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MAESTRO TRIAL – FINAL RESULTS

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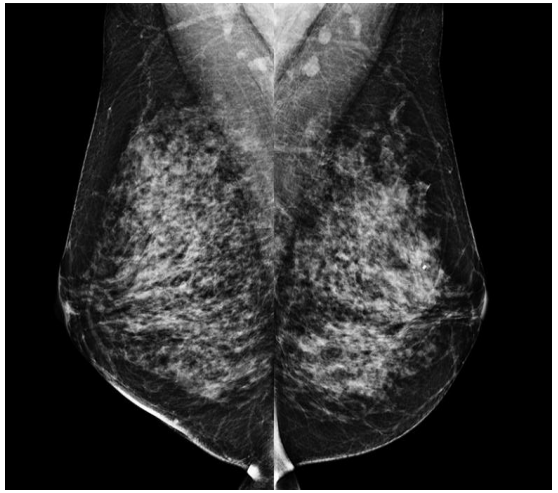
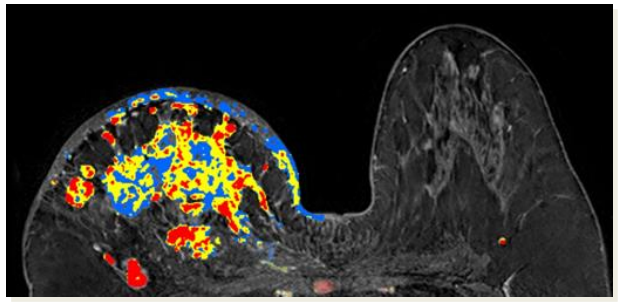
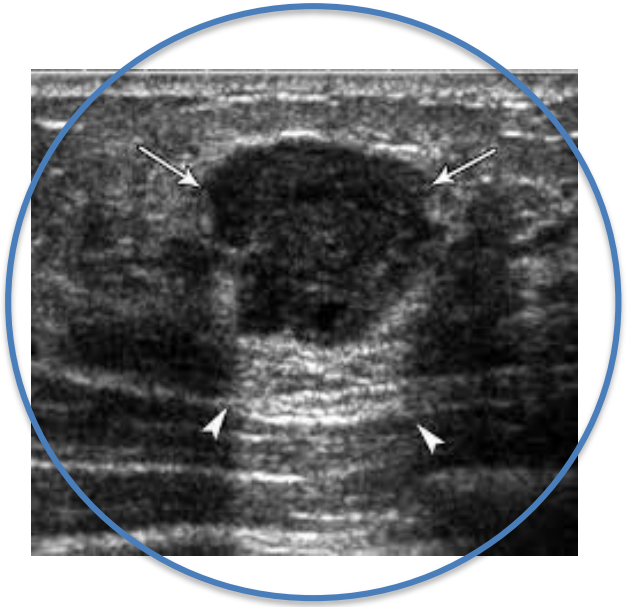
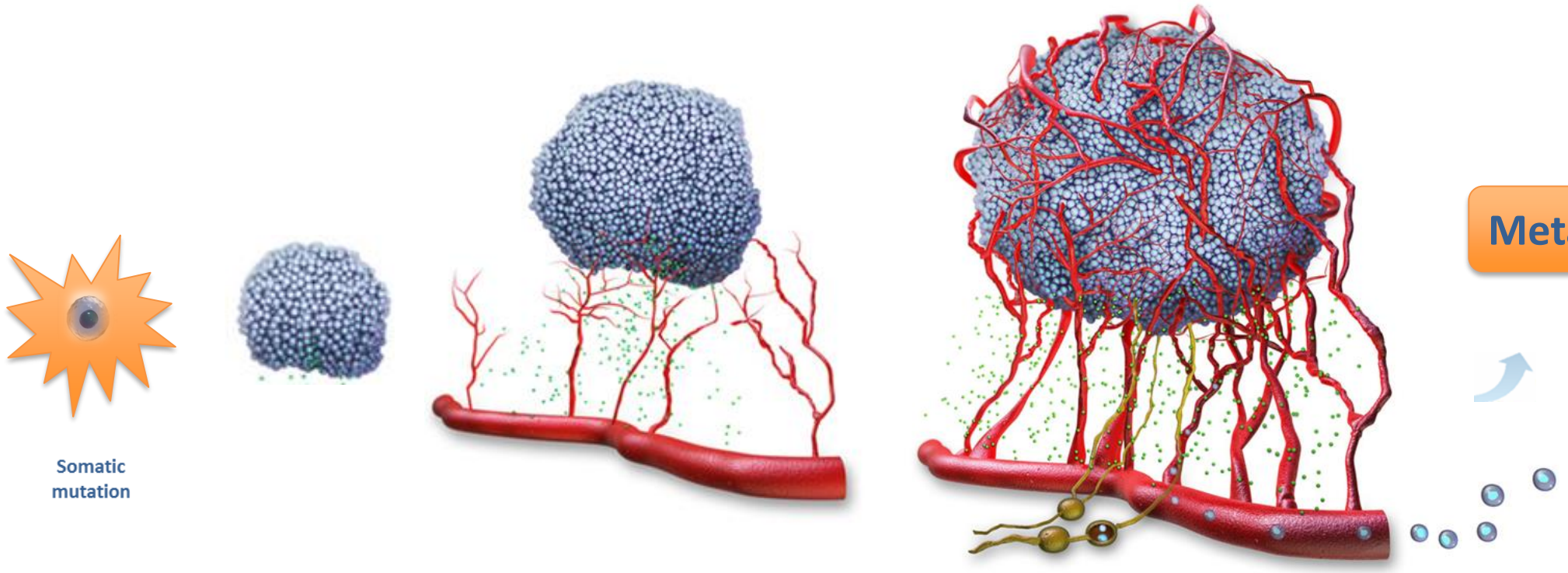
MAESTRO



