records** to view the menu of treated patients. A screen similar to Figure 6.9. will appear.

**Step 2** Tap a specific **Patient ID** to call up the records stored for that patient or tap **Select All** to call up all stored records.



**Note:** If you inadvertently selected an item or items, tap that item again or tap **Deselect All** to clear the selection(s).

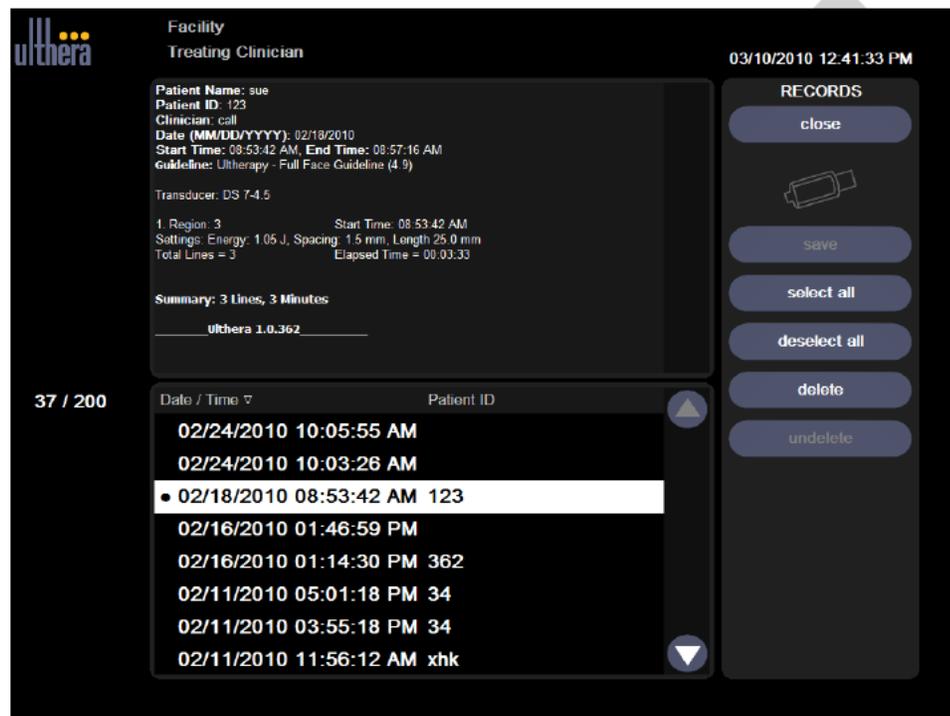


Figure 6.9 Treatment Records screen.

**Step 3** Connect the generic USB storage device (as described in Section 5.4.3 Connecting Accessories).

- The icon for this appears on the upper right hand side of the screen: it will be grayed out if the accessory is disabled and will be displayed in white if enabled.

**Step 4** Tap **Save** to export record(s) to USB thumb drive.

**Step 5** For the information to remain on the System after exporting the desired information tap **Close** to return to the Settings screen. To delete the information from the System after exporting it, see the next Section, 6.8.5.

### 6.7.5. Deleting Records from the Database



**Note:** It is advisable to store records on an accessory device before deleting information.

**Step 1** To remove one or more item(s) from the database, select the item(s) and tap **Delete**; to remove *all* items from the database, tap **Select All** and then tap **Delete All**.



**Note:** If you inadvertently delete an item or items, tap **Undelete** to restore the item(s).

Records in the **Undelete** dialogue may be permanently erased by selecting the items to be permanently erased and then tapping the **Erase** button.

**Step 2** Tap **Close** to return to the **Settings** screen.

### 6.7.6. Recovering Deleted Records/Images from the Database



**Note:** Only the 50 previously deleted records or images may be recovered.

**Step 1** To recover one or more of the 50 previously deleted records or images tap **Undelete**.

**Step 2** Select the images or records that you would like to undelete and tap **Undelete** once more.

The records or images will have now returned to the current database.

## 6.8. Troubleshooting

### 6.8.1. Ulthera System Warning and Caution Dialogs



**Warning:** These dialogs indicate that a problem was detected. See System Messages section for more details.

An example of a system warning appears in Figure 6.10. In such cases the user is given instructions on how to resolve the issue. Please follow the guidance to help solve the problem as quickly as possible and to provide proper information in case Technical Support is needed.

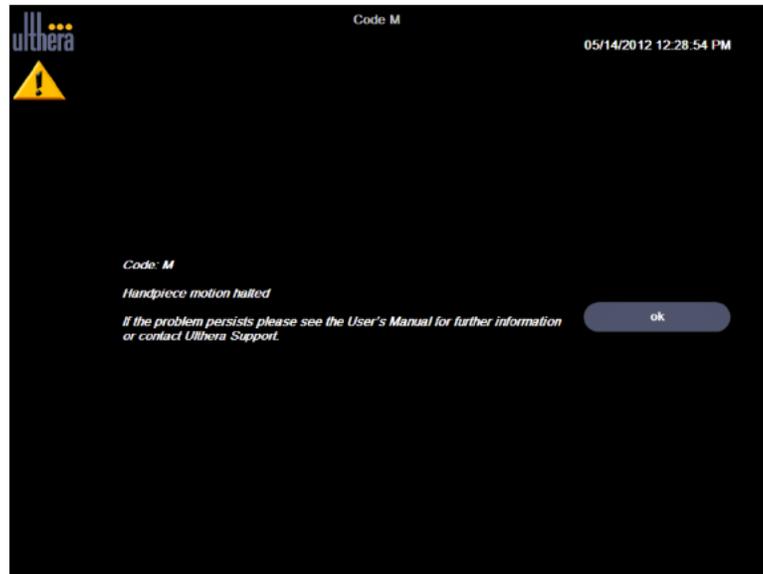


Figure 6.10 Example of System Caution Dialog.

## 6.8.2. Unsatisfactory Image Quality

### Action Required:

- Check that the display brightness is set appropriately for the transducer that is connected and the area being imaged via the **Display** controls.
- Check that enough gel is applied to the transducer.
- If the problem is not resolved, contact Ulthera, Inc. or your country representative for assistance.

## 6.9. Shutting Down the System

- Step 1** Stop any imaging and/or treatment in progress prior to shutting down the system.
- Step 2** On the **Settings** screen, tap **Shutdown**
- Step 3** Remove the Ulthera System User Access Key to prevent unauthorized usage.



**Note:** The main power switch on the rear panel of the control unit should be left in the ON position; however, it may be switched off when moving the system between rooms or for storage or cleaning.

## 7. System Messages

The Ulthera System is designed with internal checks to ensure that all aspects of the device are functioning appropriately. In the event that an information message presents itself during use, please follow the instructions on the screen or refer to the information listed below.

These messages are classified as INFORMATION SIGNALS per IEC 60601-1-8.

| Info Code | Message Displayed   | Description  |
|-----------|---|--|
| <b>B</b>  |  <p>Code B</p> <p>Internal handpiece temperature is too high</p> <p>If the problem persists please see the User's Manual for further information or contact Ulthera Support.</p>   | The internal handpiece temperature is above its limit. Allow the handpiece to cool down.   |
| <b>C</b>  |  <p>Code C</p> <p>Hardware halted</p> <p>Please restart the system.</p> <p>If the problem persists please see the User's Manual for further information or contact Ulthera Support.</p>                                  | Hardware was halted due to an event detected in the control unit.  |
| <b>E</b>  |  <p>Code E</p> <p>Communication halted</p> <p>Please restart the system.</p> <p>If the problem persists please see the User's Manual for further information or contact Ulthera Support.</p>                           | Communication was halted due to an initialization event detected in the control unit.  |
| <b>G</b>  |  <p>Code G</p> <p>Hardware halted</p> <p>Please restart the system.</p> <p>If the problem persists please see the User's Manual for further information or contact Ulthera Support.</p>                                | Hardware was halted due to an event detected in the control unit.  |
| <b>H</b>  |  <p>Code H</p> <p>Transducer motion not detected</p> <p>Please remove and reinsert the transducer.</p> <p>If the problem persists please see the User's Manual for further information or contact Ulthera Support.</p> | Transducer motion was not detected. Ensure that the transducer is properly mounted in the handpiece. Please be sure to always hit Scan N before removing transducer. Remove and reinsert the transducer. |
| <b>I</b>  |  <p>Code I</p> <p>Communication halted</p> <p>Please restart the system.</p> <p>If the problem persists please see the User's Manual for further information or contact Ulthera Support.</p>                           | Communication halted due to an event detected in the control unit.   |

| Info Code | Message Displayed   | Description  |
|-----------|---|--|
| J         | <p>Code J</p>  <p>Handpiece communication halted<br/>Please restart the system.</p> <p>If the problem persists please see the User's Manual for further information or contact Ulthera Support.</p>          | Communication halted due to an event detected in the control unit.   |
| K         | <p>Code K</p>  <p>Software halted<br/>Please restart the system.</p> <p>If the problem persists please see the User's Manual for further information or contact Ulthera Support.</p>                         | Software was halted due to an event detected in the control unit.  |
| L         | <p>Code L</p>  <p>Transducer out of lines<br/>Please replace transducer and continue.</p> <p>See User's Manual for further information.</p>  | The Transducer's remaining line count is zero. Remove and replace the Transducer.  |
| M         | <p>Code M</p>  <p>Handpiece motion halted<br/>If the problem persists please see the User's Manual for further information or contact Ulthera Support.</p>   | Inspect handpiece. Ensure that the transducer is properly mounted and latched in the handpiece.  |
| N         | <p>Code N</p>  <p>USB flash memory connectivity<br/>Please check flash drive and continue.</p> <p>See User's Manual for further information.</p>   | A problem was detected with the attached USB flash memory drive. Make sure the drive is properly formatted and has enough free space. Do not remove the drive while the system is communicating with it. |
| P         | <p>Code P</p>  <p>Hardware halted<br/>Please restart the system.</p> <p>If the problem persists please see the User's Manual for further information or contact Ulthera Support.</p>                       | Hardware was halted due to an event detected in the control unit.  |
| S         | <p>Code S</p>  <p>The red STOP button has been pressed.<br/>Please restart the system.</p> <p>If the problem persists please see the User's Manual for further information or contact Ulthera Support.</p> | The red Stop button was pressed.   |
| T         | <p>Code T</p>  <p>Internal transducer temperature is too high<br/>If the problem persists please see the User's Manual for further information or contact Ulthera Support.</p>                             | The internal transducer temperature is above its limit. Allow the transducer to cool down or use another transducer.   |
| U         | <p>Code U</p>  <p>Control unit temperature too high<br/>If the problem persists please see the User's Manual for further information or contact Ulthera Support.</p>                                       | The internal control unit temperature is above its limit. Allow the control unit to cool down. Provide proper ventilation.   |

