

**SUMMARY OF SAFETY AND
EFFECTIVENESS DATA (SSED)**

SUMMARY OF SAFETY AND EFFECTIVENESS

I. General Information

Device Generic Name:	Orthopedic Extracorporeal Shock Wave Therapy Device
Device Trade Name:	Orbasone Pain Relief System
Applicant's Name and Address:	Orthometrix, Inc. 106 Corporate Park Drive, Suite 106 White Plains, NY 10604
PMA Number:	P040039
Date of Panel Recommendation:	None
Date of Notice of Approval to Applicant:	August 10, 2005

II. Indications for Use

The Orbasone Pain Relief System is intended for extracorporeal shock wave therapy for the treatment of chronic proximal plantar fasciitis in patients 18 years of age or older that has failed to respond to conservative therapy. Chronic proximal plantar fasciitis is defined as heel pain in the area of the insertion of the plantar fascia on the medial calcaneal tuberosity that has persisted for six months or more.

III. Contraindications

Use of the Orbasone Pain Relief System is contraindicated in the following situations:

1. Over or near bone growth centers until bone growth is complete.
2. When a malignancy is known to be present in or near the treatment area.
3. Not for use in open wounds, skin rashes, swollen, inflamed, or infected areas.
4. Not for use over ischemic tissues in individuals with vascular disease where the blood supply would be unable to follow the increase in metabolic demand and tissue necrosis may result.
5. Patient has coagulation disorder or is taking anticoagulant medications, either for acute or chronic anticoagulant therapy.
6. Patient has infection at the area to be treated. This is due to the risk of spreading infection.
7. This product contains rubber latex which may cause allergic reactions.

IV. Warnings and Precautions

The warnings and precautions can be found in the device labeling.

V. Device Description

Principle of Operation:

The Orbasone Pain Relief System is a device that generates sonic wave vibrations and includes (1) energy plugs (i.e., spark gap electrode); (2) an ellipsoidal stainless steel focusing reflector; and (3) a water cushion with coupling membrane. The Orbasone uses a water-filled ellipse to reflect and transmit a sonic wave to the patient. One half of the ellipse is machined from stainless steel, while a latex membrane forms the other half. It is the latex membrane that contacts the patient.

The sonic wave is created by a hot bubble of gas formed at the center of the metal portion of the ellipsoidal reflector, using spark gap technology. The energy plugs are located at the end of the ellipsoid reflector and produce short sparks between the two points. The sparks generate the hot bubble of gas, which expands rapidly, causing a sonic wave to be delivered at a point no greater than 45 mm under the skin.

Choosing any of twelve (12) power settings may vary the amplitude of the sonic wave vibration, by dialing the knob found on the controller. During treatment, the sonic waves are delivered at a maximum rate of 110 per minute.

Additionally, the total number of sonic waves used is preset and can be as little as 100 to as many as 3000. The controller has a counter, which is set to the desired number of sonic waves before treatment begins.

VI. Alternative Practices and Procedures

Current treatment options for plantar fasciitis, a common cause of heel pain, include:

- Rest
- Heat
- Physical conditioning exercises
- Heel cushions
- Stretching
- Over-the-counter pain relievers or prescription pain relievers
- Nonsteroidal anti-inflammatory drugs (“NSAIDs”)
- Corticosteroid injections
- Taping
- Orthotics
- Night splinting
- Casting
- Surgery (i.e., endoscopic plantar fasciotomy or open plantar fascia release)

VII. Potential Adverse Effects of the Device on Health

There were 42 adverse events (AEs) reported during the clinical study in 179 patients at 3 sites. The AEs included bruising, mild edema, pain, swelling, tingling and sprained ankle. There were more AEs in the treatment group versus the sham-control group. None of the AEs was severe, and none required medical intervention or subsequent medical care. A summary of AEs that were observed during treatment with the Orbasone Pain Relief System are shown in Table 1 below:

Table 1 Adverse Events Summary

	Orbasone Group (N=96) n (%)	Sham-Control Group (N=83) n (%)
All Adverse Events	31 (32.3%) [‡]	11 (13.3%) [‡]
Bruising	13 (13.5%)	3 (3.6%)
Mild edema	9 (9.4%)	2 (2.4%)
Pain	9 (9.4%)	5 (6.0%)
Swelling	2 (2.1%)	0 (0%)
Tingling	1 (1.0%)	0 (0%)
Sprained ankle	0 (0%)	2 (2.4%)

[‡] Some patients may have more than one adverse event.

