

Radiology Advisory Panel Meeting

U-Systems

somo-v Automated Breast Ultrasound System (ABUS)

FDA Review

**Division of Radiological Devices
Office of *In Vitro* Diagnostic Device Evaluation and Safety
Center for Devices and Radiological Health
Food and Drug Administration**

Radiology Advisory Panel Meeting

U-Systems

somo-v Automated Breast Ultrasound System (ABUS)

Introduction and Background

Shahram Vaezy, PhD

Division of Radiological Devices

Office of *In Vitro* Diagnostic Device Evaluation and Safety

Premarket Approval (PMA) Objective

- U-Systems, Inc., a California-based company, has submitted a PMA application to propose expansion of the Indication for Use (IFU) of its device, somo-v Automated Breast Ultrasound System (ABUS).
- ABUS is an automated ultrasound scanning device currently cleared under a 510(k) premarket notification.
- It has not changed significantly for this PMA submission.
- Pre-clinical studies were conducted in the context of the 510(k) submission.



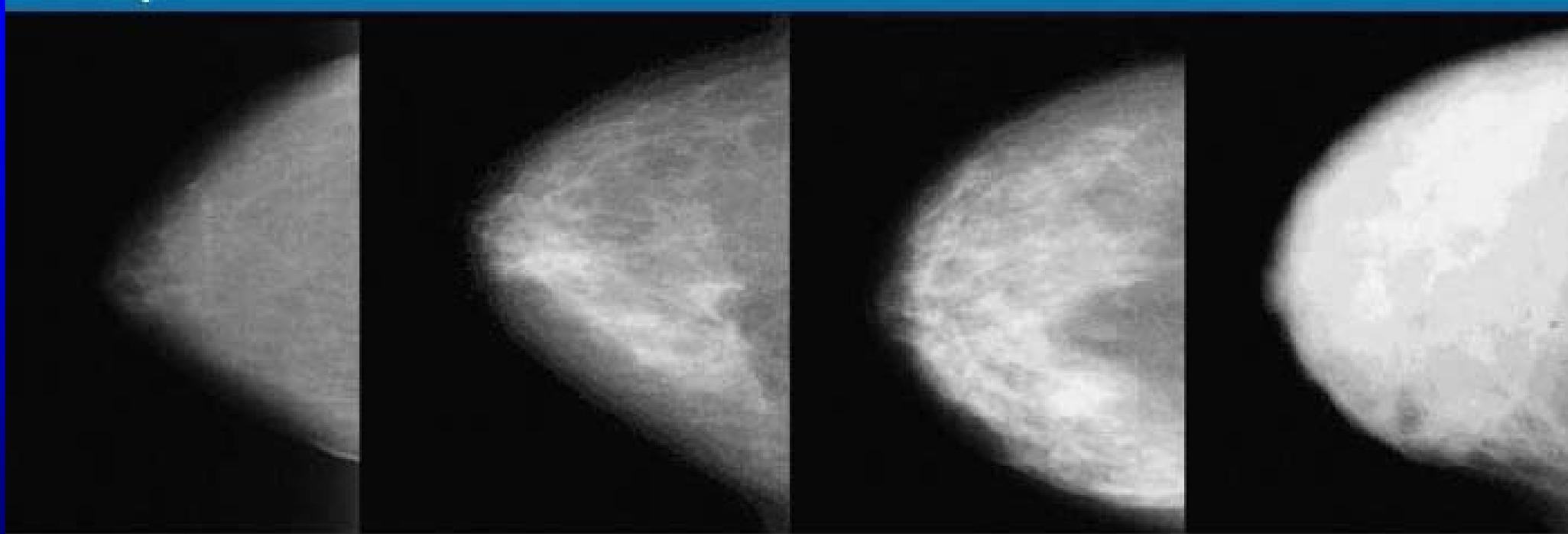
Proposed Indications for Use

- **U-Systems is planning to expand the Indications for Use (IFU).**
 - **Current IFU: The device is indicated for use as an adjunct to mammography for B-mode ultrasonic imaging of a patient's breast when used with an automatic scanning linear array transducer or a handheld transducer. The device is not intended to be used as a replacement for screening mammography.**
 - **Proposed IFU: The somo-v Automated Breast Ultrasound System (ABUS) is indicated as an adjunct to mammography for breast cancer screening in asymptomatic women for whom screening mammography findings are normal or benign (BI-RADS[®] Assessment Category 1 or 2), and breast parenchymal tissue is dense (BI-RADS[®] Composition/Density 3 or 4), and have not had previous clinical breast intervention. The device is intended to increase breast cancer detection in the described patient population.**

Breast Density/Composition

- Breast density, a mammographic finding that is not related to the perceived density of breast tissue on palpation, is a measurement of the ratio between radiodense epithelium and stroma to radiolucent fatty tissue.
- American College of Radiology categorization of breast density, using Breast Imaging-Reporting and Data System (BI-RADS®) for density/composition:
 - BI-RADS 1: The breast is almost entirely fat (<25% glandular).
 - BI-RADS 2: There are scattered fibroglandular densities (approximately 25-50% glandular).
 - BI-RADS 3: The breast tissue is heterogeneously dense, which could obscure detection of small masses (approximately 51-75% glandular).
 - BI-RADS 4: The breast tissue is extremely dense. This may lower the sensitivity of mammography (>75% glandular).
- A significant number of women (up to 75%, depending on age, ethnicity, and certain medical conditions) have dense breasts.

Breast Density/Composition BI-RADS[®] Categories



BI-RADS 1
fatty breast
< 25% dense

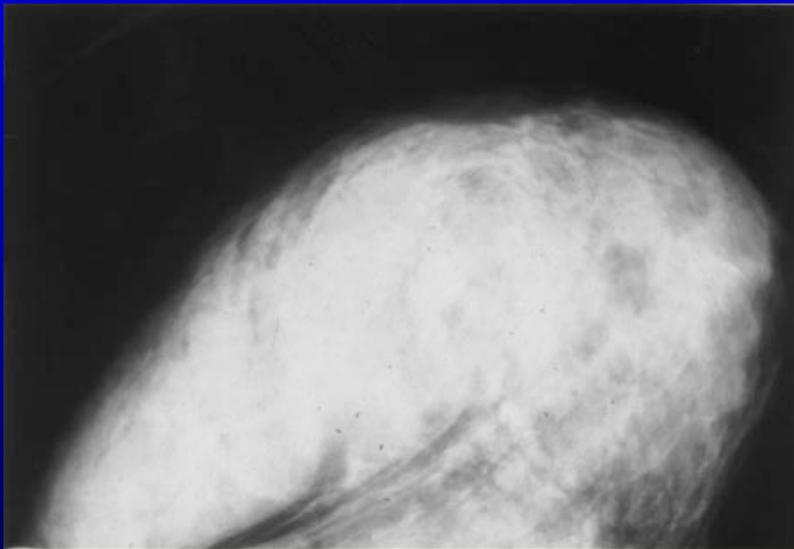
BI-RADS 2
scattered densities
25%-50% dense