| Info Code | Message Displayed  | Description   |
|-----------|--|---|
| V         | <p>Code V</p>  <p>Transducer energy delivery halted</p> <p>Tap Scan Y to resume scanning</p> <p>If the problem persists please see the User's Manual for further information or contact Ulthera Support.</p>      | <p>Excessive reflected power has been detected. If the problem persists, please try another transducer and contact Ulthera Support. Use Transducer only as instructed. Tap Scan Y to resume scanning.</p> |
| W         | <p>Code W</p>  <p>Unauthorized transducer.</p> <p>Please replace the transducer and continue.</p> <p>Please contact your local representative for further assistance.</p>   | <p>The transducer connected is not an authorized transducer. Contact your local representative for further assistance.</p>  |
| X         | <p>Code X</p>  <p>Transducer cannot be read</p> <p>Please remove and reinsert the transducer.</p> <p>If the problem persists please see the User's Manual for further information or contact Ulthera Support.</p> | <p>The transducer cannot be read. Remove and reinsert the transducer. Check that the transducer contact area is clean.</p>  |

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## 8. Cleaning and Care

### 8.1. Cleaning the Transducer and Handpiece



**Note:** Transducers are packaged and shipped non-sterile and ready to use.

Because the transducer will come in contact with the skin of a patient, the standard practice for cleaning and low level disinfection of transducers between patients is to gently but thoroughly wipe the transducers with a standard 70% isopropyl alcohol prep pad. One may also use a standard 70% isopropyl alcohol prep pad to gently wipe the handpiece and cable. Neither the transducers nor the handpiece should be submerged in liquid. Place the transducer back into its original packaging between uses.



**Warning:** Use only this procedure for cleaning. Do not use acetone or other solvents as this can damage the transducer.

### 8.2. General Care of the System

To get the best possible performance, treat the equipment carefully by adhering to the following guidelines:

1. Inspect the handpiece and connectors regularly for any problems.
2. Turn scanning off before changing transducers to ensure proper identification of transducers and to prolong the life of the system.
3. Do not drop the handpiece or transducers on the floor or other hard surfaces. This can cause permanent damage.
4. Do not twist or pull the transducer cables. This could cause damage to internal wires and connections.
5. Use aqueous ultrasound gel only. Other lubricants or lotions, particularly mineral oil, could eventually damage transducers or cables.
6. Do not use acoustic standoff pads or any objects between the transducer and patient.
7. Apply ultrasound gel only to the window of the transducer and wipe it from the transducer after completing a treatment. Avoid getting the gel on the handpiece or control unit.
8. Transducers should be cleaned between procedures. See cleaning procedure information immediately preceding this subsection.
9. Keep new transducers in sealed pouches until ready for use.

10. Place transducers back into original pouch and reseal for storage between procedures.
11. Do not hold the handpiece in a manner that can damage the chord or strain relief while removing or inserting transducers.



**Caution:** Always check the expiration date on the transducer before using.

PROPOSED DRAFT

## 9. Re-order Information

Please contact Ulthera, Inc. or your country representative to order transducers, accessories, or other items for your system.

| Description                               | Catalog/<br>Reorder Number |
|---|----------------------------|
| Ulthera Control Unit                      | UC-1                       |
| Ulthera® DeepSEE® Handpiece               | UH-2                       |
| Ulthera® DeepSEE® Transducer DS 7-3.0     | UT-1                       |
| Ulthera® DeepSEE® Transducer DS 7-3.0N    | UT-1N                      |
| Ulthera® DeepSEE® Transducer DS 4-4.5     | UT-2                       |
| Ulthera® DeepSEE® Transducer DS 7-4.5     | UT-3                       |
| Ulthera® DeepSEE® Transducer DS 10-1.5    | UT-4                       |
| Ulthera® DeepSEE® Transducer DS 10-1.5N   | UT-4N                      |
| Ulthera System Cart                       | UR-1                       |
| (Optional) Ulthera System Case            | US-1                       |
| (Optional) Ulthera System User Access Key | UK-1                       |
| (Optional) USB Storage Device             | UD-1                       |

## 10. Safety Standards and Regulatory Classifications

|   |
|---|
| FDA Product Classification 878.4590   |
| UL60601-1, IEC60601-1 Medical Electrical Equipment, Part 1: General Requirements for Safety.                    |
| Class I device, type B applied part, non AP/APG rated.  |
| Ingress protection: IPx0 (“Ordinary Equipment”) for Control Unit; IPx1 for mated transducer and handpiece.      |
| Mode of operation: Continuous.  |
| IEC60601-1-2, Electromagnetic Compatibility. CISPR 11 class A, Group 1.   |
| IEC60601-1-4, Programmable electrical medical systems   |
| IEC60601-2-37, Particular requirements for the safety of ultrasonic medical diagnostic and monitoring equipment |
| Patient contacting materials comply with ISO 10993-1  |
| NRTL Certification: Canadian Standards Association (CSA)  |
| ISO 13485 Quality Assurance Standard  |

# Appendix A – Treatment Guidelines

As displayed on the user interface and as notated in Tables A.1. & A.2. guidelines are set forth for the levels of energy, available transducer and the number of treatment lines to be delivered for each treatable region.

*Table A.1. Treatment Guideline (5.0)*

| Ultherapy Guideline (5.0) |                     |            |                   |      |      |      |       |
|---------------------------|---------------------|------------|-------------------|------|------|------|-------|
| Area                      | Region              | Transducer | Energy Levels [J] |      |      |      | Lines |
| Medial Neck               | Medial Neck 4-4.5   | DS 4-4.5   | 1.20              | 1.00 | 0.90 | 0.75 | 14    |
|                           | R-Neck 4-4.5        | DS 4-4.5   | 1.20              | 1.00 | 0.90 | 0.75 | 18    |
| Right Side 4.5            | R-Cheek 4-4.5       | DS 4-4.5   | 1.20              | 1.00 | 0.90 | 0.75 | 55    |
|                           | R-Brow 7-4.5        | DS 7-4.5   | 1.05              | 0.90 | 0.75 | 0.66 | 10    |
|                           | R-Orbit 7-4.5       | DS 7-4.5   | 1.05              | 0.90 | 0.75 | 0.66 | 10    |
| Medial Neck               | Medial Neck 7-3.0   | DS 7-3.0   | 0.45              | 0.35 | 0.30 | 0.25 | 14    |
|                           | R-Neck 7-3.0        | DS 7-3.0   | 0.45              | 0.35 | 0.30 | 0.25 | 18    |
| Right Side 3.0            | R-Cheek 7-3.0       | DS 7-3.0   | 0.45              | 0.35 | 0.30 | 0.25 | 40    |
|                           | R-Brow 7-3.0        | DS 7-3.0   | 0.45              | 0.35 | 0.30 | 0.25 | 10    |
|                           | R-Orbit 7-3.0       | DS 7-3.0   | 0.45              | 0.35 | 0.30 | 0.25 | 10    |
|                           | R-Infraorbital 3.0N | DS 7-3.0N  | 0.45              | 0.35 | 0.30 | 0.25 | 9     |
|                           | L-Neck 4-4.5        | DS 4-4.5   | 1.20              | 1.00 | 0.90 | 0.75 | 18    |
| Left Side 4.5             | L-Cheek 4-4.5       | DS 4-4.5   | 1.20              | 1.00 | 0.90 | 0.75 | 55    |
|                           | L-Brow 7-4.5        | DS 7-4.5   | 1.05              | 0.90 | 0.75 | 0.66 | 10    |
|                           | L-Orbit 7-4.5       | DS 7-4.5   | 1.05              | 0.90 | 0.75 | 0.66 | 10    |
|                           | L-Neck 7-3.0        | DS 7-3.0   | 0.45              | 0.35 | 0.30 | 0.25 | 18    |
| Left Side 3.0             | L-Cheek 7-3.0       | DS 7-3.0   | 0.45              | 0.35 | 0.30 | 0.25 | 40    |
|                           | L-Brow 7-3.0        | DS 7-3.0   | 0.45              | 0.35 | 0.30 | 0.25 | 10    |
|                           | L-Orbit 7-3.0       | DS 7-3.0   | 0.45              | 0.35 | 0.30 | 0.25 | 10    |
|                           | L-Infraorbital 3.0N | DS 7-3.0   | 0.45              | 0.35 | 0.30 | 0.25 | 9     |
|                           | R-Cheek             | DS 10-1.5  | 0.25              | 0.20 | 0.18 | 0.15 | 75    |
| Right Side 1.5            | R-Brow              | DS 10-1.5  | 0.25              | 0.20 | 0.18 | 0.15 | 15    |
|                           | R-Orbit 10-1.5      | DS 10-1.5  | 0.25              | 0.20 | 0.18 | 0.15 | 15    |
|                           | R-Infraorbital 1.5  | DS 10-1.5  | 0.25              | 0.20 | 0.18 | 0.15 | 15    |
|                           | R-Infraorbital 1.5N | DS 10-1.5N | 0.25              | 0.20 | 0.18 | 0.15 | 15    |
|                           | R-Oral 1.5          | DS 10-1.5  | 0.25              | 0.20 | 0.18 | 0.15 | 25    |
|                           | R-Oral 1.5N         | DS 10-1.5N | 0.25              | 0.20 | 0.18 | 0.15 | 25    |
|                           | L-Cheek             | DS 10-1.5  | 0.25              | 0.20 | 0.18 | 0.15 | 75    |
| Left Side 1.5             | L-Brow              | DS 10-1.5  | 0.25              | 0.20 | 0.18 | 0.15 | 15    |

