Diagnosis of Breast Masses Using Opto-Acoustics

Erin I. Neuschler, MD, A. Thomas Stavros, MD, Philip T. Lavin, PhD, Michael J. Ulissey, MD
1. Erin I. Neuschler, MD: Northwestern University Feinberg School of Medicine, Assistant Professor of Radiology, research grant from Seno Medical Instruments, Inc.

2. A. Thomas Stavros, MD: Seno Medical Instruments, Inc., Medical Director, Seno stock

3. Philip T. Lavin, PhD: Boston Biostatistics Research Foundation, Consultant to Seno Medical Instruments, Inc., analytical services provider

4. Michael J. Ulissey, MD: Breast Diagnostic Center, Seno Stock
Imagio® is an investigational device that embodies the opto-acoustic technology. The information presented in this presentation is preliminary and not based on an FDA-approved device using this opto-acoustic technology.
Some of these images are taken with the Seno Imagio® system and are not to be reproduced.

Copyright 2016 Seno Medical Instruments, Inc.  
All rights reserved.
Purpose

• Gray-scale ultrasound is limited in its specificity for characterization of breast masses

• Limited ultrasound specificity results in false positives and negative biopsies

• Can opto-acoustic (OA) imaging increase the specificity of gray-scale ultrasound for characterization of breast masses?
Basis for Opto-Acoustic Imaging

- Cancers do not grow beyond 2-mm without developing neovascularity\(^1\)
- With angiogenesis there is increased blood flow to cancerous tissue
- Cancers are generally more metabolically active and deoxygenate hemoglobin more than benign entities or normal tissue
Opto-Acoustic Imaging

• Optical energy from a laser is absorbed\textsuperscript{2,3,4}

• Light excitation causes thermalelastic expansion within a mass which then emits a pressure (acoustic) wave that is detected by an array of acoustic sensors within a hand-held breast probe\textsuperscript{5}

• Pulses of laser light at two wavelengths are applied sequentially to breast tissue
  
  • Near-infrared light (757nm) is absorbed predominantly by hypoxic (deoxygenated) blood
  
  • Laser light (1064 nm) is absorbed predominantly by normally oxygenated blood
Investigational Device - Imagio®

- Hand-held linear probe which can perform both gray-scale ultrasound as well emits optical pulses via a class 3b laser
- Dual wavelength optical pulses are used to generate the OA images
- Ultrasound images are acquired and temporally interleaved and co-registered with the OA images in real-time

Images proprietary to Seno Medical Instruments, Inc.
Opto-Acoustic Imaging: Fusion Imaging

Fusion of laser optic imaging and gray-scale imaging in real-time$^6$-$^{12}$

- Optics – high contrast resolution (about 20/1)
- Ultrasound – high spatial resolution and better penetration than laser alone in diffuse optical tomography

Fusion of anatomy and function

- Anatomy – gray-scale ultrasound anatomy as well as OA demonstration of tumor angiogenesis
- Function – OA demonstration of relative degrees of oxygenation/deoxygenation
Opto-Acoustic (OA) and Ultrasound Images
Real Time Hemoglobin Map

Malignant
more deoxygenated hemoglobin

Benign
more oxygenated or absent hemoglobin

Images proprietary to Seno Medical Instruments, Inc.
Opto-Acoustics (OA) 6-on-1 Real Time Display
1 gray scale map and 5 OA maps are complementary to each other
Invasive ductal carcinoma, grade II

![Image of OA displays](image-url)
PIONEER-01 Pilot Study

- A Pivotal Study of Imaging with Optoacoustics to diagnose breast masses detected by mammography and/or clinical findings: A New Evaluation Tool for Radiologists

- Pilot study of 100 patients was evaluated for the potential ability of OA to downgrade BI-RADS scores in benign masses

- Can OA upgrade the BI-RADS (BR) categories of malignant masses?
| 2,097 subjects | 7 blinded readers | 16 sites in the USA |
Materials and Methods

• 6 of the 16 sites contributed to the pilot cases

• Women referred for diagnostic breast ultrasound due to a palpable mass or a suspicious mammographic finding

• Patients with BI-RADS 3, 4a, 4b, 4c and 5 lesions at conventional diagnostic ultrasound (CDU) were eligible for the study

• Investigators obtained gray-scale images with the Imagio device, the internal ultrasound control, Imagio Ultrasound (IUS), immediately before acquiring the OA images
Materials and Methods

