# Upclassification of Suspicious Breast Masses Using Opto-Acoustic Imaging

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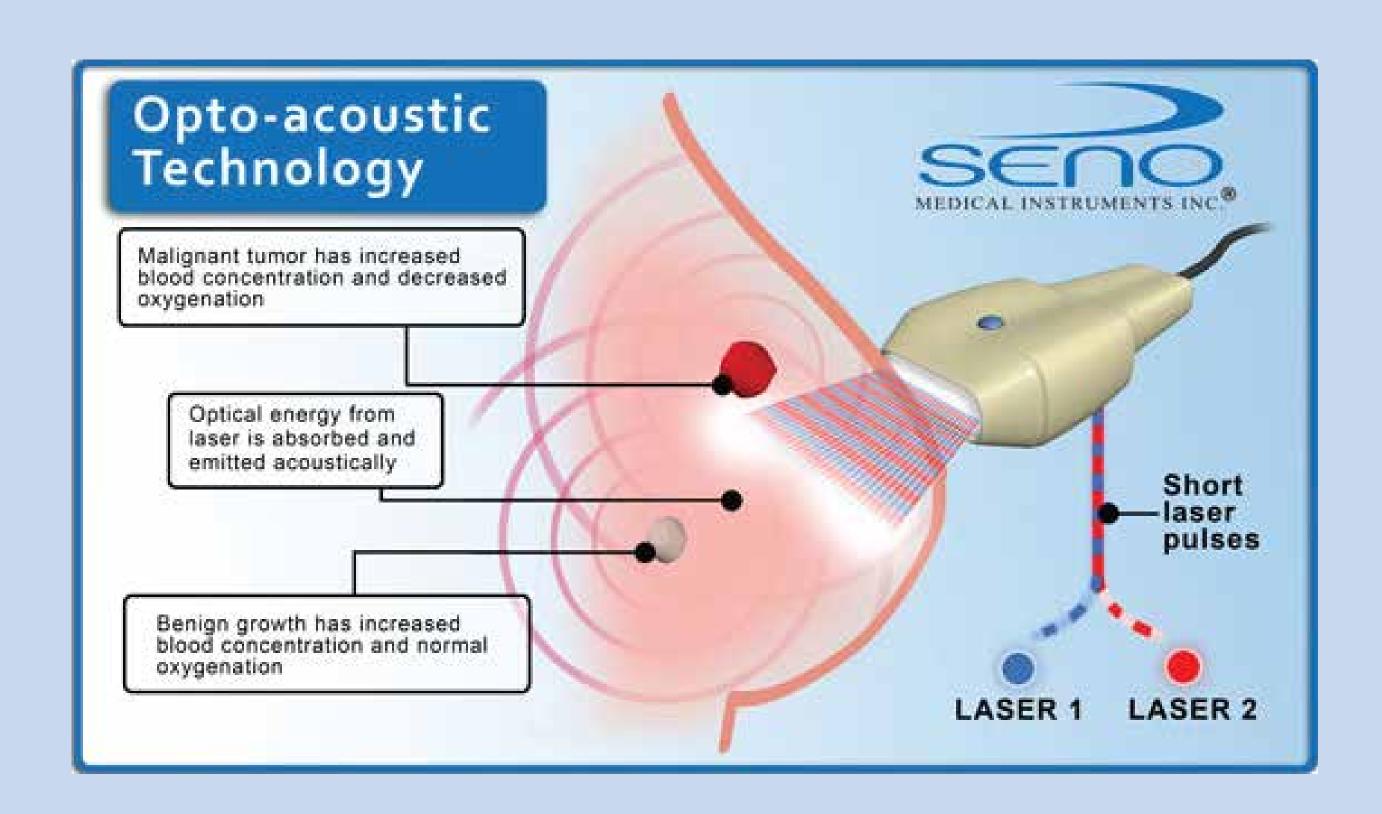
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## BACKGROUND

Imagio® (Seno Medical Instruments, Inc.) is currently an investigational medical device being tested in a Pivotal Study for FDA approval. Imagio is a fusion of dual wavelength laser opto-acoustics co-registered with B-mode gray-scale ultrasound and shows both structural and functional imaging information about potentially suspicious breast masses without the need for administering contrast agents, radionuclides, or exposing patients to x-irradiation. This fused imaging technology has been previously introduced in presentations at medical conferences. It may have the ability to increase both sensitivity and specificity of sonographically evident breast masses.