|                      |                     |            |      |      |      |      |    |
|----------------------|---------------------|------------|------|------|------|------|----|
|                      | L Orbit 10-1.5      | DS 10-1.5  | 0.25 | 0.20 | 0.18 | 0.15 | 15 |
|                      | L Infraorbital 1.5  | DS 10-1.5  | 0.25 | 0.20 | 0.18 | 0.15 | 15 |
|                      | L Infraorbital 1.5N | DS 10-1.5N | 0.25 | 0.20 | 0.18 | 0.15 | 15 |
|                      | L Oral 1.5          | DS 10-1.5  | 0.25 | 0.20 | 0.18 | 0.15 | 25 |
|                      | L Oral 1.5N         | DS 10-1.5N | 0.25 | 0.20 | 0.18 | 0.15 | 25 |
| <b>Medial Option</b> | Medial Neck 7-4.5   | DS 7-4.5   | 1.05 | 0.90 | 0.75 | 0.66 | 14 |
| <b>Right Option</b>  | R Neck 7-4.5        | DS 7-4.5   | 1.05 | 0.90 | 0.75 | 0.66 | 18 |
|                      | R Cheek 7-4.5       | DS 7-4.5   | 1.05 | 0.90 | 0.75 | 0.66 | 55 |
|                      | R Brow 7-3.0N       | DS 7-3.0N  | 0.45 | 0.35 | 0.30 | 0.25 | 10 |
|                      | R Orbit 7-3.0N      | DS 7-3.0N  | 0.45 | 0.35 | 0.30 | 0.25 | 10 |
|                      | R Infraorbital 3.0  | DS 7-3.0   | 0.45 | 0.35 | 0.30 | 0.25 | 9  |
| <b>Left Option</b>   | L Neck 7-4.5        | DS 7-4.5   | 1.05 | 0.90 | 0.75 | 0.66 | 18 |
|                      | L Cheek 7-4.5       | DS 7-4.5   | 1.05 | 0.90 | 0.75 | 0.66 | 55 |
|                      | L Brow 7-3.0N       | DS 7-3.0N  | 0.45 | 0.35 | 0.30 | 0.25 | 10 |
|                      | L Orbit 7-3.0N      | DS 7-3.0N  | 0.45 | 0.35 | 0.30 | 0.25 | 10 |
|                      | L Infraorbital 3.0  | DS 7-3.0   | 0.45 | 0.35 | 0.30 | 0.25 | 9  |

Table A.12. Treatment Guideline (5.0 PLUS)

| <b>Ultherapy – Guideline (5.0 PLUS)</b> |                     |             |                   |      |      |      |       |
|---|---------------------|-------------|-------------------|------|------|------|-------|
| Area                                    | Region              | Transducer  | Energy Levels [J] |      |      |      | Lines |
| Medial Neck                             | Medial Neck 4-4.5   | DS 4 - 4.5  | 1.20              | 1.00 | 0.90 | 0.75 | 18    |
| Right Side<br>4.5                       | R Neck 4-4.5        | DS 4 - 4.5  | 1.20              | 1.00 | 0.90 | 0.75 | 26    |
|   | R Cheek 4-4.5       | DS 4-4.5    | 1.20              | 1.00 | 0.90 | 0.75 | 77    |
|   | R Brow 7-4.5        | DS 7-4.5    | 1.05              | 0.90 | 0.75 | 0.66 | 10    |
|   | R Orbit 7-4.5       | DS 7-4.5    | 1.05              | 0.90 | 0.75 | 0.66 | 10    |
| Medial Neck                             | Medial Neck 7-3.0   | DS 7 - 3.0  | 0.45              | 0.35 | 0.30 | 0.25 | 18    |
| Right Side<br>3.0                       | R Neck 7-3.0        | DS 7 - 3.0  | 0.45              | 0.35 | 0.30 | 0.25 | 26    |
|   | R Cheek 7-3.0       | DS 7 - 3.0  | 0.45              | 0.35 | 0.30 | 0.25 | 56    |
|   | R Brow 7-3.0        | DS 7 - 3.0  | 0.45              | 0.35 | 0.30 | 0.25 | 10    |
|   | R Orbit 7-3.0       | DS 7 - 3.0  | 0.45              | 0.35 | 0.30 | 0.25 | 10    |
|   | R Infraorbital 3.0N | DS 7 - 3.0N | 0.45              | 0.35 | 0.30 | 0.25 | 9     |
| Left Side<br>4.5                        | L Neck 4-4.5        | DS 4 - 4.5  | 1.20              | 1.00 | 0.90 | 0.75 | 26    |
|   | L Cheek 4-4.5       | DS 4-4.5    | 1.20              | 1.00 | 0.90 | 0.75 | 77    |
|   | L Brow 7-4.5        | DS 7-4.5    | 1.05              | 0.90 | 0.75 | 0.66 | 10    |
|   | L Orbit 7-4.5       | DS 7-4.5    | 1.05              | 0.90 | 0.75 | 0.66 | 10    |
| Left Side<br>3.0                        | L Neck 7-3.0        | DS 7 - 3.0  | 0.45              | 0.35 | 0.30 | 0.25 | 26    |
|   | L Cheek 7-3.0       | DS 7 - 3.0  | 0.45              | 0.35 | 0.30 | 0.25 | 56    |
|   | L Brow 7-3.0        | DS 7 - 3.0  | 0.45              | 0.35 | 0.30 | 0.25 | 10    |
|   | L Orbit 7-3.0       | DS 7 - 3.0  | 0.45              | 0.35 | 0.30 | 0.25 | 10    |

|                           |                     |             |      |      |      |      |    |
|---------------------------|---------------------|-------------|------|------|------|------|----|
|                           | L Infraorbital 3.0N | DS 7 - 3.0N | 0.45 | 0.35 | 0.30 | 0.25 | 9  |
| <b>Right Side<br/>1.5</b> | R Cheek             | DS 10-1.5   | 0.25 | 0.20 | 0.18 | 0.15 | 75 |
|                           | R Brow              | DS 10-1.5   | 0.25 | 0.20 | 0.18 | 0.15 | 15 |
|                           | R Orbit 10-1.5      | DS 10-1.5   | 0.25 | 0.20 | 0.18 | 0.15 | 15 |
|                           | R Infraorbital 1.5  | DS 10-1.5   | 0.25 | 0.20 | 0.18 | 0.15 | 15 |
|                           | R Infraorbital 1.5N | DS 10-1.5N  | 0.25 | 0.20 | 0.18 | 0.15 | 15 |
|                           | R Oral 1.5          | DS 10-1.5   | 0.25 | 0.20 | 0.18 | 0.15 | 25 |
|                           | R Oral 1.5N         | DS 10-1.5N  | 0.25 | 0.20 | 0.18 | 0.15 | 25 |
| <b>Left Side<br/>1.5</b>  | L Cheek             | DS 10-1.5   | 0.25 | 0.20 | 0.18 | 0.15 | 75 |
|                           | L Brow              | DS 10-1.5   | 0.25 | 0.20 | 0.18 | 0.15 | 15 |
|                           | L Orbit 10-1.5      | DS 10-1.5   | 0.25 | 0.20 | 0.18 | 0.15 | 15 |
|                           | L Infraorbital 1.5  | DS 10-1.5   | 0.25 | 0.20 | 0.18 | 0.15 | 15 |
|                           | L Infraorbital 1.5N | DS 10-1.5N  | 0.25 | 0.20 | 0.18 | 0.15 | 15 |
|                           | L Oral 1.5          | DS 10-1.5   | 0.25 | 0.20 | 0.18 | 0.15 | 25 |
|                           | L Oral 1.5N         | DS 10-1.5N  | 0.25 | 0.20 | 0.18 | 0.15 | 25 |
| <b>Medial<br/>Option</b>  | Medial Neck 7-4.5   | DS 7-4.5    | 1.05 | 0.90 | 0.75 | 0.66 | 18 |
| <b>Right<br/>Option</b>   | R Neck 7-4.5        | DS 7-4.5    | 1.05 | 0.90 | 0.75 | 0.66 | 26 |
|                           | R Cheek 7-4.5       | DS 7-4.5    | 1.05 | 0.90 | 0.75 | 0.66 | 77 |
|                           | R Brow 7-3.0N       | DS 7 - 3.0N | 0.45 | 0.35 | 0.30 | 0.25 | 10 |
|                           | R Orbit 7-3.0N      | DS 7 - 3.0N | 0.45 | 0.35 | 0.30 | 0.25 | 10 |
|                           | R Infraorbital 3.0  | DS 7 - 3.0  | 0.45 | 0.35 | 0.30 | 0.25 | 9  |
| <b>Left<br/>Option</b>    | L Neck 7-4.5        | DS 7-4.5    | 1.05 | 0.90 | 0.75 | 0.66 | 26 |
|                           | L Cheek 7-4.5       | DS 7-4.5    | 1.05 | 0.90 | 0.75 | 0.66 | 77 |
|                           | L Brow 7-3.0N       | DS 7 - 3.0N | 0.45 | 0.35 | 0.30 | 0.25 | 10 |
|                           | L Orbit 7-3.0N      | DS 7 - 3.0N | 0.45 | 0.35 | 0.30 | 0.25 | 10 |
|                           | L Infraorbital 3.0  | DS 7 - 3.0  | 0.45 | 0.35 | 0.30 | 0.25 | 9  |

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Cosmetic Medicine

# Clinical Efficacy and Safety of Focused-Image Ultrasonography: A 2-Year Experience

Gordon H. Sasaki, MD, FACS; and Ana Tevez, RN

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## Abstract

**Background:** Focused-image ultrasonography produces controlled waves that image dermal and subdermal structures in real time, with precise thermal coagulation points in a linear pattern, for eventual nonsurgical lifting.

**Objectives:** The authors evaluate the effectiveness of single and dual planes of ultrasound treatment by varying the directions of treatment lines, depths, and cumulative joule energies and compare the safety and efficacy of treatment with these variations.

**Methods:** In this prospective, 2-part study, patients were treated by single- or dual-treatment depth with differing directions of treatment lines while the number of treatment lines and amount of energy delivered to brows or marionette lines remained constant (Study 1) or with lower or higher joule energy to opposing areas while the dual depths and number of vectored lines remained constant (Study 2). Lifting was measured using the matched-orientation function of specific mirroring software. Clinical outcomes were assessed with global aesthetic improvement scales.

