Opto-Acoustic Nomograms for Improving Breast Cancer Diagnosis

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for
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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

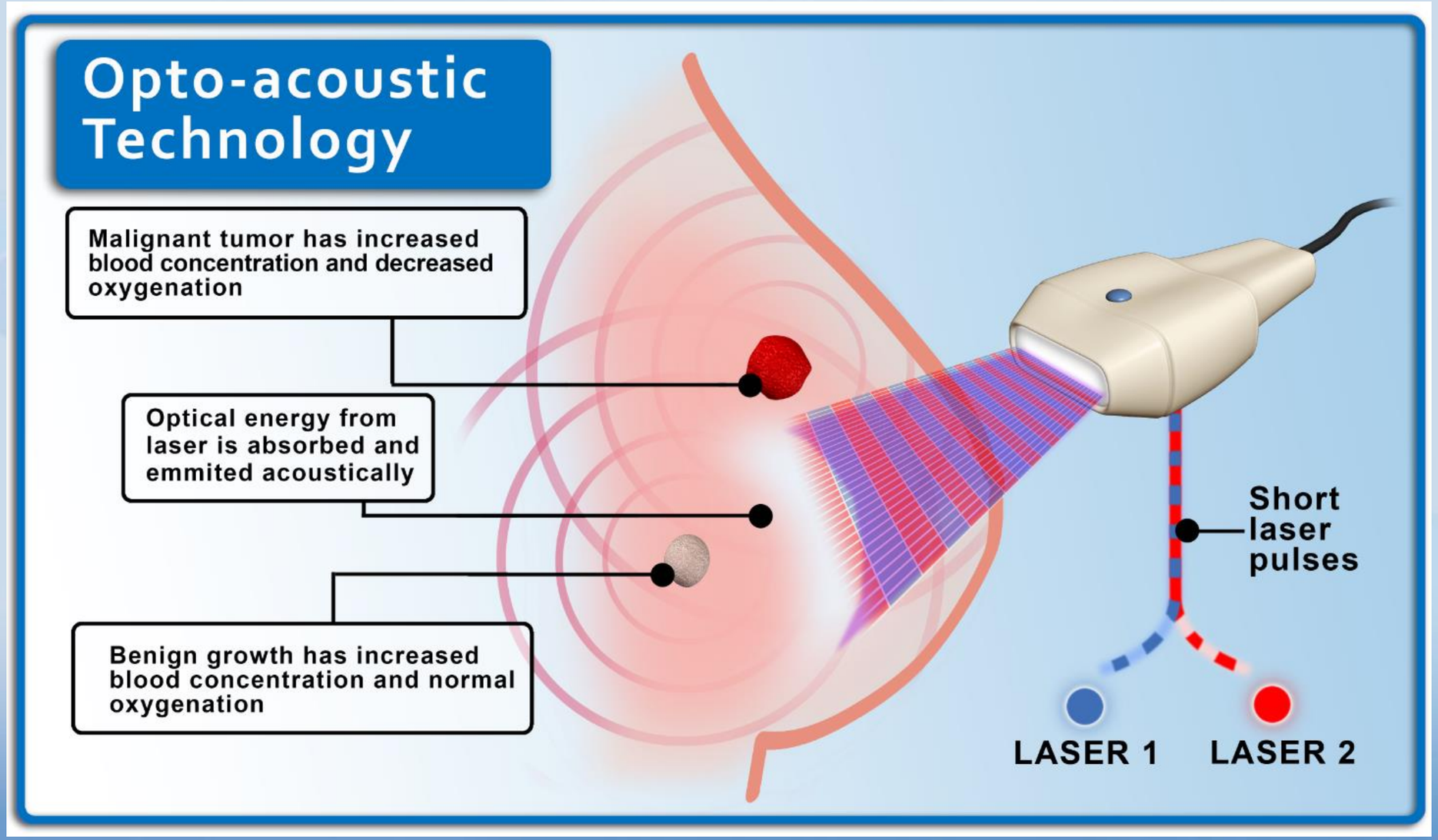
- Imagio® is currently an investigational medical device being tested for FDA review under a PMA.