BI-RADS 3
heterogeneously dense
51%-75% dense

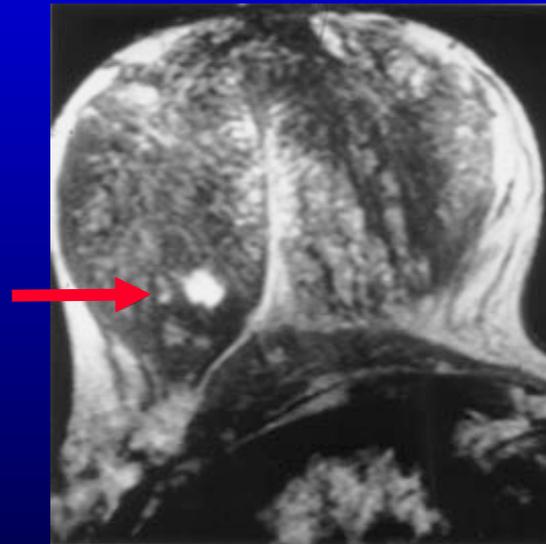
BI-RADS 4
extremely dense
> 75% dense

Clinical Need

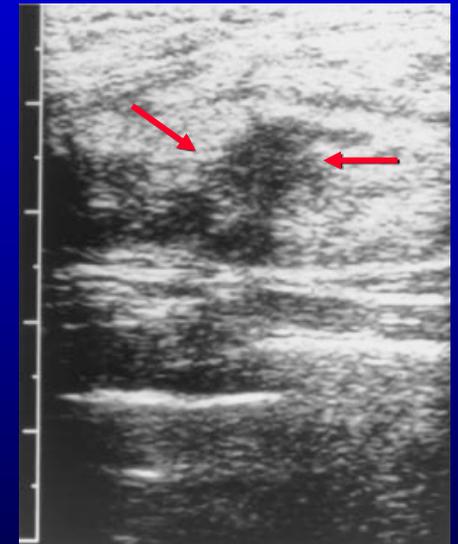
- Dense breast tissue, appearing bright in mammograms, can mask structural abnormalities such as tumors.
- There is an increased rate of breast cancer (up to 8 times higher according to some studies) in dense-breasted women in all age groups.



Mammography
Craniocaudal Oblique View



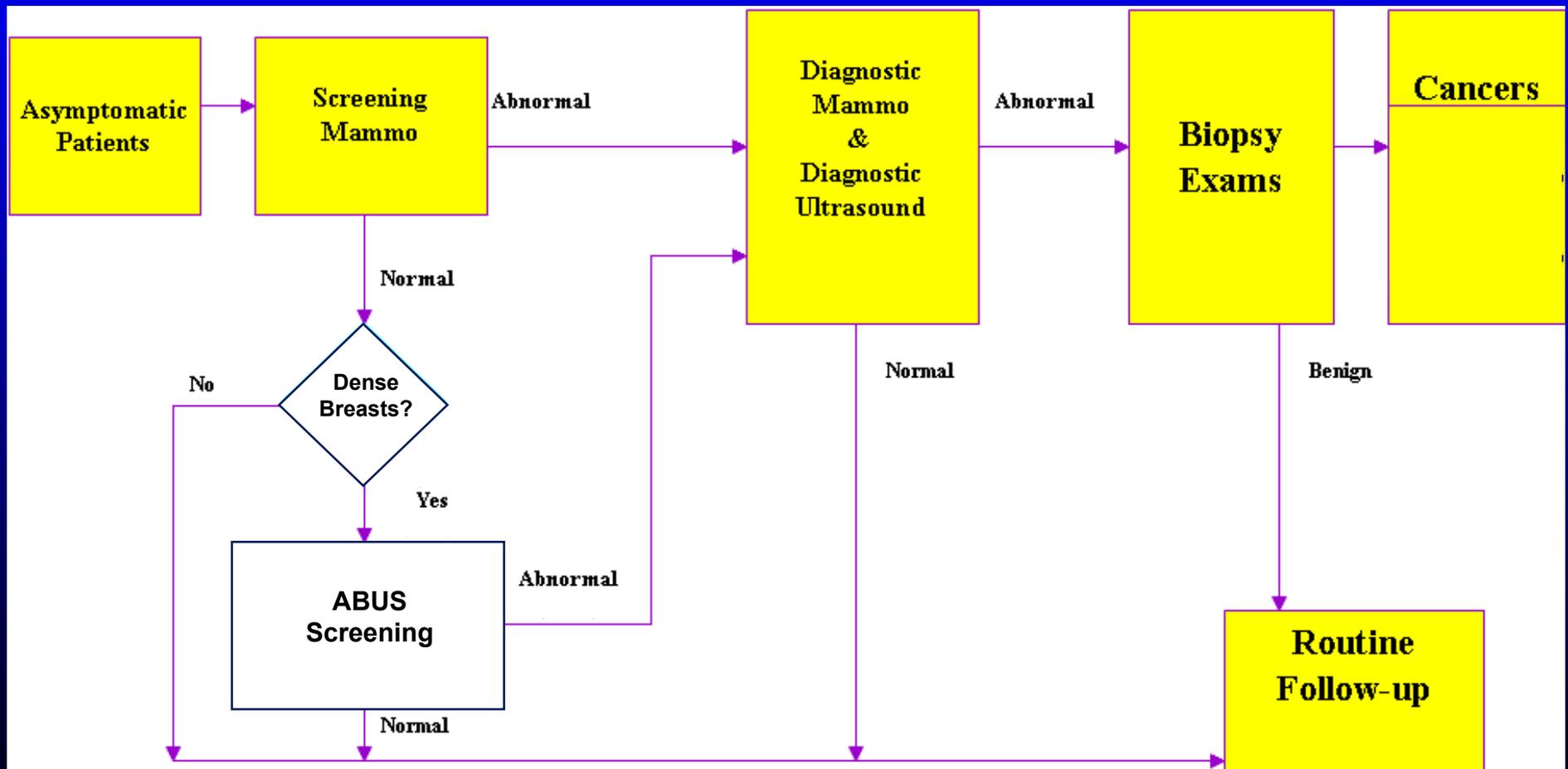
MRI
T1-weighted, Post Contrast



Ultrasound
7.5 MHz, Linear

U-Systems PMA

- U-Systems has conducted clinical studies (non-pivotal and pivotal) to demonstrate the safety and effectiveness of its ABUS device in the following clinical practice.