**Results:** Vertical vectoring of 15 treatment lines in both tissue depths produced significant lifting over the 15 horizontally-placed treatment lines in the opposing brows and marionette lines. Sites with more treatment lines and higher joule energy at dual depths resulted in significantly greater lifting (Study 2). Side effects were minimal.

**Conclusions:** Focused-imagined ultrasound therapy to facial tissues is safe and effective when performed as described.

## Level of Evidence: 3

## Keywords

cosmetic medicine, ultrasonography, focused-image ultrasound, marionette lines

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Surgery to the ptotic face and neck remains the most effective method for achieving prolonged rejuvenation of the aging face. Despite the major efficacy advantage, informed patients often prefer noninvasive devices and procedures because they are associated with minimal posttreatment downtime and lower morbidity. Because the current non-invasive energy systems<sup>1-5</sup> are unable to efficiently lift anatomical structures below the skin level, these devices are likely to be less effective than invasive procedures and the results are unpredictable. In contrast, focused ultrasound therapy<sup>6-10</sup> produces precise, propagated ultrasonic waves that penetrate deeply and produce real-time imaging of the skin and subdermal structures. The targeted tissue levels are treated with a number of lines, each containing discrete separated thermal coagulation points (TCPs), which produces eventual nonsurgical tissue lifting without affecting the surface of the skin.

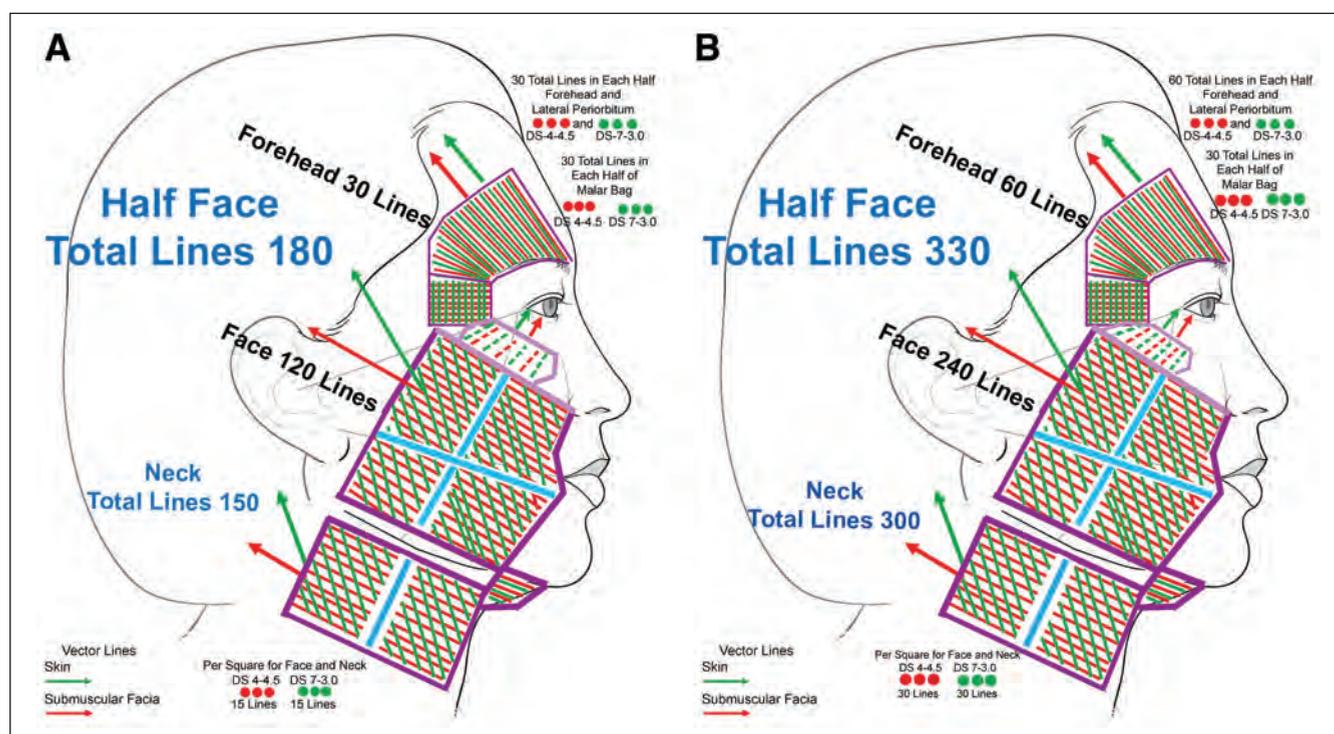
The objectives of the research described in this article were 3-fold. First, in Pilot Study 1, the effects of

single/dual levels of treatment were assessed by varying the directions of treatment lines, depths of tissue treatments, and joule energies of the exposure lines to determine the optimal set of parameters for tissue lifting. Second, in Pilot Study 2, the lifting achieved in Study 1 was compared with that obtained with higher joule energies. Third, we compared the safety and efficacy between patients treated with lower versus higher numbers of treatment lines and at lower and higher joule energies.

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**Figure 1.** Treatment maps. (A) Lower number of treatment lines and joule energy. (B) Higher number of treatment lines and joule energy.

## METHODS

### Patient Selection

Of over 100 adults recruited in six months from the study site's patient data base, only 35 were qualified, provided written informed consents, and were randomized into the two Pilot Study Groups. Inclusion criteria were mild to moderate ptosis of skin and fibromuscular layers as well as mild to moderate fat thickness to the face and neck. Exclusion criteria included severely damaged actinic skin, thin porcelain-type skin, significant ptotic skin and fibromuscular units, active systemic or local infection, acne or keloidal scarring, skin diseases that altered wound healing, and hemorrhagic disorders or hemostatic dysfunctions. Women who were pregnant or breastfeeding were excluded from participation. Subjects who had undergone facial surgery, including ablative and nonablative skin procedures, were excluded until 1 year after their procedure. Study participants were treated in compliance with guidelines established by the International Organization for Standardization, US Food and Drug Administration, and Institutional Review Boards.

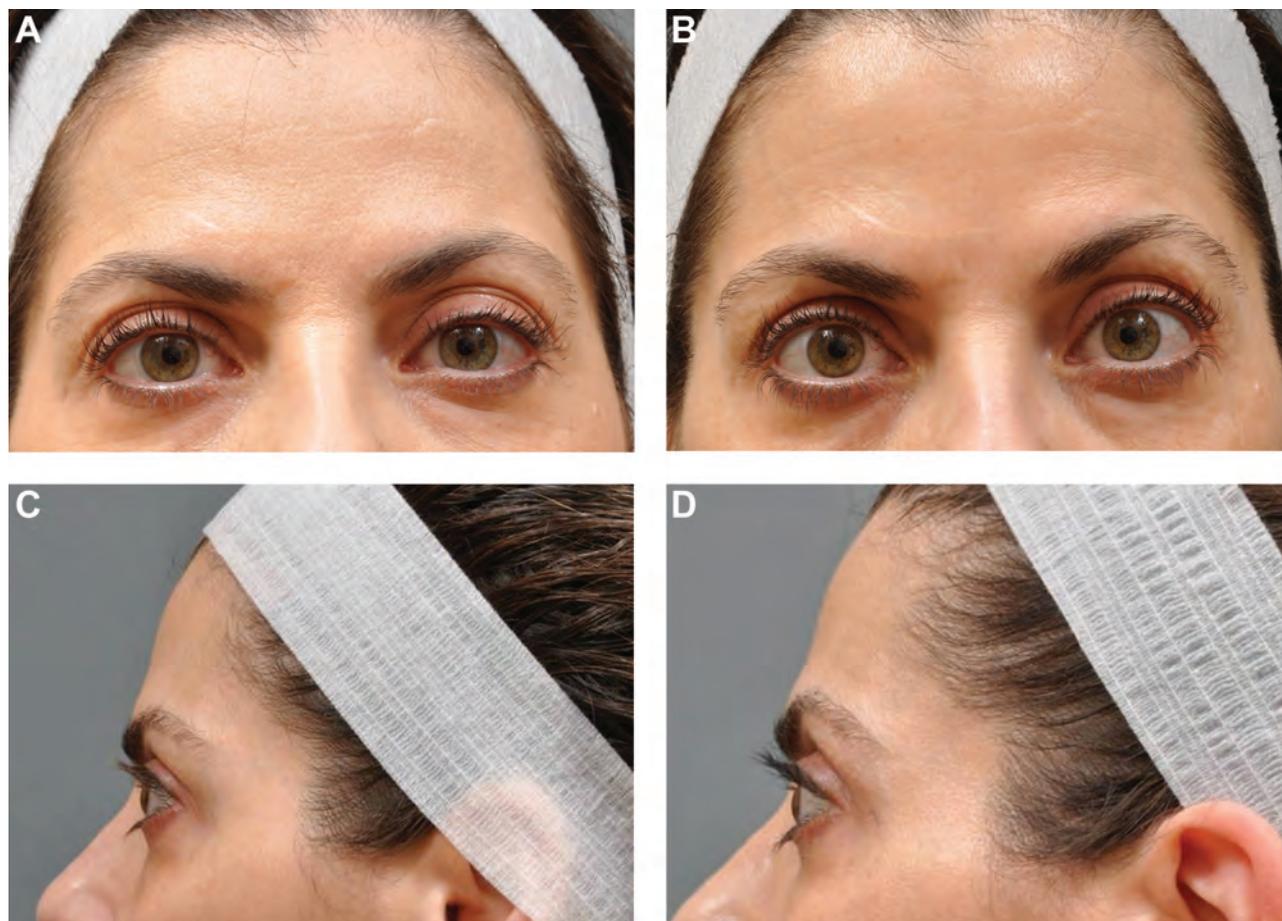
### Pretreatment Protocol

One week before treatment, patients were asked to discontinue the use of topical skin care products such as

isotretinoin, glycolic acid, and salicylic acid. On the day of treatment, they were asked to avoid application of facial creams, lotions, powders, and foundations. All metal jewelry was removed from the facial area. Patients washed their faces with a mild cleanser prior to their procedure. Patients who had a history of viral infections received a course of prophylactic antiviral medication, which lasted from 2 days before to 6 days after the procedure.