- 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.

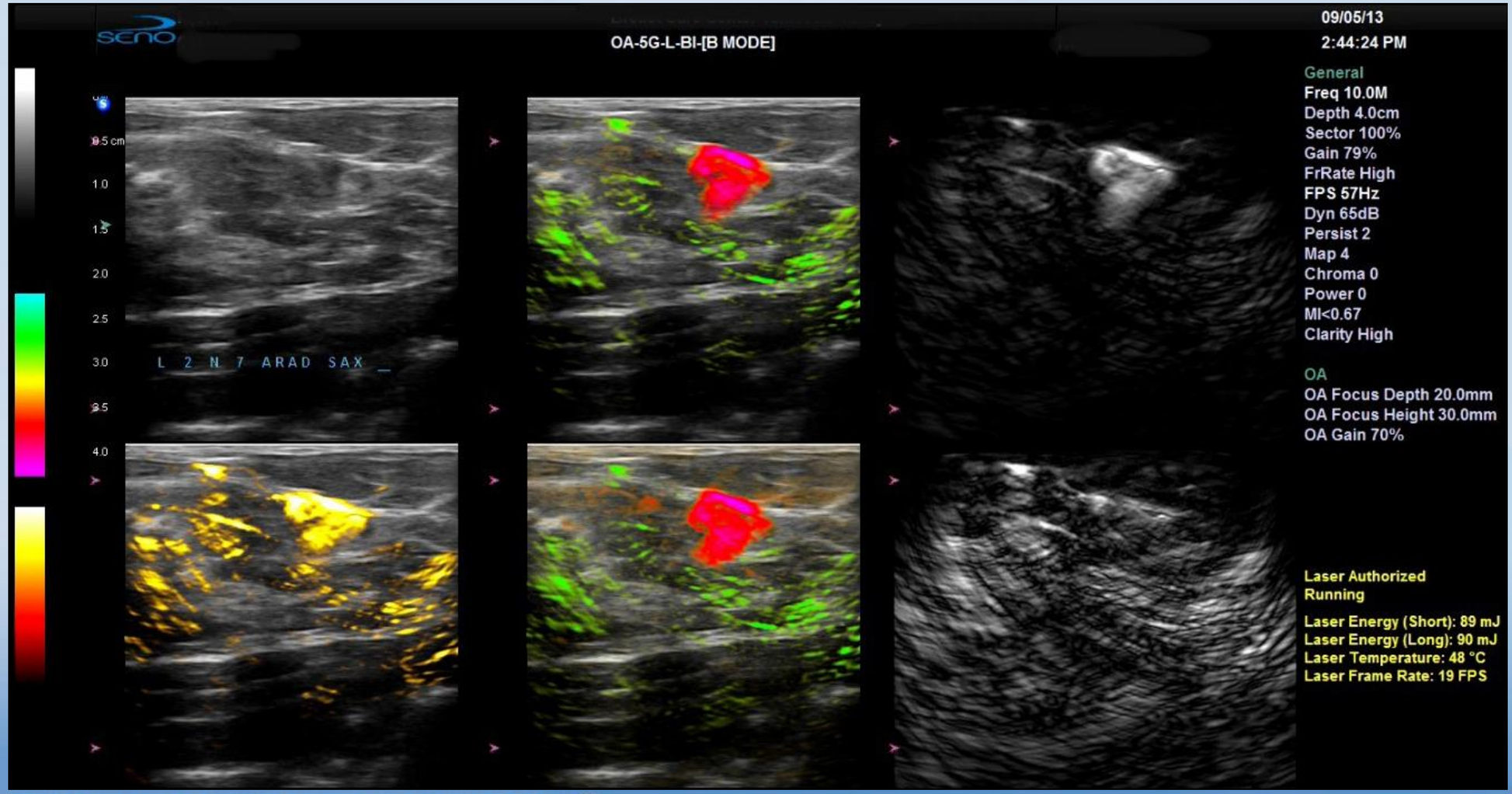
IMAGIO® DEVICE

IMAGIO SYSTEM