FDA Review of U-Systems' PMA

- **U-Systems' PMA submission was reviewed in the context of the proposed indications for use, and its potential impact on the clinical practice of mammography.**

FDA Review Team

Shahram Vaezy, PhD	Lead Reviewer, Biomedical Engineer Division of Radiological Devices
Helen Barr, MD	Director, Division of Mammography Quality and Radiation Programs
Brian Garra, MD	Medical Officer, Division of Imaging and Applied Mathematics
Berkman Sahiner, PhD	Scientist, Division of Imaging and Applied Mathematics
Norberto Pantoja-Galicia, PhD	Statistician, Division of Biostatistics
Colin Anderson-Smiths, MPH	Epidemiologist, Division of Epidemiology
David Brown, PhD	Chief Scientist, Division of Imaging and Applied Mathematics

Outline of FDA Presentations

- Introduction and Background; **Shahram Vaezy, PhD**
- Clinical Study Design; **Berkman Sahiner, PhD**
- Statistical Results; **Norberto Pantoja-Galicia, PhD**
- Clinical Significance; **Brian Garra, MD**
- Panel Discussion; **Shahram Vaezy, PhD**

Radiology Advisory Panel Meeting

U-Systems

somo-v Automated Breast Ultrasound System (ABUS)

Clinical Study Design

Berkman Sahiner, PhD

Division of Imaging and Applied Mathematics
Office of Science and Engineering Laboratories

Outline

- **General considerations**
 - **Controlled multi-reader multi-case (MRMC) study**
 - **ROC methodology**
- **Pivotal study**
 - **Endpoints**
 - **Case selection**
 - **Image interpretation**
 - **Readers**

Reader Performance Without and With ABUS

- Does the addition of ABUS to x-ray mammography (XRM) help radiologists in separating cancer and non-cancer groups in the target screening population?
- Controlled multi-reader multi-case study
 - ROC methodology

Clinical Use vs. Controlled Multi-Reader Multi-Case Studies

• Clinical Use Study

- Reader decision affects patient management
 - Multiple readers usually do not read the same case
- No enrichment
- Reading conditions may be difficult to control
 - Real world, multi-institutional
- Can lead to absolute scale performance estimates
 - e.g., cancers per 1000 women

• Controlled MRMC Study

- Reader decision may not affect patient management
 - Multiple readers can read the same case
- Enrichment
 - Esp. when prevalence is low
- Well-controlled reading conditions
 - Some components in clinical reading may be absent
- Compare two modalities
 - e.g., mammo alone vs. mammo+ABUS

Controlled MRMC Studies

- Do not provide absolute measures of figures of merit
 - Possible differences in prevalence, availability of prior images, patient history, reader mindset
- Have been used to bring to market several imaging devices
 - Full-field digital mammography (FFDM)
 - Compared to screen-film mammography
 - Digital breast tomosynthesis (DBT)
 - Combined with XRM compared to XRM alone
 - Computer-aided detection (CAD)
 - Compared to reader alone

Receiver Operating Characteristics

- **Clinical decisions**
 - Often binary: e.g. call the patient back vs. do not call the patient back
- **ROC methodology**
 - Multiple levels of confidence in disease presence
 - Reduces sources of variability
 - Decision threshold
 - Can be especially useful when one modality is expected to have higher sensitivity but lower specificity than the other

Study Objective: Primary

- Compare reader performance in detecting breast cancer, as defined by the area under the ROC Curve (AUC)
 - when ABUS and XRM are combined (XRM+ABUS), vs.
 - XRM alonein the target population

Study Objectives: Secondary

- **Evaluate reader sensitivity and specificity when XRM and ABUS are combined compared to XRM alone**

Indications for Use (IFU)

- “The Sono•v Automated Breast Ultrasound System (ABUS) is indicated as an adjunct to mammography for breast cancer screening in **asymptomatic women for whom screening mammography findings are normal or benign (BI-RADS Assessment Category 1 or 2), and breast parenchymal tissue is dense (BI-RADS Composition/Density 3 or 4), and have not had previous clinical breast intervention.** The device is intended to increase breast cancer detection in the described patient population.”

Case Selection

Multi-Center Registry Study

Over 14,000 Subjects

- **Asymptomatic, female, 25 or older**
- **> 50% parenchymal density on XRM at study entry**
 - **Clinical investigator, density BI-RADS 3 or 4**
- **In the past 12 months**
 - **No breast surgeries or interventional procedures,**
 - **No history of cancer diagnosis and/or treatment**
- **Currently not pregnant or breastfeeding**
 - **nor planning to become pregnant in the following 15 months**

Case Selection

Pivotal Study

- **Cases (N=200) were selected from the registry study for the pivotal study**
 - **Cases for primary analysis (N=164)**
 - **Supplemental cases (N=21)**
 - **Control cases (N=15)**

Case Selection

Inclusion Criteria – Primary Analysis Dataset

- All inclusion criteria of the registry study
- **XRM BI-RADS Assessment Category 1 or 2 (normal or benign) by registry clinical site investigator**
- **Evaluable XRM and ABUS exams**
 - No significant protocol deviations that could be expected to bias reader interpretation,
 - Available source records for verification purposes, and
 - Complete electronic data capture (EDC) records.

Case Selection

Exclusion Criteria – Primary Analysis Dataset

- XRM assessed BI-RADS Density score 1 or 2 (<50% parenchymal density) by registry clinical site investigator
- XRM assigned BI-RADS Assessment Category other than 1 or 2 by registry clinical site investigator
- Cases demonstrating administrative or technical errors:
 - e.g., **XRM or ABUS image quality inadequate** due to technologist error in labeling, positioning or acquisition technique.

Relevance: Discussion Topic #3: Does training provide a thorough understanding of the ABUS device capabilities and limitations to provide a technologist (and physicians) the information necessary to perform a quality ABUS exam?

Exclusion Criteria – Primary Analysis Dataset (Cont.)

- For non-cancer cases, a relevant medical history or existing benign breast findings, which could otherwise be classified as abnormal without knowledge of
 - patient history
 - access to relevant clinical data
 - review of prior images

This condition excludes non-cancer cases that underwent

- breast biopsy
- cyst aspiration
- breast enhancement surgery
- mastectomy and lumpectomy
- breast radiation for breast cancer

at any time in the past

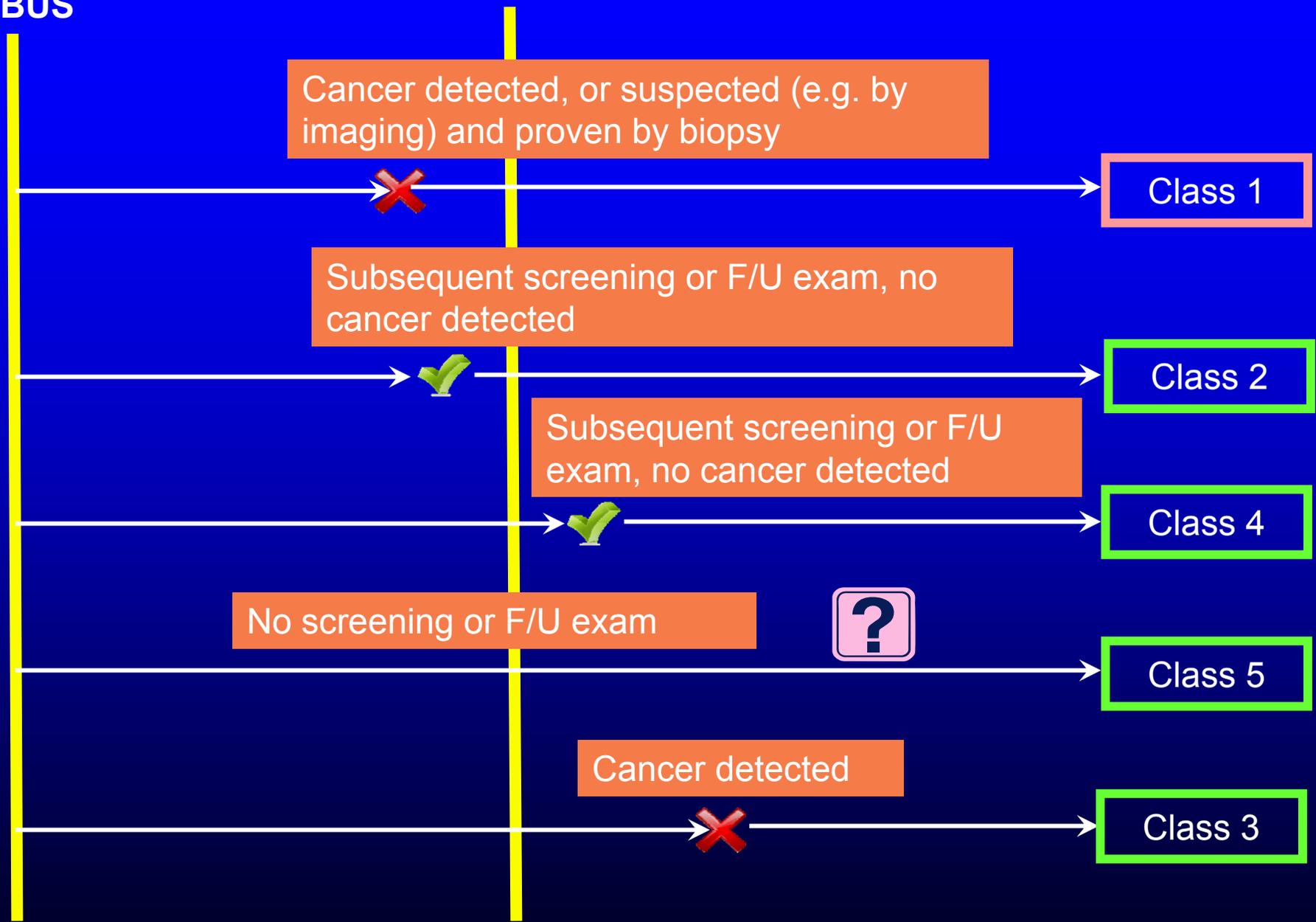
Relevance: Discussion Topic #2: Can collected data be generalized to include this specific patient population as part of the target population?