After photographic documentation, squares measuring  $2.5 \times 2.5$  cm were marked at selected treatment sites such as the brow complex, crow's feet, malar bag region, mid-face, and neck, as shown in Figures 1 and 2. The predicted pathways of the frontal nerve rami (1.5 cm superolateral to the orbital rim), the marginal mandibularis rami (medial to the marionette line), and the deep, long, lateral branch of the supraorbital sensory nerve (1-1.5 cm medial to the superior temporal crest line) were outlined as a reminder to (1) lower the quantity of delivered energy, (2) lessen the downward pressure of the transducer on the skin surface, (3) select a transducer associated with a higher level of tissue treatment, and/or (4) avoid placement of any treatment lines.

Treatment was avoided over areas containing mechanical implants, electrical devices, or soft-tissue augmentation materials. Treatment was not administered on tissues directly over a patient's eyes or in any area where ultrasound energy could potentially reach the eyes. Ultrasound therapy should not be applied directly over the thyroid gland.



**Figure 2.** (A, C) This 52-year-old woman presented with orbital hooding and ptosis of the lateral brows. The forehead tissue above her right lateral brow was treated with the 7 MHz, 4.5 mm (15 vertical lines; 267.8 joules) and the 7 MHz, 3.0 mm (15 vertical lines; 155.2 joules) and above her left lateral brow with 7 MHz, 4.5 mm (30 vertical lines; 535.6 joules) and 7 MHz, 3.0 mm (30 vertical lines; 310.5 joules). (B, D) Six months posttreatment. The left lateral brow demonstrates increased elevation compared with the right lateral brow.

## Treatment Protocol

A full description of the ultrasound system used in this study (Ulthera System; Ulthera, Inc., Mesa, Arizona; approved by the US Food and Drug Administration in September 2009) is available in an online-only appendix at [www.aestheticsurgeryjournal.com](http://www.aestheticsurgeryjournal.com).

After a thin layer of ultrasound transmission gel was applied to the transducer's window, the selected transducer was positioned onto the marked skin-treatment square and activated to begin imaging of the skin and subdermal structures. Upon activation of the transducer, a series of TCPs were deposited at the selected tissue level in a straight line. This sequence was repeated within each treatment square with the selected number, direction, and depth of treatment lines, according to the study protocols (described later), to complete the procedure. The ultrasound transmission gel was reapplied frequently to ensure proper tissue imaging and coupling. For the few patients who acknowledged a low pain threshold or who experienced moderate discomfort during treatment, a pain

management program was initiated in a graded fashion. It consisted of administering oral analgesic or sedative medication, giving distractive hand and foot massages, reducing skin temperature with an air coolant device, lowering joule settings (by one level for each transducer or by shortening the length of treatment lines), and, if necessary, administering selective nerve blocks or limited amounts of buffered lidocaine (subcutaneously). The majority of patients who received treatment to the midface and neck did not require a local nerve block or lidocaine because of the adequate thickness of those tissues. A patient treated on the forehead/brow may require local anesthesia or nerve blocks because of the thinness of tissues overlying the frontal bone. After completion of treatment and removal of the ultrasound gel, patients were able to return immediately to their usual lifestyle and activities. Medical skin-care regimens resumed within 1 week. The entire 2-year study began in October 2009 and ended in October 2011. The Pilot Study 1 extended from October 2009 to April 2010, while Pilot Study 2 took place between April 2010 and October 2010.

**Table 1. Pilot Study 1: Treatment Mapping of Depths, Number of Vector Lines, and Joule Energy**

|         | Right Brow   | Left Brow   |
|---------|--|---|
| Group 1 | 7 MHz, 3.0 mm (15 vertical lines) <sup>a</sup>   | 7 MHz, 3.0 mm (15 horizontal lines) <sup>a</sup>  |
| Group 2 | 7 MHz, 4.5 mm (15 vertical lines) <sup>b</sup>   | 7 MHz, 4.5 mm (15 horizontal lines) <sup>b</sup>  |
| Group 3 | 4 MHz, 4.5 mm (15 vertical lines) <sup>c</sup>   | 4 MHz, 4.5 mm (15 horizontal lines) <sup>c</sup>  |
| Group 4 | 7 MHz, 3.0 mm (15 vertical lines) <sup>a</sup><br>7 MHz, 4.5 mm (15 vertical lines) <sup>b</sup>           | 7 MHz, 3.0 mm (15 horizontal lines) <sup>a</sup><br>7 MHz, 4.5 mm (15 horizontal lines) <sup>b</sup>    |
| Group 5 | 7 MHz, 3.0 mm (15 vertical lines) <sup>a</sup><br>7 MHz, 4.5 mm (15 horizontal lines) <sup>b</sup>         | 7 MHz, 3.0 mm (15 horizontal lines) <sup>a</sup><br>7 MHz, 4.5 mm (15 vertical lines) <sup>b</sup>      |
|         | Right Marionette Fold  | Left Marionette Fold  |
| Group 6 | 7 MHz, 3.0 mm (15 superolateral lines) <sup>a</sup>  | 7 MHz, 3.0 mm (15 horizontal lines) <sup>a</sup>  |
| Group 7 | 4 MHz, 4.5 mm (15 superolateral lines) <sup>c</sup>  | 4 MHz, 4.5 mm (15 horizontal lines) <sup>c</sup>  |
| Group 8 | 7 MHz, 3.0 mm (15 superolateral lines) <sup>a</sup><br>4 MHz, 4.5 mm (15 superolateral lines) <sup>c</sup> | 7 MHz, 3.0 mm (15 horizontal lines) <sup>a</sup><br>4 MHz, 4.5 mm (15 horizontal lines) <sup>c</sup>    |
| Group 9 | 7 MHz, 3.0 mm (15 superolateral lines) <sup>a</sup><br>4 MHz, 4.5 mm (15 horizontal lines) <sup>c</sup>    | 7 MHz, 3.0 mm (15 horizontal lines) <sup>a</sup><br>4 MHz, 4.5 mm (15 superolateral lines) <sup>c</sup> |

<sup>a</sup>0.45 J/TCP × 23 TCPs/25-mm line × 15 lines = 155.2 J.

<sup>b</sup>1.05 J/TCP × 17 TCPs/25-mm line × 15 lines = 267.8 J.

<sup>c</sup>1.2 J/TCP × 17 TCPs/25-mm line × 15 lines = 306 J.

### Pilot Study 1

Twenty-seven patients (9 groups of 3 patients each) received treatment to opposing brows and marionette folds by varying vector directions and single/dual tissue treatment depths, while keeping constant other aspects of the treatment map such as the number of lines (15, each 25 mm long) at the highest level of joules/TCP at each site (Table 1). For each group, the matching site on the opposing side of the face received identical total amounts of energy delivered at the same tissue depths; the only variation was the direction of the 15 lines of treatment.

The patients in Groups 1, 2, 3, 6, and 7 had their ipsilateral and contralateral brows and marionette lines treated at either the visualized dermal or fibromuscular layer, as determined by the transducer's preset fixed focal depth, with 15 lines and equivalent joules per side (7 MHz, 3.0 mm, 15 lines, 155.2 J; 7 MHz, 4.5 mm, 15 lines, 267.8 J; 4 MHz, 4.5 mm, 15 lines, 306 J). Six months after treatment, the percentage of change in tissue lifting (vs baseline) was measured for each patient using Canfield Mirror software (Canfield Scientific, Inc., Fairfield, NJ).

**Table 2. Pilot Study 2: Treatment Mapping of Depths, Number of Vectored Lines, and Total Joule Energy**

|         | Right Brow  | Left Brow   |
|---------|---|---|
| Group 1 | 7 MHz, 3.0 mm (15 vertical lines) <sup>a</sup><br>7 MHz, 4.5 mm (15 vertical lines) <sup>c</sup>        | 7 MHz, 3.0 mm (30 vertical lines) <sup>b</sup><br>7 MHz, 4.5 mm (30 vertical lines) <sup>d</sup>        |
|         | Right Marionette Fold   | Left Marionette Fold  |
| Group 2 | 7 MHz, 3.0 mm (15 superolateral lines) <sup>a</sup><br>4 MHz, 4.5 mm (15 horizontal lines) <sup>e</sup> | 7 MHz, 3.0 mm (30 superolateral lines) <sup>b</sup><br>4 MHz, 4.5 mm (30 horizontal lines) <sup>f</sup> |

<sup>a</sup>0.45 J/TCP × 23 TCPs/25-mm line × 15 lines = 155.2 J.

<sup>b</sup>0.45 J/TCP × 23 TCPs/25-mm line × 30 lines = 310.5 J.

<sup>c</sup>1.05 J/TCP × 17 TCPs/25-mm line × 15 lines = 267.8 J.

<sup>d</sup>1.05 J/TCP × 17 TCPs/25-mm line × 30 lines = 535.6 J.

<sup>e</sup>1.2 J/TCP × 17 TCPs/25-mm line × 15 lines = 306 J.

<sup>f</sup>1.2 J/TCP × 17 TCPs/25-mm line × 30 lines = 612 J.

Patients in Groups 4 and 5 received dual-plane treatment of complementary brows. A total of 30 lines and 423 J were delivered to fibromuscular and dermal layers of each side along either vertical-vertical, horizontal-horizontal, or crisscrossing lines. Groups 8 and 9 underwent dual-plane treatment (30 lines, 461.2 J) to opposing marionette lines in 1 of 3 directions: horizontal-horizontal, crisscrossing, or superolateral-superolateral. Six months after treatment, tissue lifting was measured with Canfield software.