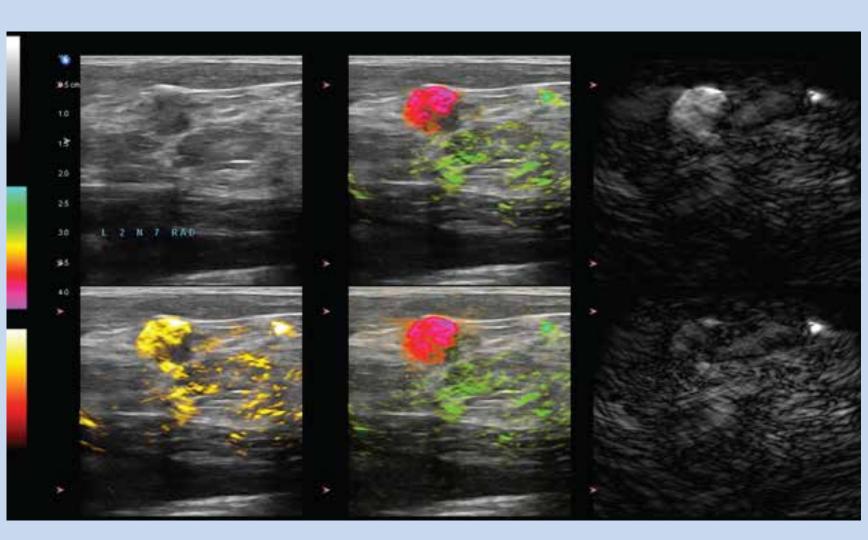
## OBJECTIVES

Breast cancer diagnostic methodologies have been optimized to achieve increased sensitivity at the expense of relatively low specificity. Seno Medical's opto-acoustic (OA) imaging fuses real time co-registered, temporally interleaved laser optic and ultrasound imaging showing dual functional (hemoglobin de-oxygenation) and morphology findings for breast masses using a hand-held probe. We present data from the PIONEER Pilot Study (n=100). We have shown improved specificity for OA relative to the ultrasound component (IUS) and the site determination by conventional diagnostic ultrasound (CDU). We now examine the BI-RADS upgrades for 36 malignant masses achieved by OA versus IUS and the site determinations using CDU.



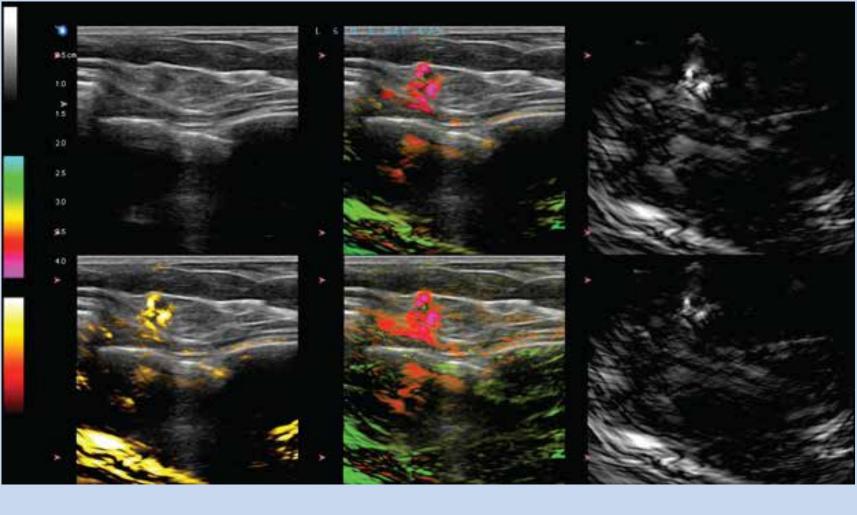
### METHODS

A total of 7 independent registration readers (IRRs) blindly assessed all 36 malignant masses using IUS first and OA second without any knowledge of clinical data or outcome. Among these masses, there were 2 Bl-RADS 4b, 12 Bl-RADS 4c, and 22 Bl-RADS 5 according to participating site radiologists' CDU evaluations. IRRs trained to identify and score three OA internal features and two OA external features for all masses were immediately offered the results of two nomograms based on their OA feature scores to predict the Probability of Malignancy (POM), which was then used to assign a Bl-RADS category.