Other potential adverse events not seen during the study, but observed with other similar devices, include:

- Decreased sensation in the treated foot;
- Petechia;
- Tendon rupture;
- Rare allergic or sensitivity reaction to the latex membrane;
- Hematoma;
- Neural injury or irritation resulting from the local anesthetic injection or shock wave treatment; and
- Anesthesia complication, including allergic reactions to local anesthetic agents.

VIII. Marketing History

The Orbasone Pain Relief System is CE-marked and is authorized for sale in Europe and Canada. The Orbasone Pain Relief System has not been withdrawn or recalled for safety or effectiveness.

IX. Summary of Nonclinical Studies

Bench Testing (Hydrophone)

Acoustic output measurements were made in accordance with the parameters defined in the FDA *Draft of Suggested Information for Reporting Extracorporeal Shock Wave Lithotripsy Device Shock Wave Measurements* (1991). Acoustic output measurements were recorded using a PVDF, spot-poled, membrane-type hydrophone. The hydrophone was integrally connected to a preamplifier system equipped with a self-monitoring arrangement to assist in determining the status of the sensor during testing.

The reflector of the Orbasone Pain Relief System was positioned so the ellipsoidal axis was vertical (parallel to the Z-axis of the scanning gantry). A jig was constructed with a steel pointer centered with the rim of the ellipsoidal reflector and vertically raised to the point known as F2. The hydrophone was then fixed to the scanning gantry at a position normal to the Z-axis and installed into the secondary tank. The bottom of this tank was made of the same latex rubber membrane material that is employed during patient treatments. This was deemed appropriate in order to account for the effects (if any) this interface component might have on the device output.

The beam energy of the Orbasone Pain Relief System is listed for the energy output settings of 10 KV (minimum), 16 KV (mid-range) and 22 KV (maximum).

Setting	Energy (mJ)
10 KV	0.26
16 KV	0.35
22 KV	0.42

Electrical Safety

The Orbasone Pain Relief System complies with the following electrical safety standards:

- JIS T 1001 and JIS T 1002
- EN 60601.1

Electromagnetic Interference

The Orbasone Pain Relief System has been tested for EMC in accordance with EN50501.1.

Software Verification and Validating and Risk Analysis

Software verification validation testing results and risk analysis demonstrate that the Orbasone Pain Relief System possesses software safety control features, as well as hardware safety redundancies, that work together to minimize patient and user risk.

Biocompatibility

The membrane that contacts a patient's skin is latex, and, accordingly, required labeling is included in the Orbasone Pain Relief System Operator Manual. The latex is supplied

by Fuji Latex of Tokyo, Japan, which supplies this same latex to manufacturers of gloves and condoms distributed in the U.S.

Animal Testing of Finished Device

A study was conducted in beagle dogs to determine the effects of repeated administration of ultrasonic waves produced by the Orbasone Pain Relief System. The left knee joints of four male beagle dogs were exposed once to 1,000 pulses at 22 kV. A single animal was sacrificed at the following times: immediately after treatment; one day after treatment; three days after treatment; and seven days after treatment. Animals were observed for clinical signs of morbidity and mortality prior to treatment, 6 hours after treatment, and daily until sacrifice, at which time the left and right knee joints were removed for gross and microscopic evaluation. No animals died during the course of the study, and no abnormal clinical signs were observed. No gross or microscopic changes were noted in the knee joints of the exposed animals.

X. Summary of Clinical Study

A clinical study was conducted to provide data on the safety and effectiveness of the Orbasone Pain Relief System in treating heel pain associated with chronic proximal plantar fasciitis in the U.S.

A. Study Design and Objectives

This study was a multicenter, randomized, sham-controlled, prospective, double-blind trial consisting of consecutively enrolled patients with foot pain who were randomized to either a group receiving treatment with the Orbasone Pain Relief System or a control group receiving sham treatment. For the sham-control patients, no water was pumped into the reflector head. Although the Orbasone appeared to operate normally, the absence of a transmitting media prevented the shockwave energy from reaching the patient's foot. Subjects were followed for 12 weeks after a single treatment. There were 3 U.S. study sites.