### Pilot Study 2

There were 2 groups in Study 2 (Table 2). The 4 patients in Group 1 had their ipsilateral brows treated with a lower number of lines and joule energy of vertical-vertical lines (7 MHz, 3.0 mm, 15 lines, 155.2 J; 7 MHz, 4.5 mm, 15 lines, 267.8 J) and their contralateral brows treated with a higher number of treatment lines and joule energy of vertical-vertical lines (7 MHz, 3.0 mm, 30 lines, 310.5 J; 7 MHz, 4.5 mm, 30 lines, 535.5 J). Similarly, the 4 patients in Group 2 had their ipsilateral marionette lines treated by a lower number of treatment lines and joule energy of superolateral-horizontal lines (7 MHz, 3.0 mm, 15 lines, 155.2 J; 4 MHz, 4.5 mm, 15 lines, 306 J) and their contralateral marionette lines treated by a higher number of treatment lines and joule energy of superolateral-horizontal lines (7 MHz, 3.0 mm, 30 lines, 310.5 J; 4 MHz, 4.5 mm, 30 lines, 612 J). Six months later, the percentage of change in tissue lifting (vs baseline) was measured for each patient with Canfield software.

### Clinical Experience With Vectored Lines and Joule Energy Levels

Based on the results of Study 1, we treated 107 patients in our clinic between October 2009 and October 2010 with

ultrasonography applied to fewer treatment lines and at lower joule energies (Figure 1, left panel) to the brows, crow's feet, face, and neck. Inclusion criteria remained the same as those listed for the pilot studies. The treatment regimen was as follows: (1) 423 J to each lateral brow and crow's feet (7 MHz, 3.0 mm, 15 lines; 7 MHz, 4.5 mm, 15 lines); (2) 461.2 J to each malar bag (7 MHz, 3.0 mm, 15 lines; 4 MHz, 4.5 mm, 15 lines) and 1845 J to each half of the face (7 MHz, 3.0 mm, 60 lines; 4 MHz, 4.5 mm, 60 lines); and (3) 2306 J to the entire neck (7 MHz, 3.0 mm, 75 lines; 4 MHz, 4.5 mm, 75 lines). Above the superolateral brow, the fibromuscular layer and dermal treatment lines were administered in vertical directions, but these were administered horizontally within crow's feet sites. Within the malar bag site, all fibromuscular and dermal treatment lines were placed in a superomedial direction. In the face and neck, fibromuscular treatment lines were positioned in a horizontal direction, and dermal treatment lines were placed superolaterally. The superolateral layer was treated before the dermis to minimize heat retention in a given site, which could result in increased thermal injury to tissues. Patients were evaluated photographically in the follow-up period and completed questionnaire assessments at 6 months.

Based on the results of Study 2, 55 patients treated between November 2010 and August 2011 (Figure 1B) received ultrasonography to twice the number of treatment lines and, therefore, increased joule energy to each site (except the malar bag area, where treatment remained the same as before). The regimens were as follows: (1) 846 J to each lateral brow and crow's feet (7 MHz, 3.0 mm, 30 lines; 7 MHz, 4.5 mm, 30 lines); (2) 461.2 J to each malar bag (7 MHz, 3.0 mm, 15 lines; 4 MHz, 4.5 mm, 15 lines) and 3690 J to each half of the face (7 MHz, 3.0 mm, 120 lines; 4 MHz, 4.5 mm, 120 lines); and (3) 4612 J to the entire neck (7 MHz, 3.0 mm, 150 lines; 4 MHz, 4.5 mm, 150 lines).

## Photographic and Statistical Analysis

In Studies 1 and 2, a custom-designed Canfield VISIA Analysis and Photographic System (Canfield Scientific, Inc, Fairfield, NJ) was used for baseline and follow-up photography with standardized lighting (0°, 45°, and 90° views). The matched-orientation function of the Mirror software was used to compare baseline and posttreatment distance changes (mm) between reference points on a standardized facial positioning table. Each photographic image was automatically tagged with a specific label that could not be edited.

An average of 3 vertical displacements of each brow (midpupil, lateral canthus, and lateral tail of brow) from the intercanthal horizontal axis, or the average of 3 superolateral displacements of each marionette line along a fixed reference line (extending from inferior tragal notch to midpoint of marionette line), was used to compare measurements for each subject and between each group. A disadvantage of using the brow or marionette fold as a reference point for measurements is the inherent vagary of mobile groomed structures. However, data were subjected

to 1-way analysis of variance to test for significance between and within groups and for homogeneity of variances. Data were analyzed using Scheffé's post hoc test for multiple comparisons of mean differences, standard errors, and 95% significance at the probability level of .05.

The validated Fitzpatrick Wrinkle, Fold, and Tissue Laxity Scale (FWFTLS)<sup>12</sup> was used to classify and score patients from baseline photographs and was performed by 2 independent investigators who were blinded to protocols and patients. Categorization was as follows: Class I, mild, score of 1 to 3; Class II, moderate, score of 4 to 6; Class III, severe, score of 7 to 9. Aesthetic treatment efficacy from baseline to 6 months was rated by the same 2 independent investigators using the Investigator Global Aesthetic Improvement Scale (IGAIS) from standardized photographs (0 = no change, 1 = mild improvement, 2 = moderate improvement, 3 = significant improvement). Patients used a Subject Global Aesthetic Improvement Scale (SGAIS) (0 = no change, 1 = mild change, 2 = moderate change, 3 = significant change) to assess their results at the 6-month mark. During treatment, patients assessed their level of heat-pain perception on a 10-point scale (0 = no pain, 10 = extreme pain).

## RESULTS

The cumulative demographic data for 27 patients in Pilot Study 1 included the following distributions: 27 female; average age 46.1 (range 25-67 years); 16 Caucasians and 11 Hispanics. The cumulative demographic data for 8 patients in Pilot Study 2 had the following distributions: 8 females; average age 49.6 (range 43-56); 5 Caucasians and 3 Hispanics.

### Pilot Study 1

**Groups 1, 2, 3, 6, and 7.** Six months after treatment, the brows and marionette lines that had received superolaterally-placed treatment lines showed significantly higher lifting (vs baseline values) than the opposite sides treated by horizontal lines, according to post hoc testing analyses, independent of tissue depth or joule energy. The respective results were as follows: Group 1,  $5.7 \pm 1.2\%$  vs  $1.0 \pm 0.3\%$ ; Group 2,  $6.6 \pm 0.5\%$  vs  $3.6 \pm 0.7\%$ ; Group 3,  $5.6 \pm 1.3\%$  vs  $2.4 \pm 0.8\%$ ; Group 6,  $3.8 \pm 0.7\%$  vs  $2.0 \pm 0.5\%$ ; Group 7,  $3.8 \pm 0.7\%$  vs  $1.8 \pm 0.2\%$  (all  $P = .05$ ).

**Groups 4 and 5.** Six months after treatment, post hoc testing analyses showed a significantly higher percentage of tissue lifting (vs baseline) for areas that had received dual-depth treatments in vertical-vertical directions compared with horizontal-horizontal directions (Group 4,  $7.2 \pm 1.4\%$  vs  $3.7 \pm 0.7\%$ , respectively;  $P = .05$ ). Dual-plane treatment of opposing brows with crisscrossing lines resulted in significantly higher lifting for areas in which treatment lines had been applied horizontally to the fibromuscular layers and vertically to the dermis, compared with horizontal application to the dermis and vertical application to fibromuscular layers (Group 5,  $6.0 \pm 1.4\%$  vs  $3.1 \pm 0.9\%$ , respectively;  $P = .05$ ).

**Table 3. Clinical Study: Demographics of Lower and Higher Treatment Groups (Lines, Joule Energy)**

|  | First Group (Lower Lines/<br>Energy)  | Second Group (Higher<br>Lines/Energy) |
|--|---------------------------------------|---------------------------------------|
| No. of patients and gender   | 6 males (5.6%)<br>101 females (94.4%) | 2 males (3.6%)<br>53 females (96.4%)  |
| Age, y   | 53.5 (range, 25-77)                   | 64.4 (range, 26-74)                   |
| Treatment areas, n   |                                       |                                       |
| Forehead   | 55                                    | 37                                    |
| Midface  | 77                                    | 49                                    |
| Neck   | 43                                    | 58                                    |
| Ethnicity, n (%)   |                                       |                                       |
| White  | 65 (60.8)                             | 26 (47.3)                             |
| Hispanic   | 22 (20.5)                             | 15 (27.3)                             |
| Asian  | 15 (14.0)                             | 8 (14.5)                              |
| Other  | 5 (4.7)                               | 6 (10.9)                              |
| Fitzpatrick skin type classification, n (%)                        |                                       |                                       |
| I  | 3 (2.8)                               | 0 (0.0)                               |
| II   | 23 (21.5)                             | 15 (27.3)                             |
| III  | 50 (46.8)                             | 24 (43.7)                             |
| IV   | 29 (27.1)                             | 14 (25.4)                             |
| V  | 2 (1.9)                               | 2 (3.6)                               |
| Fitzpatrick Wrinkle, Fold, and Tissue Laxity Scale (FWFTLS), n (%) |                                       |                                       |
| Class I, mild (score 1-3)  | 46 (43.0)                             | 18 (32.7)                             |
| Class II, moderate (score 4-6)                                     | 55 (51.4)                             | 33 (60.0)                             |
| Class III, severe (score 7-9)                                      | 6 (5.6)                               | 4 (7.3)                               |

**Groups 8 and 9.** Post hoc analyses at 6 months showed significantly higher tissue lifting (vs baseline) for dual-plane treatment given in the superolateral–superolateral direction (Group 8,  $2.4 \pm 0.2\%$ ;  $P = .05$ ) compared with horizontal–horizontal application (Group 8,  $1.1 \pm 0.3\%$ ;  $P = .05$ ). Similarly, dual-plane treatment of opposing marionette lines with crisscrossing lines resulted in significantly higher lifting for tissues in which the lines had been delivered horizontally to the fibromuscular layers and superolaterally to the dermis compared with the reverse of these procedures (ie, superolaterally to the fibromuscular layer and horizontally to the dermis) (Group 9,  $2.7 \pm 0.2\%$  vs  $1.4 \pm 0.2\%$ ;  $P = .05$ ).

## Pilot Study 2

At the 6-month evaluation, post hoc analyses showed that all patients in Group 1 had achieved significantly greater brow lifting from the higher number of lines and joule energy levels, delivered in dual planes (60 lines, 846 J,  $4.3 \pm 0.2\%$ ;  $P = .05$ ), compared with the lower number of lines and energy used to treat the opposite side (30 lines, 423 J,  $1.9 \pm 0.3\%$ ;  $P = .05$ ), also delivered in dual planes (Figure 2). Similarly, at the 6-month mark, all patients in Group 2 had achieved significantly greater lifting of the marionette lines (vs baseline) when more lines had been treated and higher joule energy applied in dual planes (60 lines, 922 J,  $2.4 \pm 0.3\%$ ;  $P = .05$ ), compared with the fewer lines and lower energy used in dual-plane treatment of the opposite side (30 lines, 461 J,  $0.3 \pm 0.2\%$ ;  $P = .05$ ).

