Opto-Acoustic Nomograms for Improving Breast Cancer Diagnosis

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Disclosure of Commercial Interest

Dr. Lavin and Dr. Stavros have a financial relationship with Seno Medical Instruments, Inc. that may have a direct or indirect interest in the content as follows:

- Dr. Lavin performs contract research support for Seno Medical Instruments, Inc.
- Dr. Stavros is the Medical Director for Seno Medical Instruments, Inc.
- Dr. Lavin and Dr. Stavros hold Seno Medical Instruments, Inc. stock options
Disclaimer

Imagio® is an investigational device that uses opto-acoustic technology. The information presented in this presentation is preliminary and not based on an FDA-approved device. Accordingly, the images, videos, text and audio contained in each of these modules represent preliminary information. All of this information is being validated in a pivotal clinical study.
OA Background

• Imagio® is currently an investigational medical device being tested for FDA review under a PMA.

• It utilizes dual wavelength laser opto-acoustic (OA) imaging technology co-registered with conventional diagnostic ultrasound in real time to gain both structural (demonstration of neo-angiogenesis) and functional imaging (showing relative degree of de-oxygenation) information of potentially suspicious breast masses. Imagio does this without having to administer radioactive contrast agents or expose patients to radiation.

• The purpose of this study is to evaluate if nomograms derived from OA findings can help independent readers (blinded to clinical outcomes) differentiate benign vs. malignant breast masses.
IMAGIO® DEVICE
Malignant tumor has increased blood concentration and decreased oxygenation

Optical energy from laser is absorbed and emitted acoustically

Benign growth has increased blood concentration and normal oxygenation
IMAGIO 6 UP IMAGE

Grade 3 Invasive Ductal Carcinoma
IMAGIO 6 UP IMAGE
Grade 1 Invasive Ductal Carcinoma
Fibroadenoma
OA Data

• PIONEER study consists of two separate studies:
  – n=100 Pilot Study (reported here) and the subsequent
  – n=1,997 Pivotal Study to support PMA to help diagnose suspicious BI-RADS 3-5 masses by sites

• Independent Readers (IRs) used OA to assess 3 internal and 2 external features:
  – Internal: vascularity, hemoglobin, deoxygenation
  – External: boundary zone, peripheral zone

• Readers trained to evaluate the OA features
Nomograms Construction

• Construction based on 80 biopsied masses out of a total of 102 masses in 100 Pilot subjects
  ▪ Masses: 41 benign, 38 malignant, 1 high risk (held aside)
  ▪ 22 not biopsied (BI-RADS 3 being followed for 12 months) and not included in this analysis

• Nomograms designed using logistic and linear regression models based on the 5 features
  – Logistic: benign vs. malignant
  – Linear: probability of malignancy (POM)

• Expert reader (TS) assessed and scored 5 OA features on all 80 pilot cases blinded to clinical information and biopsy results

• OA feature scoring performed by expert reader (blinded) was used to create nomograms
Methods

• First, expert reader scored Pilot cases blinded to clinical outcomes
• Independent readers also blinded to clinical outcomes
• IUS component evaluated first
  — Readers advised not to downgrade IUS POM >30%
• Independent readers scored OA features
• Nomogram predictions offered real-time to help blinded readers assess POM and BI-RADS
• Real-time nomogram provided immediately once readers scored the 5 OA features
• Readers had option to use nomogram results
Feature Differentiation

• Features scored on a 0-5/6 ordinal scale
• There were significantly lower scores for benign vs. malignant masses for the feature distributions:
  – Vascularity (11/15 IRs)
  – Hemoglobin (10/15 IRs)
  – Deoxygenation (10/15 IRs)
  – Boundary Zone (14/15 IRs),
  – Peripheral Zone (13/15 IRs)

• No significant differences for the artifact score
Sensitivity and Specificity

• Overall sensitivities were 96.5% for IUS and 98.1% for OA across all IRs (not statistically different)
  – No downside offering nomogram

• Overall specificities were 36.7% for IUS and 42.7% for OA across all IRs

• Mean specificities using the averaged nomogram was 53.8% representing 17% more absolute improvement in OA specificity, already 6% more favorable than IUS
Nomogram Specificity Gain

| PIONEER Pilot OA Specificity Enhancement Using Averaged Prediction Models |
|-------------------------------------------------|----------------|
| Observed | Nomogram 10% Threshold |
| Reader | |
| Sensitivity | Specificity |
| All IRs | 98.1% | 42.7% | 53.8% |

11% Absolute Gain in Specificity for Pre-defined Averaged 10% Prediction Threshold
Conclusions

- OA features can be independently and quickly mastered by practicing IRs to consistently differentiate masses.

- Nomograms offer further confidence to enhance decision making to differentiate benign from malignant using OA.
  - no significant sensitivity downside
  - further specificity upside

- If confirmed in the Pivotal Study, OA findings with nomograms might be useful in differentiation and thus spare biopsies.
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