The objectives of this study were to: (1) collect safety and effectiveness data to support a PMA for the Orbasone Pain Relief System; and (2) provide confirming data supporting the safe and effective use of the Orbasone Pain Relief System for the desired indication.

B. Effectiveness and Safety Endpoints

Primary Endpoint: Subject assessment of pain using a 10 cm Visual Analog Scale ("VAS"), Pain on walking the first few minutes after awakening (within 24 hours of follow-up visit) change from baseline at 3 months (12 weeks) post-treatment.

Secondary Endpoint: Percentage of patients who achieved a 40% reduction from baseline VAS at 3 months post-treatment.

Safety Endpoints: Adverse events and subject complaints; assessment of peripheral neuropathy using Semmes-Weinstein monofilament test, toe clawing; assessment of vascular function using ankle brachial index.

C. Inclusion and Exclusion Criteria

Inclusion Criteria:

- Male or female greater than 21 years of age.
- Chronic proximal plantar fasciitis that persisted for at least six months prior to study enrollment as assessed by patient history. The patient had been under the care of a physician for this duration and had been in compliance with a prescribed stretching program.
- Failure to respond to at least four forms of conventional treatment, to include NSAIDs and three other conservative therapies (e.g., physical therapy; use of orthotics; ultrasound; analgesics; corticosteroid injections; shoe modifications; strapping of the foot; and night splints).
- Subject pain self-assessment of ≥ 6 cm on a 10 cm VAS scale.
- Single site of tenderness with local pressure over the medial calcaneal tuberosity on passive dorsiflexion of the foot.

Exclusion Criteria:

- Previous attempt with any other conservative therapies within two weeks of treatment; corticosteroid injection within one month of treatment.
- Previous surgery for plantar fasciitis.
- Bilateral foot pain.
- Subjects diagnosed with peripheral vascular disease and those with non-palpable pulses of the dorsal pedis or posterior tibial artery underwent testing with a standard Ankle Brachial Index Test ("ABI"). Subjects with ABIs of less than 1.0 were excluded from the study.
- Radiographic evidence of another cause for heel pain (e.g., rheumatoid arthritis; bone cyst or tumor; infection).
- History or documented evidence of:
 - autoimmune disease;
 - metabolic disorders;
 - Type I or Type II diabetes mellitus;
 - peripheral neuropathy such as nerve entrapment, tarsal tunnel syndrome;
 - systemic inflammatory disease such as rheumatoid arthritis, ankylosing spondylitis, Reiter's syndrome, etc.;
 - bleeding disorders or hemophilia;
 - known latex allergy;
 - known sensitivity or allergy to xylocaine; or
 - calcaneal stress fracture.
- Anticoagulant therapy (including aspirin prophylaxis) within 7 days prior to treatment.
- Patients with implanted defibrillators.
- Patients with prosthetic devices implanted in the area to be treated.

- Treatment area with open wound, skin rash, swelling, or inflammation.
- Active or unresolved infection in the involved foot.
- Pregnancy.
- Patients with pacemakers.

D. Study Procedures

Following screening, eligible subjects received a single treatment with either the Orbasone Pain Relief System or the sham control. Treatment parameters were: 2000 pulses at 20 to 21 KV at a frequency of 110 pulses/minute. Duration of treatment were 30 to 60 minutes. The total energy density was <math><1,000 \text{ mJ/mm}^2</math>. All patients received an injection of up to 10 mL (depending on patient size) of 0.5% bupivacaine into the area of the medial calcaneal branch of the tibial nerve. A summary of the study procedures is provided below in Table 2.

Table 2 Study Procedures

Parameter/Information	Screening/ Pre-treatment	Week 4	Week 8	Week 12
Medical history	√			
Physical exam*	√			
Radiographic evaluation**	√			√
Informed consent	√			
Inclusion/exclusion criteria	√			
Subject self-assessment of pain	√	√	√	√
Medication log	√	√	√	√
Adverse events/complaints		√	√	√

*Vascular, motor, and sensory function in the treated foot were evaluated at the follow-up visits.