Cancer and Non-Cancer Cases

- Cancer cases (class 1)
- Non-cancers cases (class 2, 3, 4 and 5)

XRM Screening + ABUS

365 Days



N=11,663

Asymptomatic, mammo. BI-RADS 1 or 2, density >50%, no protocol deviations, complete EDC

N=31

Class 1 cases (Cancer)

-31

N=11,632

Potential for non-cancer pool: No cancer detected within 1 year of initial screening

44%

-5126

< 1 yr between initial screening and case selection date

N=6,506

At least 1 year between initial screening and case selection date

38%

-2498

Cases ineligible because of previous breast intervention (PBI)

N=4,008

Cases in non-cancer pool

**Relevance: Discussion Topic #2:
Can collected data be
generalized to include this
specific patient population as
part of the target population?**

Cancer Cases

- **N=31**
- **All cancers detected in the registry study**
- **15 cases underwent previous breast intervention**

Non-Cancer Cases

- From the non-cancer pool (N=4008), 400 cases randomly selected
- Among 400 randomly-selected cases:
 - 21% (N=83+2) excluded based on ABUS quality control assessment
 - 8% (N=30) excluded because complete exams were not available
 - 1% (N=5) excluded because exam file not compatible with workstation software
- Second random selection after exclusions:
- 133 non-cancer cases

Cancer and Non-Cancer Cases

Class	Number of Cases	Case Type
Class 1	31	Cancer
Class 2	6	Non-Cancer
Class 3	0	Non-Cancer
Class 4	104	Non-Cancer
Class 5	23	Non-Cancer
Total	164	Primary Analysis

Image Interpretation – Pivotal Study

- Sequential reading
 - XRM alone
 - Followed by XRM+ABUS

Image Interpretation – Pivotal Study

- For each reading condition, each case
 - BI-RADS 0, 1 or 2
 - Likelihood of malignancy (LOM) on a [0, 100] scale
 - ROC analysis
- For each BI-RADS 0 case
 - Forced BI-RADS (for case): 1, 2, 3, 4a, 4b, 4c, 5
 - Sensitivity, specificity
 - Lesion location
 - Location sensitivity

Readers

- **61 radiologists solicited**
- **33 met the qualification criteria, which included**
 - **Minimum interpretation requirements for XRM and breast ultrasound**
 - **Experience (min. 10 years) and/or fellowship requirements in breast imaging**
- **17 readers selected**
 - **based on their availability during study dates**

Readers

- **Practice:**
 - 7: academia
 - 6: private
 - 4: community clinics
- 9 readers with breast imaging fellowship
- 3-18 years experience in breast imaging
- Mammography review rate (per year)
 - Mean [range]: 5,490 [1,850-14,600]
- Breast US review rate (per year)
 - Mean [range]: 1,079 [603-5,000]

Reader ABUS Training

- **Module 1:**
 - Self-study, five online tutorials, case study presentations
- **Module 2:**
 - Interactive, real-time webinar with an ABUS expert
- **Module 3:**
 - 10-hour training at the U-Systems headquarters, hands-on sessions
- **Skill set exercise**
 - 25 cases
 - 10 biopsy-confirmed cancers
 - 10 benign biopsy-confirmed lesions
 - 5 negative cases

Radiology Advisory Panel Meeting

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Statistical Analyses Results

Norberto Pantoja-Galicia, PhD
Diagnostic Devices Branch
Division of Biostatistics
Office of Surveillance and Biometrics

Overview

- Previous Reader Studies 1, 2 and 3
- Pivotal Reader Study Results (Study 4)
 - Primary analysis (AUC)
 - Secondary analysis (sensitivity, specificity)
- Selection Criteria
- Additional Analyses
- Risk-Benefit Analysis

Previous Studies (& Pivotal)

Study	N	Readers	Intended population (Dense breast tissue)	Comments
1	300	12 *	All	AUC difference not statistically significant
2	308	3 **	All	Explored effect of reader experience with ABUS on ABUS performance
3	200	13	XRM –	Not filed. Non-cancers selected based on ABUS reading
4	200	17	XRM –	Pivotal Study (To be discussed)