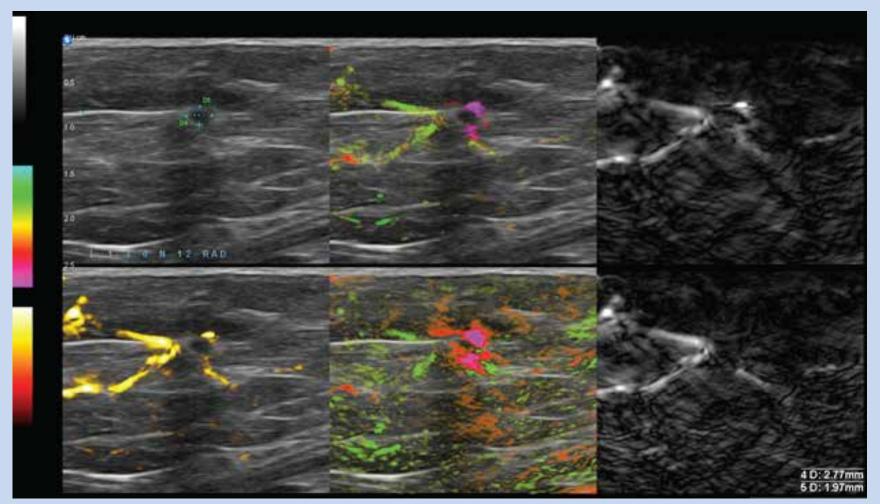
#### Figure 1 (002-011)

This 7 mm mass was classified as BI-RADS 4b by gray-scale ultrasound. OA shows primarily internal suspicious findings with absent peripheral findings. There is intense deoxygenated blush filling the central tumor nidus and the boundary zone. The mass was upgraded to BI-RADS 5 based upon the OA findings. The histology was grade 3 invasive papillary carcinoma. The appearance of primarily internal OA findings with relative paucity of peripheral findings is typical for grade 3 invasive breast carcinomas.



#### Figure 2 (001-011)

This 6 mm mass was classified BI-RADS 4a on gray-scale ultrasound. OA shows extensive de-oxygenated blush in the peripheral part of the nodule and within the boundary zone between the nodule and the surrounding tissue. The mass was upgraded to BI-RADS 4c based upon the OA findings. The center of the mass contains little hemoglobin or deoxygenation because of necrosis and/or fibrosis centrally. The histology showed grade 2 invasive duct carcinoma. The appearance of mixed internal and external findings is typical for grade 2 invasive breast carcinomas.