## Clinical Patients

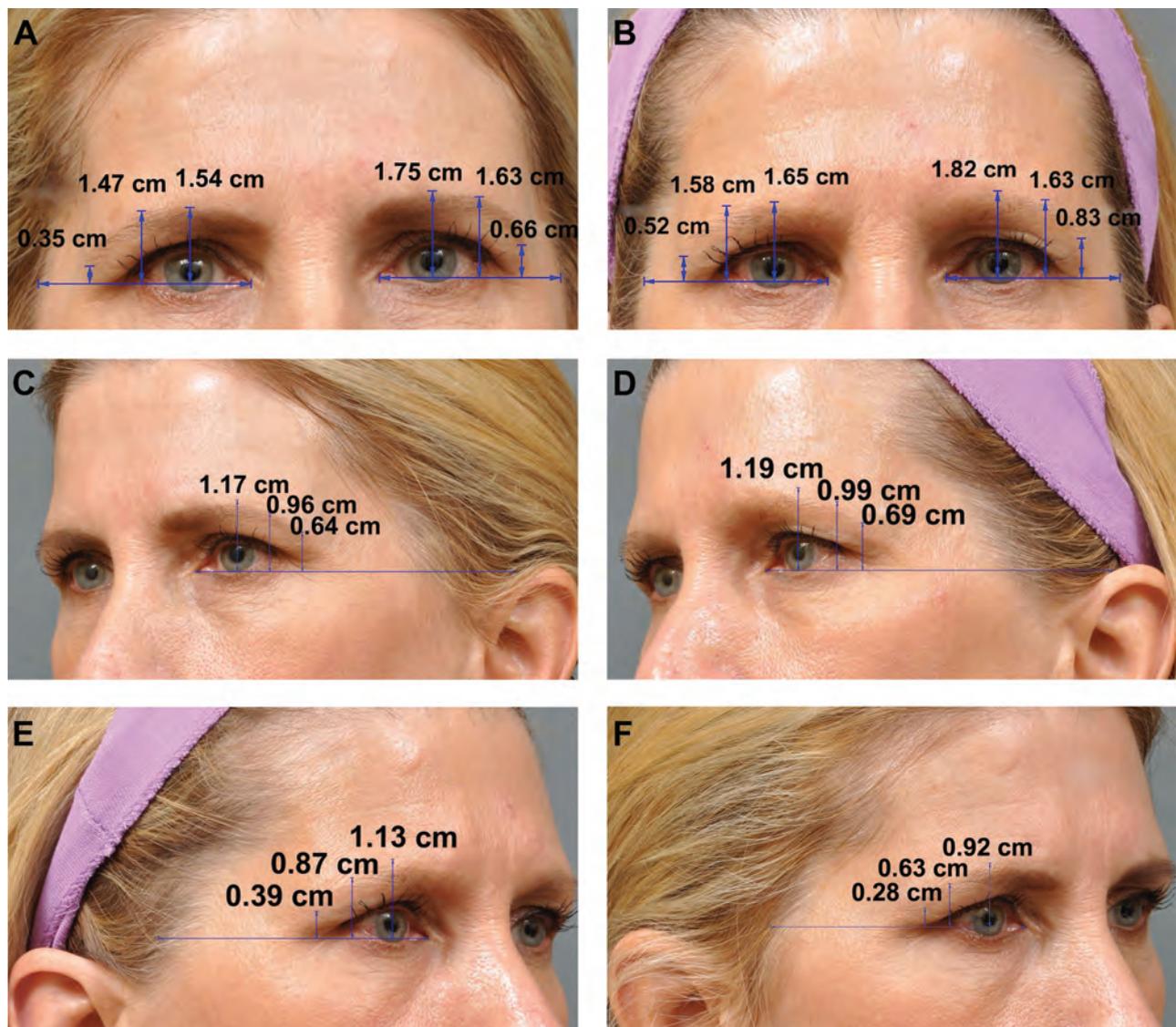
The cumulative demographic data of patients in the 2 clinical groups (fewer treatment lines, lower joule energy; more treatment lines, higher joule energy) are summarized in Table 3.

Two independent evaluators found that fewer than 2% of patients in these groups demonstrated mild improvements by IGAIIS grading as early as 6 weeks. At 3 months, 51.4% of patients in the first group (fewer lines, lower energy) were classified as responders (mild, 47.2%; moderate, 52.8%). By 6 months, the percentage of responders in this group had increased to 70.3% (mild, 31.1%; moderate, 68.9%).

In contrast, 71.2% of patients in the second group (more lines, higher energy) were judged to be responders at 3 months (mild, 34.0%; moderate, 47.6%; significant, 18.4%). By 6 months, the percentage of responsiveness in the higher-energy group had increased to 80.2% (mild, 10.4%; moderate, 63.4%; significant, 26.2%). The FWFTLS classification at baseline of patients who experienced mild, moderate, or significant responses at 6 months, in either group, was as follows: Class I, 55%; Class II, 30%. The FWFTLS categorizations of patients who demonstrated negligible responses at 6 months (29.7% of the first group; 19.8% of the second group) were Class I, 15.5%, 17.8%; Class II, 41.1%, 33.7%; Class III, 43.4%, 48.5% (first and second groups, respectively). Clinical results of treatment to the brow complexes appear in Figures 3 and 4; the malar bags appear in Figure 5; and the midface and neck regions are shown in Figures 6 and 7.

## Side Effects and Complications

No patient in Pilot Studies 1 or 2 or in the clinical study experienced any significant adverse event, such as long-standing sensory changes, permanent paresis/paralysis, blistering, ulceration, scarring, dyschromia, or fat atrophy during the 6-month follow-up period. However, 3 patients



**Figure 3.** (A, C, E) This 51-year-old woman presented with orbital hooding and asymmetrical ptosis of the lateral brow. (B, D, F) Six months after the forehead tissue above her lateral brows received dual-level treatment with 7 MHz, 4.5 mm (30 vertical lines; 535.6 J) and 7 MHz, 3.0 mm (30 vertical lines; 310.5 J), her lateral brows show moderate elevation, with exposure of the double lid lines from reduction of the orbital hooded regions.

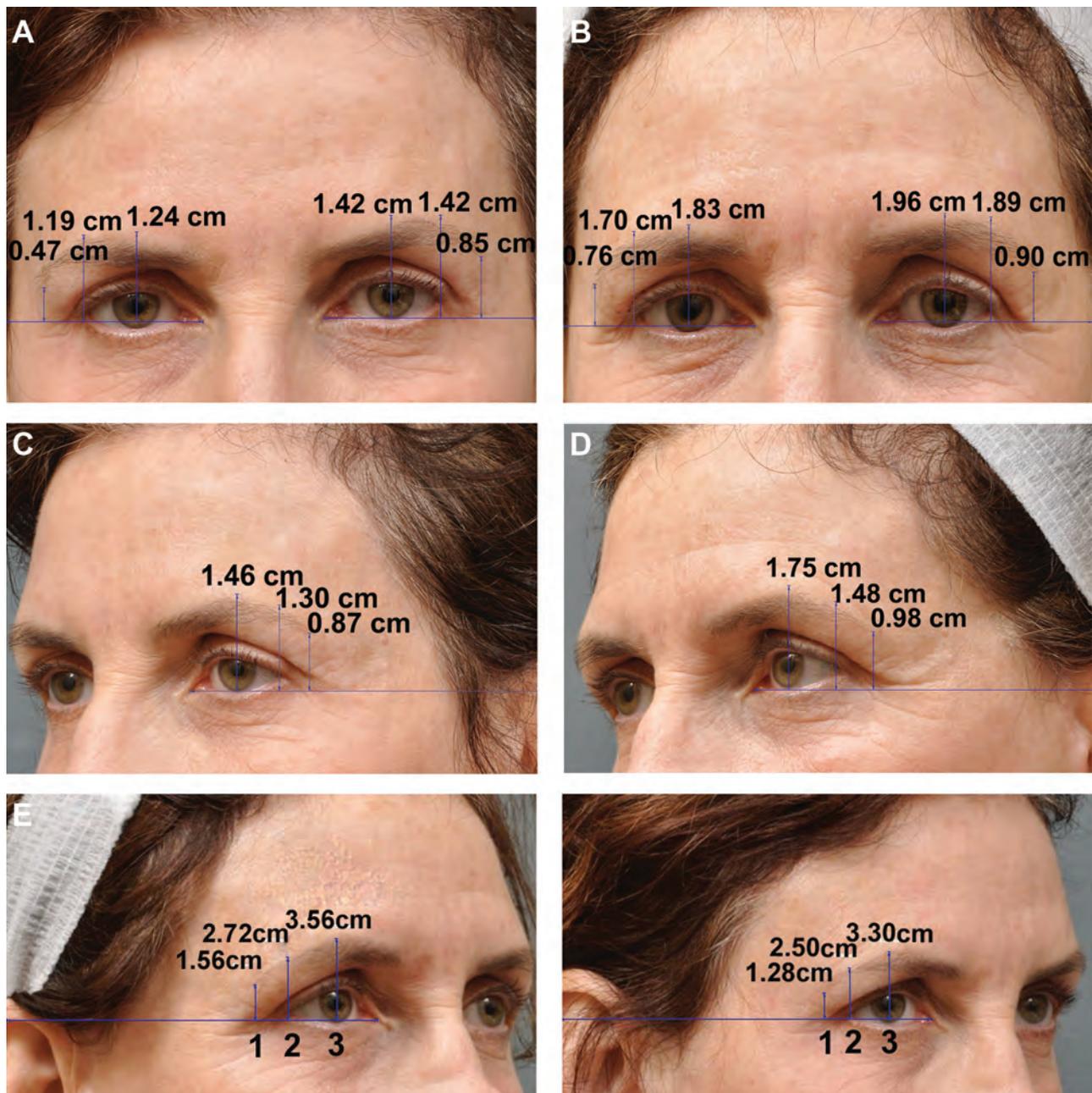
had transient dysesthesia (numbness or hypersensitivity) to the deep branch of the supraorbital nerve, which lasted for 3 to 7 days. All patients experienced transient erythema for 1 to 2 hours and mild swelling for several days. Mild bruising generally resolved within 1 to 2 weeks. The uncommon occurrence of striated linear skin patterns spontaneously resolved within a few weeks.