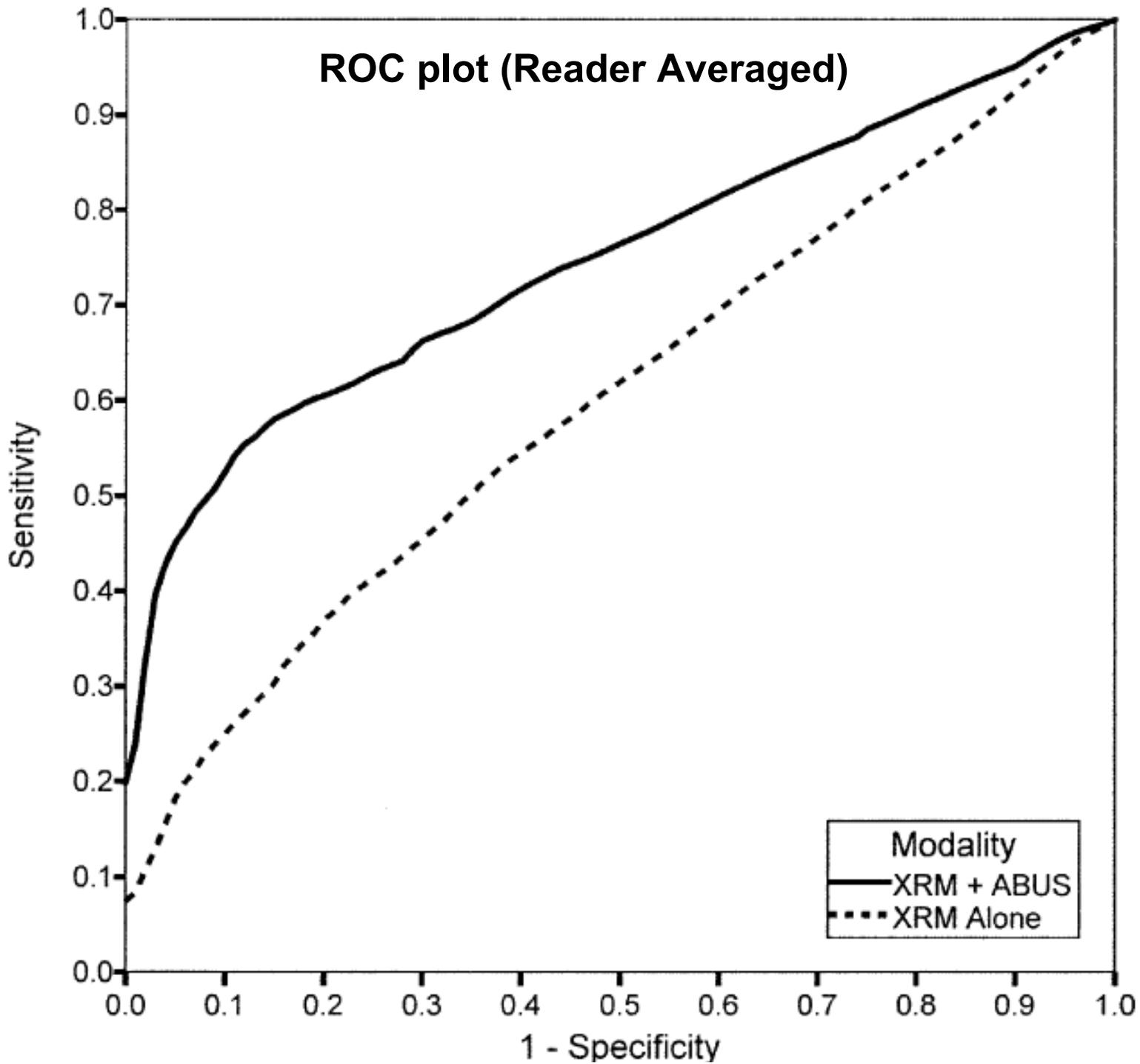
* 1/12 ABUS experienced; ** 3/3 ABUS experienced

• Opportunity to refine intended use population (All → XRM –)

Cases and Readers

- *Subjects for all studies (1-4) retrospectively selected from prospective multi-center registry study*
- *Most of the cancers in prospective study were **shared** across the four (CRRS) studies (e.g. all 22 cancers in study 3 were also in Pivotal Study + 9 new cancers)*
- *The sets of **readers** used in each study were mutually exclusive.*

PIVOTAL STUDY



Primary analysis

AUC (Reader Averaged)

31 cancers, 133 non-cancers

Method	XRM (95% CI)	XRM + ABUS (95% CI)	Difference (95% CI)
Primary *	0.604 (0.535,0.672)	0.747 (0.671,0.822)	0.143 (0.074, 0.212)

- **DBM* method used for primary analysis (nonparametric AUC)**
- **Statistical significance was met**

* Dorfman-Berbaum-Metz (DBM) method which assumes a mixed-effects ANOVA model for jackknife pseudovalues of AUC to account for multiple readers and case effects (original method in Dorfman, Berbaum, Metz, 1992 Invest Radiol 27(9):723-31)

Secondary analysis

- **Sensitivity, Specificity (Reader Averaged)**
- **BI-RADS cut point = 4**
 - **BI-RADS 1, 2, 3 is a test negative result.**
 - **BI-RADS 4, 5 is a test positive result.**

Metric	N	XRM	XRM + ABUS	Difference (95% CI)
Location-Sensitivity †	31	18.8%	49.9%	31.1%* (19.4, 43.8)%
Sensitivity	31	27.1%	57.7%	30.6%* (18.1, 43)%
Specificity	133	88.1%	84%	-4.1%** (-9.3, 0.4)%

† Cancer correctly detected and localized

* Statistical significant increase; ** non statistical significant decrease

Comparison using positive and negative likelihood ratios (PLR, NLR)

PLR: ratio of true positive fraction to false positive fraction

NLR: ratio of false negative fraction to true negative fraction

Metric	XRM	XRM + ABUS	Difference (95% CI)
Location-PLR	1.58	3.13	1.55 (0.37, 2.78)
Location-NLR	0.92	0.60	-0.32 (-0.48, -0.19)
PLR	2.28	3.61	1.33 (0.10, 2.72)
NLR	0.83	0.50	-0.32 (-0.46, -0.18)

BI-RADS
cutoff = 4

- PLR \uparrow implies greater Positive Predictive Value with ABUS
- NLR \downarrow implies greater Negative Predictive Value with ABUS
- Results do not depend on prevalence

* Biggerstaff, *Stat Med*, 2000, 19:649-663

Selection Criteria

DT 1,2

- Selection criteria different for cancers vs. non-cancers.
- Cancers excluded only if prior breast intervention (PBI) in the last 12 months (protocol registry)
 - 15 of 31 (48%) cancers had prior breast interventions (more than 1 year prior to exam)
- Non-cancers excluded if patient had prior breast intervention (protocol pivotal)
 - However, 1 non-cancer with PBI
- **Non-cancers with PBI were not studied** (except one)
- Cancers with PBI were in the study

AUC: without Prior Breast Interventions (PBI)

Method	XRM (95% CI)	XRM + ABUS (95% CI)	Difference (95% CI)
Primary *	0.604 (0.527,0.676)	0.747 (0.665,0.823)	0.143 (0.075,0.217)
Excluding PBI **	0.566 (0.479,0.662)	0.782 (0.678,0.878)	0.215 (0.105,0.329)

Bootstrap Method

- * *Not excluding PBI. (N = 164 = 31 cancers + 133 non-cancers)*
- ** *Excluding PBI. (N=164 - 15 cancers - 1 non-cancer with PBI),
N = 148 = 16 cancers + 132 non-cancers*

Sensitivity, Specificity (Reader Averaged)

- *Excluding PBI*
- *BI-RADS cut point = 4*
 - *BI-RADS 1, 2, 3 is a test negative result.*
 - *BI-RADS 4, 5 is a test positive result.*

Metric	N	XRM	XRM + ABUS	Difference (95% CI)
Sensitivity	16	22.4%	64%	41.5% (24, 60)%
Specificity	132	88.1%	84%	-4.1% (- 9,1)%

Positive and Negative Likelihood Ratios (PLR, NLR)

- Excluding PBI
- BI-RADS cutoff = 4

Metric	XRM	XRM + ABUS	Difference (95% CI)
PLR	1.88	3.99	2.11 (0.55, 3.76)
NLR	0.88	0.43	-0.45 (-0.67, -0.25)

- **PLR ↑ implies greater Positive Predictive Value with ABUS**
- **NLR ↓ implies greater Negative Predictive Value with ABUS**
- **Results do not depend on prevalence**

* Biggerstaff, *Stat Med*, 2000, 19:649-663

Intended Use Population

- IFU indicates the intended population are women that “have not had previous clinical breast intervention”
- Prior breast intervention (PBI)

Inclusion of statement in IFU	Comment
IFU with statement	Women with PBI are not part of the intended population (15 cancers, 1 non-cancer had PBI)
IFU without statement	15 cancers had PBI. All non-cancers (except one) do not have PBI.