**Pre-treatment radiographs (standard views) were mandatory for every patient screened to rule out any other potential non-plantar fasciitis cause of heel pain. Post-treatment radiographic evaluations were conducted on an as needed basis.

A health care professional who did not administer the treatment performed the follow-up evaluations and remained masked as to the treatment assignment throughout the follow-up period.

Subjects were permitted to continue their pretreatment program, including stretching, orthotics, and night splints. Use of acetaminophen was permitted as needed for pain. Patients were instructed to discontinue analgesic medication at least 4 half-lives prior to each post-treatment assessment (i.e., 16 hours for acetaminophen).

E. Study Population

262 patients were screened for this study, and 215 were enrolled. Of these 215 patients, 36 did not return for treatment; therefore, 179 patients were randomized and treated. A total of six patients who were randomized and treated had the following protocol violations, but were included in the intent-to-treat analysis: two patients had a baseline VAS score of <6 cm, and therefore, did not meet the inclusion criterion of a baseline VAS pain score of ≥ 6 cm, and four patients reported a duration of pain of less than six months prior to enrollment, and therefore, did not meet the inclusion criterion of chronic proximal plantar fasciitis that has persisted for at least six months prior to study enrollment. Of these 179 patients 96 patients were assigned to the active treatment group and 83 were assigned to the sham control group. A summary of patient accountability is provided in Table 3.

Table 3 Patient Accountability

	Orbasone n (%)	Sham-control n (%)	Total N (%)
Screened			262
Enrolled			215 ^a
Randomized and Treated	96	83	179
Completed	96 (100%)	82 (98.8%)	178 (99.4%)
Terminated Prematurely	0 (0%)	1 (1.2%)	1 (0.6%)
Lost to Follow-up	0 (0%)	1 (1.2%)	1 (0.6%)
Included in primary analysis of effectiveness	96 (100%)	82 (98.8%)	178 (99.4%)
Completed 4 Week Visit	95 ^b (99%)	83 (100%)	178 (99.4%)
Completed 8 Week Visit	93 ^b (96.9%)	80 ^b (96.4%)	173 (96.6%)
Completed 12 Week Visit	96 (100%)	82 ^b (98.8%)	178 (99.4%)

^a 36 subjects did not return for treatment.

^b Some subjects did not return for scheduled follow-up visits.

F. Patient Demographics

Patient demographics and treatment history are summarized in Table 4. Duration of pain was marginally significant on baseline demographics. There were no other significant differences between the treatment and control patients.

Table 4 Patient Demographics

Demographic Variables	Treatment Patients	Control Patients	p-value ^a
Age (years)			Treatment: 0.2654 Site: 0.0041
Mean	49.8	48.5	
SE	1	1.3	
Median	51	48.1	
Range	26.1-75	24.9-80.8	
Gender			Treatment: 0.5431 Site: 0.0913
Female	62	49	
Male	34	34	
Height (inches)			Treatment: 0.2438 Site: 0.9811
Mean	66.6	67.4	
SE	0.5	0.4	
Median	66.5	67	
Range	51-77	60-78	
Weight (pounds)			Treatment: 0.7089 Site: 0.4623
Mean	182.6	183.1	
SE	4.3	4.4	
Median	176.5	185	
Range	105-305	100-290	
Affected Foot			Treatment: 0.6292 Site: 0.2121
Right	42	40	
Left	51	40	
Duration of Pain (months)			Treatment: 0.0560 Site: 0.3854
Mean	25.3	34.9	
SE	3.3	4.2	
Median	14.8	19.8	
Range	3.2-260.5	6.2-176.3	
Baseline Pain Score (cm)			Treatment: 0.5774 Site: 0.0882
Mean	7.69	7.76	
SE	0.11	0.12	
Median	7.55	7.70	
Range	5.2-10.1 ^b	5.8-10	

^aKruskal-Willis test. "Treatment" = difference between Active Treatment and Sham Control; "Site" = Difference across sites.

^b Patient #45 has a baseline pain score of 10.1, which exceeded the maximum allowable score of 10. This patient is included in all analysis for completeness with the value of 10.1 changed to 10 for analysis.