#### Figure 3 (014-025)

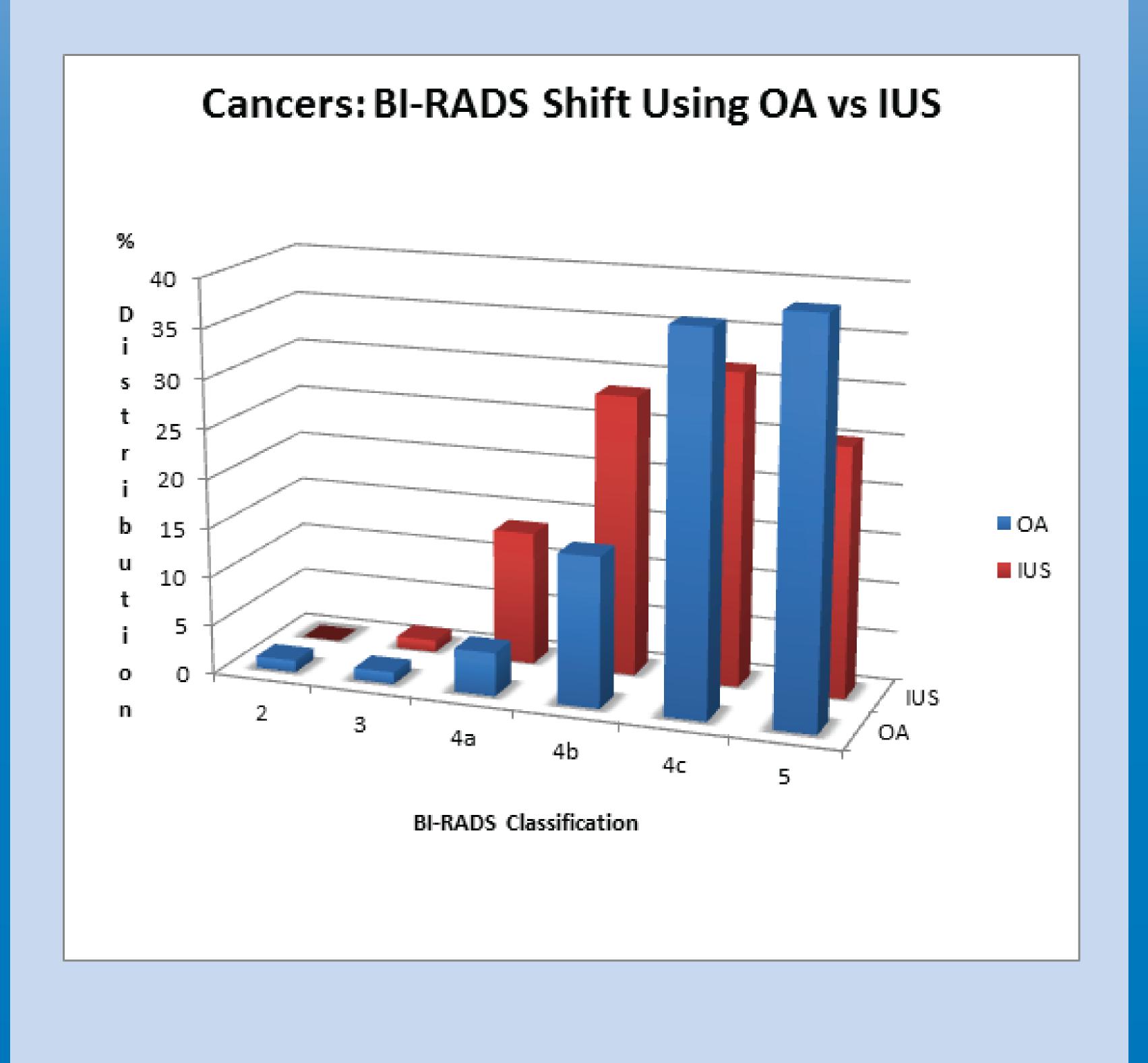
This 3 mm mass was classified as BI-RADS 4a by gray-scale ultrasound. Although masses generally do not develop neovascularity until at least 2 mm in maximum diameter, this mass has developed abundant external findings that are readily demonstrable by OA. Although we see no internal suspicious OA findings, there is a prominent deoxygenated blush in the boundary zone and there are easily appreciated exygenated peripheral radiating feeding parasitized native arteries on all 5 OA maps. The mass, despite its small size, shows OA findings over an area of several centimeters and was apgraded to BI-RADS 5 based upon OA findings. The histology was grade 1 invasive duct carcinoma. The appearance of primarily external peripheral suspicious OA findings with complete absence of internal findings is typical of grade 1 invasive breast carcinomas.

## RESULTS

Combining data from all 7 readers, OA findings enabled upgrades of site CDU-determined BI-RADS categories 43% of the time for BI-RADS 4b and 29% for BI-RADS 4c; in contrast, the overall percentages of IUS upgrades versus site CDU were 21% for BI-RADS 4b and 10% for BI-RADS 4c. Relative to IUS, the overall percentages of OA upgrades were 58% for BI-RADS 4b and 34% for BI-RADS 4c. When OA was added to IUS, there was a favorable shift towards declaring BI-RADS 5.

Overall, 12% of all OA reads resulted in upgrades in contrast to 4.4% for IUS alone with each compared to site CDU BI-RADS classifications.

OA and IUS had comparable sensitivity.



## CONCLUSIONS

OA was more likely than IUS to result in a BI-RADS upgrade of a malignant mass. When OA was added to IUS, there was a favorable shift towards declaring BI-RADS 5.

If subsequently confirmed, OA findings may help identify more cancers prior to biopsy. The 1,995 PIONEER Pivotal Study will potentially provide confirmation.

## CLINICAL RELEVANCE

The ability to upgrade BI-RADS 4b and 4c for cancer masses is an unmet need. If verified, these findings could provide additional evidence to confirm a malignant mass earlier and spare subsequent diagnostic evaluations. This may help plan the efficient identification and excision of malignant masses.