Generalization to screening population

- We recognize this study has limitations, which might affect the generalizability of the results to the intended use population, for example:
 - Study is enriched with cancers
 - Radiologists read images knowing that their readings do not affect patient management;
 - Radiologists scored the image without the use of clinical history;
- Nonetheless, we can attempt to project the results from the study to the screening population to provide a rough assessment of ABUS in practice.

Attempt to project results to screening population

(Dense breast tissue, XRM-, No PBI)

BQ3

- Analysis of 100,000 Women
- Assume Cancer prevalence 0.22% (prospective study)
- Sensitivity 22.4%, 64% for XRM, XRM+ABUS (*BI-RADS cut point = 4*)
- Specificity 88.1%, 84% for XRM, XRM+ABUS

Screening	XRM	XRM+ABUS	Change
<i>Cancer (223)</i>			
True Positives	50	143	93
False Negatives	173	80	-93
<i>Non-Cancer (99777)</i>			
False Positives	11871	15931	4060
True Negatives	87906	83846	-4060

- **93** more cancer patients may be referred to additional imaging
- **4060** more non-cancer patients may be referred to additional imaging work up unnecessarily
- **1 more True Positive** for every **44 more False Positives** (ratio 93/4060)

Attempt to project results to screening population

(Dense breast tissue, XRM-, No PBI)

BQ3

- Analysis of 100,000 Women
- Assume Cancer prevalence 0.22% (prospective study)
- Sensitivity 64% for XRM+ABUS (*BI-RADS cut point = 4*)
- Specificity 84% for XRM+ABUS

Screening	XRM	XRM+ABUS	Change
<i>Cancer (223)</i>			
True Positives	0	143	143
False Negatives	223	80	-143
<i>Non-Cancer (99777)</i>			
False Positives	0	15931	15931
True Negatives	99777	83846	-15931

- **143** more cancer patients may be referred to additional imaging
- **15931** more non-cancer patients may be referred to additional imaging work up unnecessarily
- **1 more True Positive** for every **112 more False Positives** (ratio 143/15931)

Unverified non-cancers

- 23 unverified non-cancers “class 5”.
- Addressed in an analysis of robustness to missing verification of true disease status.

Missing Data: Exclusions for Q/C problems

- 30% (120/400) non-cancers had Q/C problems
- 0% (0/31) cancers reported with Q/C problems

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Clinical Significance

Brian S. Garra, MD

Division of Imaging and Applied Mathematics
Office of Science and Engineering Laboratories

THE CLINICAL NEED

A BETTER TOOL FOR IMAGING DENSE BREASTS

- **Mammography Sensitivity Declines Greatly in Non – Fatty (“Dense”) Breast Tissue**
- **BI-RADS Classification for Breast Tissue Incorporates The Concept of Lower Sensitivity**
 - **Cat 4: “Extremely Dense Which Lowers the Sensitivity of Mammography”**
 - **Cat 3: “Heterogeneously Dense Which May Lower the Sensitivity of Mammography”**

MAMMOGRAPHIC SENSITIVITY

REFERENCE	SENSITIVITY	
	BI-RADS 1-2 ($\leq 50\%$)	BI-RADS 3-4 ($> 50\%$)
1	.93	.57
2	.80	.56
3	.50 ($\leq 40\%$)	.26 ($> 40\%$)

1. Kolb et. al. (analog), Radiology 2002;225:165 (27, 825 women, 246 cancers)
2. LeConte et. al. (analog), AJR 2003;180:1675 (4236 women, 50 cancers)
3. Berg et. al. (analog & digital), JAMA 2008;299:2151 (2637 women, 40 cancers)

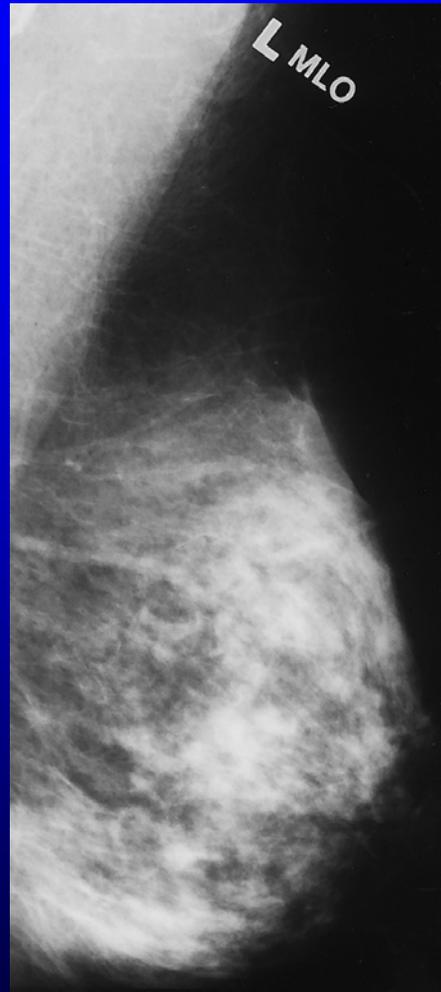
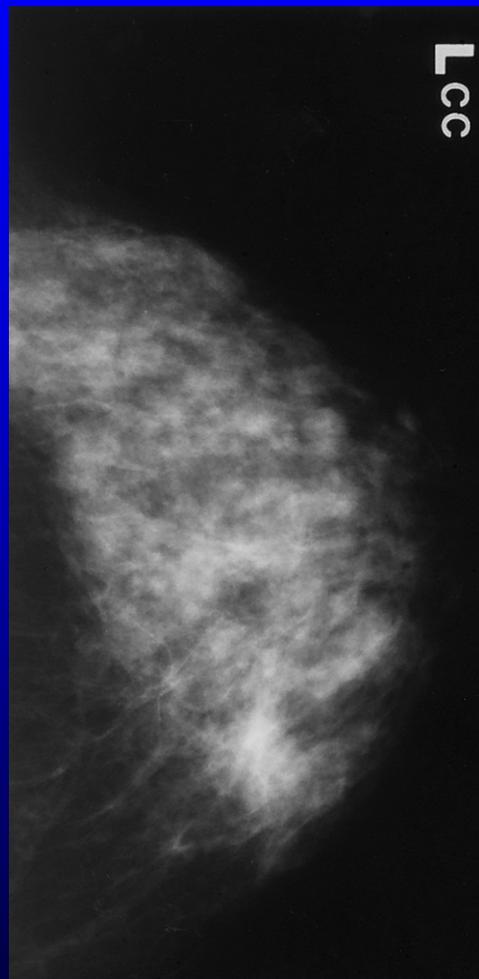
MAMMOGRAPHY & US