G. Effectiveness Results

a) Primary Endpoint

The primary endpoint for this study was self-reported VAS scores at 4, 8, and 12 weeks after treatment. A baseline VAS score was obtained at week 0 before treatment. These scores are summarized below in Table 5.

Table 5
VAS Scores for Active and Sham Patients Through 12 Weeks Post Treatment

		Baseline	Week 4	Week 8	Week 12
Active Treatment (cm)	N	96	95	93	96
	Mean	7.69	4.95	3.98	3.11
	SE	0.11	0.26	0.27	0.30
	Median	7.55	5.0	3.70	2.4
	Range	5.2-10.1	0.2-9.9	0.07-10	0-9.8
Sham Control (cm)	N	83	83	80	82
	Mean	7.76	5.94	5.49	5.51
	SE	0.12	0.30	0.32	0.35
	Median	7.70	6.4	6.15	6.5
	Range	5.8-10	0-10	0-10	0-10

The primary analysis of these data is a growth-curve/mixed-effects model. The terms in the model are site, age, baseline VAS, week, pain duration, treatment group, treatment group by week interaction and baseline VAS by treatment group interaction. When duration of pain was added to the statistical model, it did not alter the result.

Treatment group effects:

Treatment group, week, and treatment group by week are all significant ($p = 0.0022$, $p < 0.001$, and 0.0002 , respectively), which indicates that the treatment group effect changes over the course of the study and should not be viewed as constant over weeks. Control individuals initially reported some decrease in VAS that leveled out, whereas the treatment group started out with a larger decrease in VAS, which continued to decrease faster than the control group throughout the 12 weeks.

b) Secondary Endpoint

The secondary endpoint for these data is a yes/no response: Did the subject's VAS score decrease from week 0 to week 12 by 40%? This endpoint was analyzed using a generalized linear model. The effect of treatment group is significant ($p < 0.001$). Table 6 below shows the results by site and treatment group. The treated group has a higher percent of subjects passing this criterion at all sites. There is also a significant

site effect ($p = 0.001$) indicating that the differences in these percentages from control to treatment group is variable across sites.

Table 6
Number of Patients Who Achieved a 40% Reduction from Baseline VAS
12 Weeks Post Treatment

	Week 12			
	Site 1	Site 2	Site 3	All Sites
Active Treatment				
No (N)	13	9	6	28
Yes (N)	21	9	38	68
Percent Yes	61.8%	50%	86.4%	70.8%
Sham Control				
No (N)	14	13	25	52
Yes (N)	15	1	14	30
Percent Yes	51.7%	7.1%	35.9%	36.6%

Subjects also were asked what treatment they thought they received after the final (Week 12) visit. In the Active Treatment group, 68/96 (71%) correctly guessed that they received an active treatment, 27/96 (28%) incorrectly guessed that they received the sham treatment, and 1 (1%) was not sure. In the Sham Control group, 43/83 (52%) correctly guessed that they received a sham treatment, 35/83 (42%) incorrectly guessed that they received an active treatment, and (5/83) 6% were not sure. These results indicate that subjects who responded could correctly guess what treatment they received ($p=0.0003$). Review of the comments made by the subjects to support their guesses indicates that their guess was primarily based on the extent of pain relief.

Gender Analysis/Bias

The statistical analysis showed no significant correlation between age, gender, weight, duration of pain, and treatment effectiveness.

H. Safety Results

The adverse events are presented in Section VII above.

XI. Conclusions Drawn From Studies

The preclinical and clinical data provide reasonable assurance that the Orthometrix Orbasone Pain Relief System is safe and effective for patients with symptoms of chronic proximal planter fasciitis of at least 6 months duration who had failed conservative therapy when used in accordance with device labeling.

XII. Panel Recommendation

In accordance with the provisions of section 515(c)(2) of the act as amended by the Safe Medical Devices Act of 1990, this PMA application was not referred to the

General Surgical Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XIII. CDRH Decision

FDA issued an approval order August 10, 2005.

The applicant's manufacturing facility was inspected and found to be in compliance with the Quality System Regulation (21CFR 820).

XIV. Approval Specifications

Directions for Use: See the Device Labeling.

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions and Adverse Events in the labeling.

Post Approval Requirements and Restrictions: See Approval Order.