Momentary discomfort (stinging, pain, heat) occurred during the procedure but dissipated immediately after the energy was deposited. According to patient ratings, the highest level of pain during the procedure was in the brow and periorbital areas (rated 5.7 out of 10). Pain to the face (3.7 out of 10) and neck (3.6 out of 10) was considered

acceptable. Very few patients experienced pain or hypersensitivity during the first week.

## DISCUSSION

Although patient selection remains fundamental to the success of any face- or neck-lifting procedure, candidates present with a range of variation in skin and soft-tissue characteristics that include, but are not limited to, gradations of skin aging, tissue laxity, and distributions of subcutaneous fat. Because less-impressive results are anticipated for nonsurgical lifting procedures (vs surgical



**Figure 4.** (A, C, E) This 65-year-old woman presented with significant orbital hooding and ptosis of the mid to lateral brows. (B, D, F) Nine months after she received dual-level treatment with 7 MHz, 4.5 mm (30 vertical lines; 535.6 J) and 7 MHz, 3.0 mm (30 vertical lines; 310.5 J) across the lateral half of each brow, her lateral brows demonstrate significant elevation, with simultaneous reduction of the hooded area.

treatments), the presence of mixed anatomical findings becomes relevant in the interpretation of incremental outcomes in comparative studies of noninvasive techniques. Unlike surgical methods, noninvasive tissue lifting by heating mechanisms is believed to occur after application of sufficient thermal injury (65°C-70°C) to collagen fibers, which enables them to reorganize and contract later, usually by 3 months posttreatment, with results lasting up to 1 year.<sup>13</sup> Temperatures higher than 80°C result in coagulation

and fibrosis of collagen fibers. Therefore, the “ideal” candidates for nonsurgical thermal energy treatments should possess collagen fibers of optimal quantity and size as well as the most advantageous fiber orientation to allow maximal thermal absorption. In addition, the absence of tissue heaviness and fullness assists the lifting effects after thermally-induced collagen shortening. These attributes usually are characteristic of patients who have mild or moderate degrees of chronologic or photoactinic aging,



**Figure 5.** (A) This 64-year old woman had undergone 2 previous facelift procedures (1997, 2007) and had received noninvasive monopolar radiofrequency treatments to her brow complexes and midface in our office (2007). She inquired about nonsurgical treatment of her malar bags with focused-image ultrasonography. (B) Eighteen months after dual-level treatments with 4 MHz, 4.5 mm (30 superomedial lines; 612 J) and 7 MHz, 3.0 mm (30 superomedial lines; 310.5 J), which extended from the malar bag down to the middle portion of the anterior midface, the patient shows reduction of the malar bag and smoother contouring and lifting of the anterior midface tissues.

tissue ptosis, and facial heaviness.<sup>14</sup> Most studies of non-invasive procedures have demonstrated modest to moderate subjective<sup>15-20</sup> and objective<sup>21,22</sup> results. The authors of these reports have noted wide variation in consistency and predictability of results (40%-80% response) 1 year after standardized noninvasive treatments in studies that used quantifiable methods of documentation and criteria of clinically relevant outcomes.

The onset of collagen denaturation after 60°C to 70°C exposure, the commencement of tissue contraction by 3 months, and the duration of clinical lifting responses (~1 year) appear to be similar after treatment by radiofrequency, ultrasonography, or laser energy sources.<sup>11</sup> However, focused-image treatments represent a unique energy-based method that combines visualization of targeted structures beneath the skin surface and deliverance of either 17 or 23 TCPs in a single line or multiple lines to the fibromuscular and/or dermal levels of tissue.

Our pilot studies were designed to mitigate the effects of anatomical diversities by treating opposing brows or marionette lines in the same patient, with each site serving as its internal control over baseline values. In Pilot Study 1, vertical or superolateral vectoring at one brow or marionette line in the 3 patients in Groups 1, 2, 3, 6, and 7 resulted in statistically-significant percentages of change in tissue lifting in comparison to horizontal vectoring on the opposite side. Each corresponding site was treated at the same single-treatment depth, with an equal amount of joules and number of treatment lines. Comparisons of absolute percentage changes in tissue lifting (by matched Mirror imaging) between the groups demonstrated the difficulty of detecting significant clinical differences among small sets because of variations in patients and treatments.

A more meaningful approach was to compare the effects of different treatments to opposing sides in the same patient.

Since the norm in clinical practice is to treat routinely at dual levels, each subject's corresponding brows (lateral vs horizontal-horizontal) were treated at the fibromuscular and dermal layers, respectively. Dual-level treatments in vertical directions to brows (Group 4, vertical-vertical vs horizontal-horizontal) or marionette lines (Group 8, superolateral-superolateral) resulted in statistically-significant changes in tissue elevation compared with results after horizontal vectoring on the opposing side, with an equal number of treatment lines and joule energy. The objective results for patients from Groups 5 and 9, treated in criss-crossing dual-depth patterns to opposite sites with equal amounts of joules and treatment lines, emphasize the following: (1) the power of vertical- or superolateral-vectoring lines applied to skin over similarly directed lines to the fibromuscular layer and (2) the less-dominant influence of horizontally (vs vertically) directed vector lines to the skin and fibromuscular layers. These cumulative findings emphasize the importance of selecting the appropriate number and direction of treatment lines, as well as treatment depth, to optimize clinical outcomes.

The purpose of Pilot Study 2 was not only to validate the importance of the number of vertical or superolateral vectors at both the dermal and fibromuscular levels but also to assess, by objective measurements, the potential value of increasing the amount of joule energy in each layer to improve outcomes. The data confirmed a direct correlation between the amount of tissue lifting (brow and marionette lines) and the quantity of energy deposited into the fibromuscular and dermal layers. Although each



**Figure 6.** (A, C) This 47-year-old woman desired a noninvasive procedure to lift and tighten her anterior midface, jowls, and neck. (B, D) One year after treatment at dual levels to the anterior midface with 4 MHz, 4.5 mm (30 horizontal lines/2.5 cm × 2.5 cm square; 2448 J in 4 squares) and 7 MHz, 3.0 mm (30 superolateral lines/2.5 cm × 2.5 cm; 1242 J in the same 4 squares). The neck received 4 MHz, 4.5 mm (30 horizontal lines/2.5 cm × 2.5 cm square; 3060 J in 5 squares) and 7 MHz, 3.0 mm (30 superolateral lines/2.5 cm × 2.5 cm square; 1552.5 J in the same 5 squares). Moderate tightening is evident in the nasolabial folds, jowls, lateral neck, and submentum.

group of this pilot study comprised just a few patients, results suggest that the combination of vertical vectoring, a higher number of treatment lines, greater joule energy, and dual-plane delivery are significant considerations for planning individualized treatment.

The treatment parameters and outcomes of the 2 pilot studies were used as template guides to clinically treat 2 larger (but closely matched) groups of patients with different amounts of energy. This provided an opportunity to assess the safety and efficacy of treatment with lower versus higher numbers of lines and joule energies. After IGAIS assessments, observable positive responses in either group were difficult to discern within 6 weeks of treatment. After 3 months, approximately 51.4% of the first clinical group of patients and 71.0% of the second clinical group of patients (whose average age was 10 years older) were graded as showing a degree of response. It is noteworthy that 18.4%

of the responders in the second group demonstrated significant changes. By 6 months, the percentages of responders had increased to 70.3% in the first group and 80.2% in the second. Although no patient in the first group exhibited a significant change, 26.2% of responders in the second group were found to have significant lifting at 6 months. Interestingly, the majority of patients in both groups (85%) who had responded by month 6 had been assigned to FWFTLS Class I or Class II at baseline. According to the 6-month SGAIS assessments, patients considered their improvement to be slightly better than that documented by the investigators (IGAIS evaluation).

Although favorable baseline clinical findings and optimal treatment parameters were associated with successful outcomes in some of our patients, little is known about which clinical factors are reliable predictors of desirable outcomes. A recent study<sup>23</sup> suggests that there are few



**Figure 7.** (A, C) This 60-year-old woman requested a nonsurgical procedure to improve her anterior midface, pre-jowl, and neck areas. (B, D) One year after a single dual-level treatment to the anterior midface with 4 MHz, 4.5 mm (30 horizontal lines/2.5 cm × 2.5 cm square; 2448 J in 4 squares) and 7 MHz, 3.0 mm (30 superolateral lines/2.5 cm × 2.5 cm square; 1242 J in the same 4 squares). The neck was treated with 4 MHz, 4.5 mm (30 horizontal lines/2.5 cm × 2.5 cm square; 3060 J in 5 squares) and 7 MHz, 3.0 mm (30 superolateral lines/2.5 cm × 2.5 cm square; 1552.5 J in the same 5 squares). The patient demonstrates significant smoothing of her nasolabial folds and jowls, along with sharper demarcation of the mandible margin and submentum.

baseline clinical indicators of success. In our study, responses were negligible in many patients who appeared to have favorable clinical prognosticators. Thus, patient selection is a challenging task. Realistic expectations remain the cornerstone for patient success and acceptance of this technique. Further studies are underway to optimize treatment maps for multiple tissue layers at labeled sites, and to treat unusual findings in off-label areas.

## CONCLUSIONS

This research demonstrates the effectiveness of optimizing a single standardized treatment algorithm to lift tissues at 2 levels of the forehead, face, and neck by increasing the number of vectored lines and ultrasonic TCP of energy. In the pilot studies, vertical treatment lines and higher energy deposition increased the percentage of tissue lifting. In the larger clinical study, greater responses were

achieved in the patients who had more lines treated and received higher joule energy (vs fewer lines and lower joule energy). Only minor side effects occurred. Further studies will be needed to optimize patient selection and to advance this technology for more effective outcomes in labeled and off-label sites.

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