COMPLEMENTARY MODALITIES

- On Mammography:
 - Masses are: High Contrast in Low Density Fatty Breasts
 - Low Contrast In Dense Breasts
- On US:
 - Solid Tumors are Hypoechoic With Low Contrast in Hypoechoic Fatty Breasts
 - High Contrast in Dense (Echogenic) Breasts

MAMMOGRAPHY & US

DENSE BREAST



Negative BI-RADS Cat 3 Breast With 12mm Lesion Seen on US
(from Kaplan et. al. Radiology 2001)

MAMMOGRAPHY & US

FATTY BREAST



In a Fatty Breast, Cancer is White Against Gray On Mammo and Gray Against Gray on US

**So Ultrasound Can Detect Lesions
Reliably in Dense Breast Tissue
(In Literature: sensitivity 0.76 – 0.96)**

PROBLEMS WITH HANDHELD SCREENING ULTRASOUND

- **Time Consuming: Up to 30 Minutes For Traditional Scanning Methods**
- **Operator Dependency**
 - **Variable Operator Skills**
 - **Incomplete Coverage of the Breast**
 - **Difficulty Determining Precise Location of Lesions**
 - **RT Perceptual Errors Lead to Missed Lesions**

A SOLUTION: VOLUME (3D) ULTRASOUND IMAGING

- Acquiring a Series of Closely Spaced Adjacent Slices Through an Organ or Region for Later Review
- 2D or 3D Display of the Volume Imaging Data
- U-Systems ABUS is An Example of This Type of System



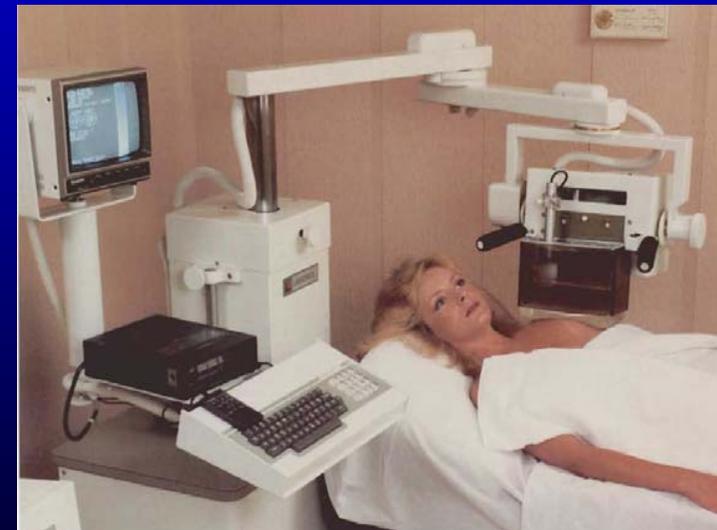
VOLUME ULTRASOUND

HISTORY

- Many Early Machines Were Automated or Semi-automated
- 1970's : Large # of Closely Spaced Images Representing a Tissue Volume (Technicare) – But No Decent Display
- PACS (90's) Allowed Users to Scroll Through Large “stacks” of Images From CT, MRI, and finally Ultrasound in 2000
- 3D Display is Often Reserved for Complex Cases



Ausonics Octoson Breast Scanner 1975



Labsonics Automated Breast Scanner 1986

VOLUME ULTRASOUND TYPES

- **MANUAL:** Handheld Transducer Manually Swept
 - In Plane Measurements Only
 - Easy and Fast to Perform
- **SEMI-AUTOMATED:** Transducer is Swept Manually -- With Position Sensor
 - Allows Measurements in Elevational Plane
 - Combining Multiple Sweeps is Possible
- **AUTOMATIC:** Transducer is Swept by Motor With Position Sensors

AUTOMATED VOLUME SCANNING MITIGATES THE PROBLEMS OF HANDHELD US

- **Rapid Systematic Breast Coverage (18 min total)**
- **Precise Location Information About Lesions**
- **Minimize Perceptual Misses -Allows Interpreter to Go Back Over Areas Multiple Times With Multiple Views**
- **Exam Consistency - Each Exam is Conducted in Precisely the Same Manner**