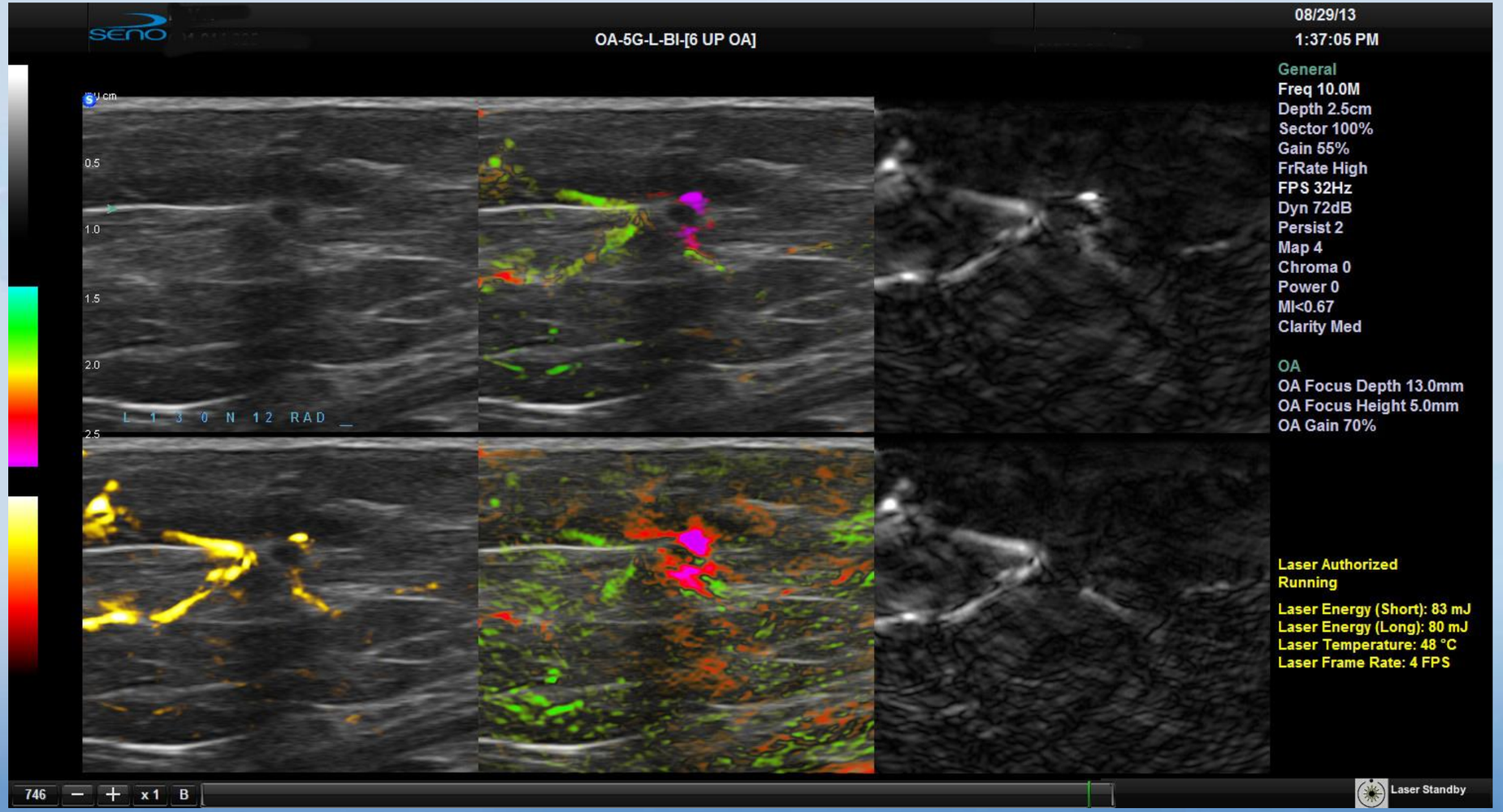
IMAGIO 6 UP IMAGE

Grade 3 Invasive Ductal Carcinoma

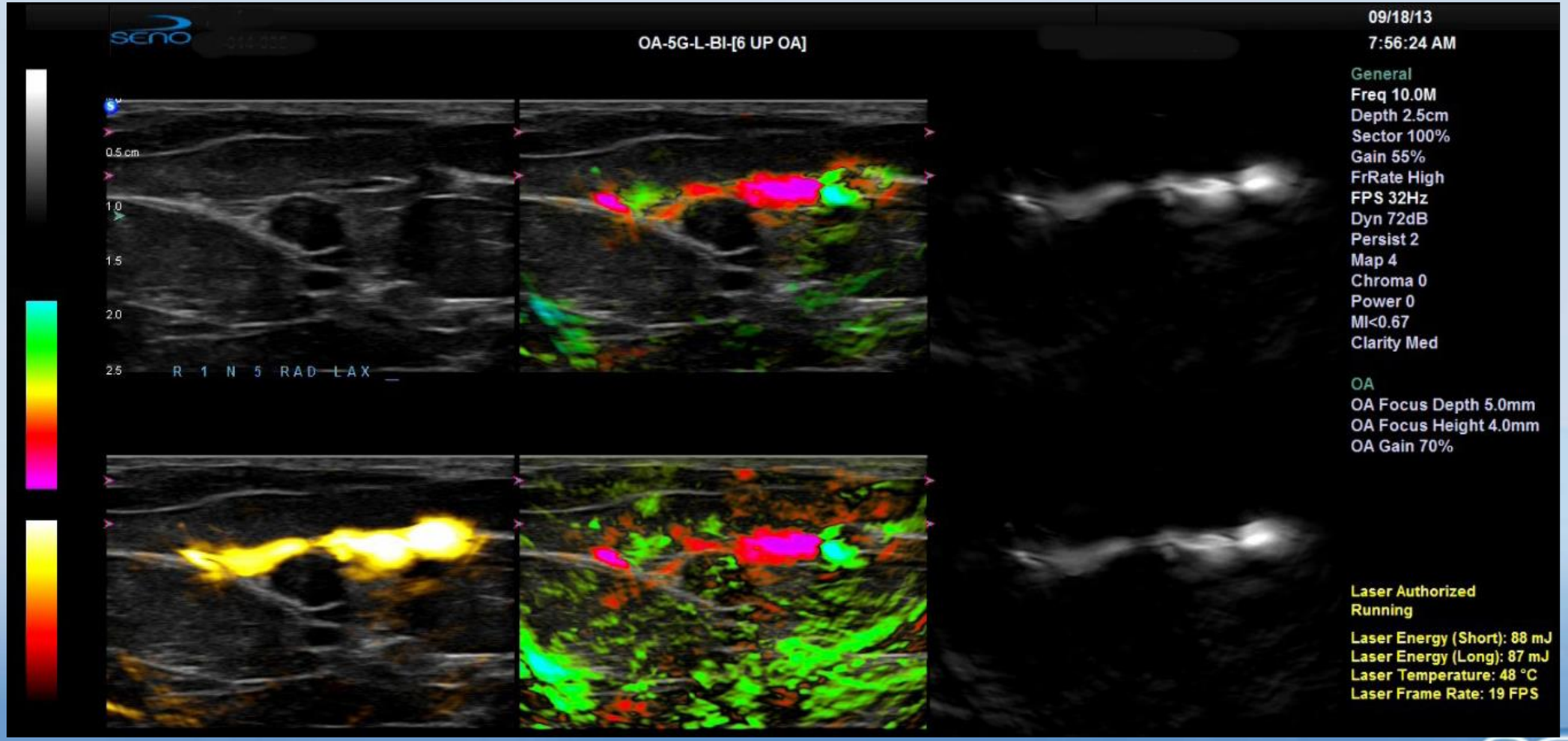


IMAGIO 6 UP IMAGE

Grade 1 Invasive Ductal Carcinoma



IMAGIO 6 UP IMAGE
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	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.