- Independent readers (IRs) blinded to clinical data, site imaging and pathology.
- 7 IRs were trained by expert reader to identify and score three OA internal features and two OA external features for each mass.
- IRs were offered the results of two nomograms (that were calculated from their OA feature scores) to help predict the Probability of Malignancy (POM).
- 2% or less POM → downgrade to BI-RADS 3.
- 0% POM → downgrade mass to BI-RADS 2.
OA Findings

Internal OA Findings
• Internal vessels
• Internal blush
• Internal hemoglobin

External OA Findings
• Capsular or boundary vessels
• Peri-tumoral vessels
Materials and Methods

• 103 masses from the 100 pilot study cases
• 101 were evaluable
• 6 masses were not biopsied and did not have 12 month follow-up
• 95 masses were either biopsied or had 12 month follow-up
  ▪ 84 biopsied masses (39 malignant and 45 benign)
  ▪ 11 masses were coded BR 3 and had 12 month follow-up
Results

- IRs had 97.0% sensitivity for IUS and OA
- IRs had a 44.3% specificity with OA, which was a 7.6% improvement over IUS
- There were higher OA scores for malignant vs. benign masses for each feature score
Results – Benign Masses: OA vs. CDU

• Using OA, 52% of benign masses classified as BR 4a by CDU were downgraded to BR 3 or 2

• Using OA, 35% of benign masses classified as BR 4b by CDU were downgraded to BR 3 or 2

• Using OA, 24% of benign masses classified as BR 3 by CDU were downgraded to BR 2
Results – Benign Masses: OA vs. IUS

• Using OA, 37% of benign masses classified as BR 4a by IUS were downgraded to a BR 3 or 2

• Using OA, 11% of benign masses classified as BR 4b by IUS were downgraded to a BR 3 or 2

• Using OA, 37% of benign masses classified as BR 3 by IUS were downgraded to BR 2
benign BR 4a masses - shift in BI-RADS category after OA versus IUS

Data Proprietary to Seno Medical Instruments, Inc.
benign BR 4b masses - shift in BI-RADS category after OA versus IUS

Data Proprietary to Seno Medical Instruments, Inc.
Case #1

0.9 cm mass in left breast at 3:00, 7 cm from the nipple

- CDU: BI-RADS 4B
- IUS: BI-RADS 4B
OA
FIBROADENOMA

0.9 cm mass in left breast at 3:00, 7 cm from the nipple

- CDU: BI-RADS 4B
- IUS: BI-RADS 4B
- OA: BI-RADS 3
Results – Malignant Masses: OA vs. CDU

- Using OA, the IRs **upgraded** 33% of the malignant masses classified as BR 4b by the CDU to 4c or 5

- No masses were given a BR 4a by the site-CDU
Results – Malignant Masses: OA vs. IUS

- Using OA, the IRs upgraded 42% of the malignant masses classified as 4a by the IUS to 4c or 5
- Using OA, the IRs upgraded 57% of the malignant masses classified as 4b by the IUS to 4c or 5
malignant BR 4a masses - shift in BI-RADS category after OA versus IUS

Number of reads:

- 2: 5.6%
- 3: 5.6%
- 4a: 13.9%
- 4b: 33.3%
- 4c: 30.6%
- 5: 11.1%

Total reads: 100.0%

Net shift: 63.8%

BI-RADS category

Data Proprietary to Seno Medical Instruments, Inc.
malignant BR 4b masses - shift in BI-RADS category after OA versus IUS

BI-RADS category

number of reads

post OA

pre OA

Data Proprietary to Seno Medical Instruments, Inc.
Case #2

1.1 cm mass in right breast at 9:00, 5 cm from the nipple

• IUS: BI-RADS 4A
DCIS Grade 2 (Solid Type)

1.1 cm mass in right breast at 9:00, 5 cm from the nipple

- IUS: BI-RADS 4A
- OA: BI-RADS 4C
Results

• Using OA, more BR 2 and 3 categories were assigned for biopsy-proven benign lesions.

• Using OA, for biopsy-proven malignant lesions there were more BR 4c and 5 categories assigned.
Conclusions

• Benign masses classified as BR 3, 4a, and 4b by IUS and CDU could be downgraded 1-3 categories while malignant masses may be upgraded one to two categories with OA.

• If the findings are confirmed by the Pivotal study, OA findings may help identify masses that do not require biopsy, and in some cases, even avoid short interval follow-up.

• Conversely, OA findings may increase suspicion and add certainty to the need for biopsies in malignant masses.
References


Thank You

eneuschl@nm.org