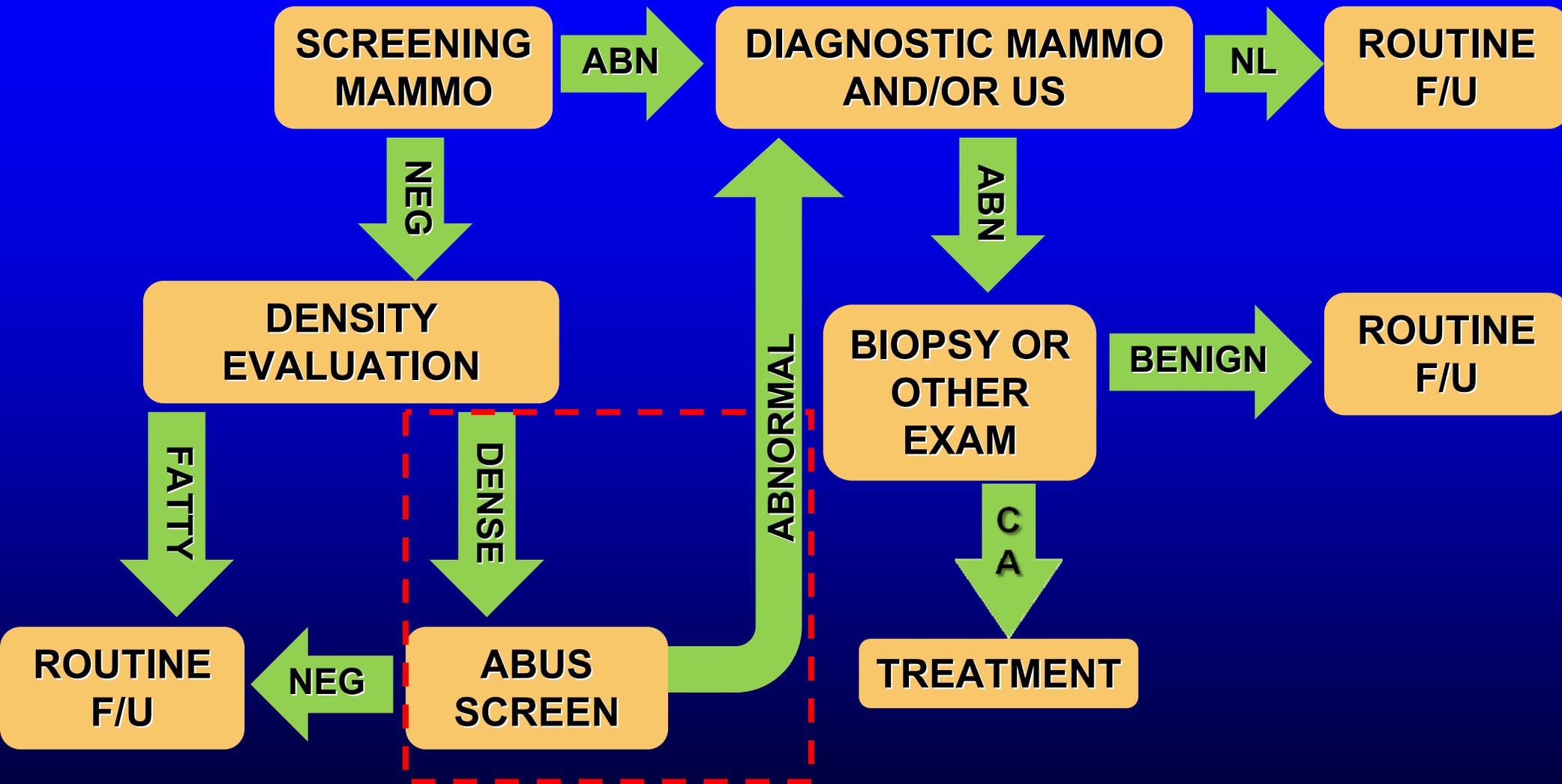
EFFECTS ON CLINICAL PRACTICE

ABUS INDICATIONS FOR USE

KEY CHANGES

- **Claim to Increase Detection of Breast Cancer**
- **Limitation to Women With Dense Breasts on Mammography**
- **Use Following a Screening Mammogram- in a Screening Environment**
- **Prior Clearance Was For Use of the Device as an Adjunct to Mammography Without Additional Specifics**

PROPOSED WORKFLOW



WORKFLOW EFFECTS

- **Current Workflow Risks Missing Cancers in Women With > 50% Glandular Tissue**
 - **Later DX of Cancer: ↑ Node Positive Disease & Cancer Size**
- **ABUS Workflow Risks ↑ False Positives**
 - **Additional Diagnostic Workups**
 - **Is the Increase in FP Enough to be a Problem?**
 - **Will Extending the ABUS to Pts With Prior Procedures Result in More False Positives (Panel Topic 2) ?**
- **Will Technical Failures be a Problem?**

TRAINING ISSUES

(Discussion TOPIC 3)

READER TRAINING RATIONALE

- **Extensive Training Was Used in Pivotal Study**
- **The ABUS Provides a Different Type of Image (A 3D Rendered Image Set)**

OPERATOR TRAINING RATIONALE

- **23% Technical Failures**
- **Device Positioning Unlike Handheld**
- **Previous Experience With Prior Automated Units**

Radiology Advisory Panel Meeting

U-Systems

somo-v Automated Breast Ultrasound System (ABUS)

Panel Discussion

Shahram Vaezy, PhD
Division of Radiological Devices
Office of *In Vitro* Diagnostic Device Evaluation and Safety

Discussion Topic #1

Generalizability of the Clinical Study Results

Please discuss the generalizability of the clinical study results in support of the proposed indication for use. In your discussion, please consider the relative importance of the following in determining the acceptability of the data:

- The resulting data set with respect to exclusion criteria were different between the cancer and non-cancer cases.
 - Approximately 1/3 of the normal cases were excluded due to clinical breast intervention at any time in the past.
 - Approximately 1/2 of the cancer cases had prior intervention prior to the past 12 months.
- The exclusion criteria allowed technical reasons for excluding cases. Approximately 20% of cases were excluded due to poor ABUS image quality.

Discussion Topic #2

Indications for Use (IFU)

The current IFU excludes women who have had previous clinical breast intervention, (e.g., breast surgeries or other interventional procedures, or a history of cancer diagnosis and/or treatment). The study was designed to exclude these patients as a means to eliminate the confounding effects of past clinical breast intervention. Please discuss the generalizability of the clinical study results with respect to this specific patient population. Please consider the following points in your discussion:

- the potential impact of previous clinical breast interventions on device performance and clinical outcome
- whether additional clinical data would be needed to demonstrate comparable clinical outcomes for women with previous clinical breast intervention
- whether the data can be generalized to include these women in the indications for use, to allow removing the exclusion of women with previous clinical breast intervention in the IFU

Discussion Topic #3

Training Program

Please discuss the acceptability of the proposed training program for the ABUS system as described by the sponsor. In your discussion, please consider the following:

- the amount of training required in the pivotal study to achieve the stated outcomes**
- the impact of training on the clinical outcomes of the non-pivotal and pivotal studies**
- the technical difficulties resulting in the exclusion of 20% of the cases due to image quality**
- the important training considerations for technologists to achieve the proficiency needed to achieve comparable outcomes as those observed in the pivotal study**
- the important training considerations for physicians to achieve the proficiency needed to achieve comparable outcomes as those observed in the pivotal study**

Ballot Vote Question #1

Is there a reasonable assurance that the ABUS device is safe for the proposed indication for use?

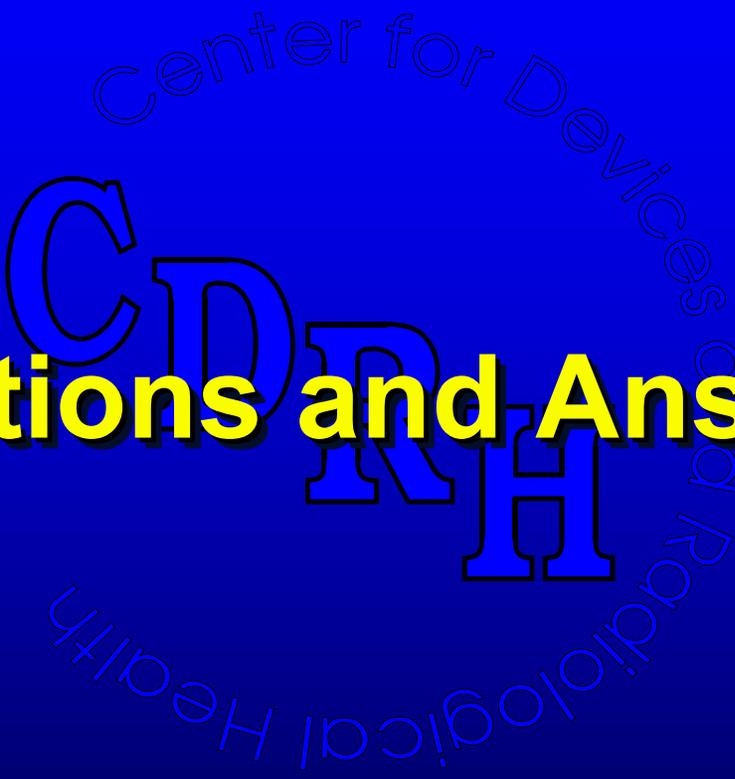
“The sono-v Automated Breast Ultrasound System (ABUS) is indicated as an adjunct to mammography for breast cancer screening in asymptomatic women for whom screening mammography findings are normal or benign (BI-RADS® Assessment Category 1 or 2), and breast parenchymal tissue is dense (BI-RADS® Composition/Density 3 or 4), and have not had previous clinical breast intervention. The device is intended to increase breast cancer detection in the described patient population.”

Ballot Vote Question #2

Is there a reasonable assurance that the ABUS device is effective for the proposed indication for use?

Ballot Vote Question #3

Do the benefits of the ABUS device for the proposed indication for use outweigh the risks of the device for the proposed indication?

The logo for the Center for Devices and Radiological Health (CDRH) is a circular watermark in the background. It features the text "Center for Devices and Radiological Health" around the perimeter and the acronym "CDRH" in the center.

Questions and Answers