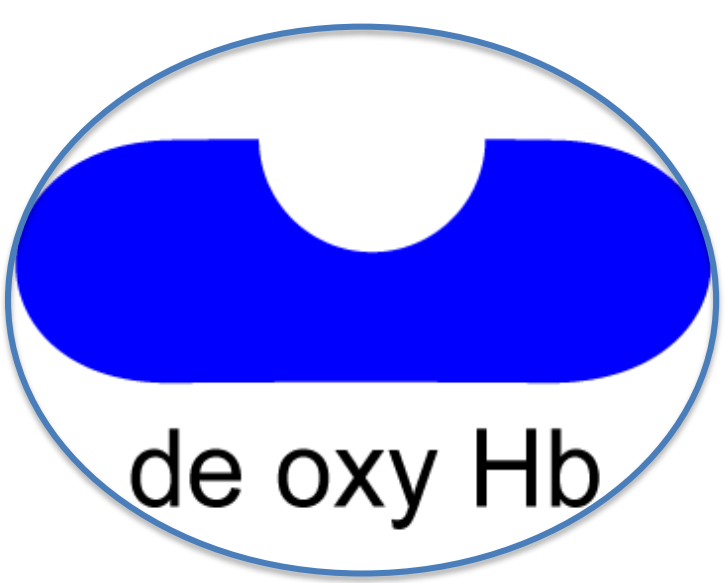




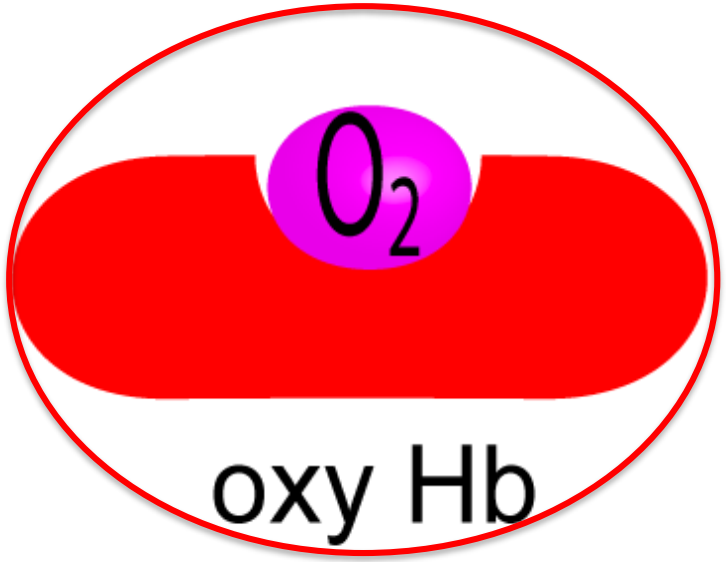
Angiogenesis



How does OA work?



Malignant



Benign

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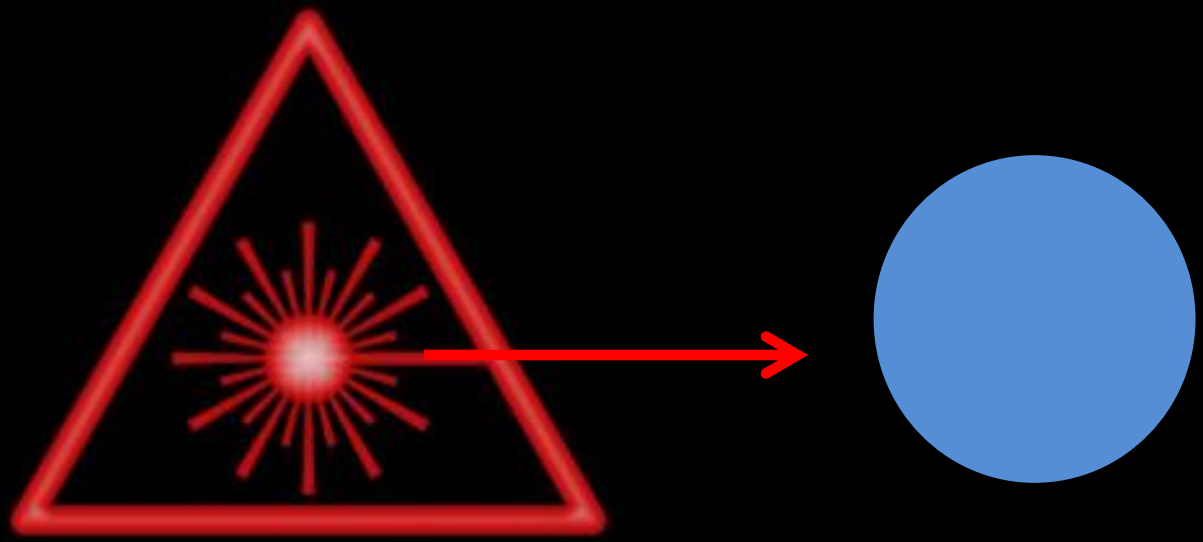

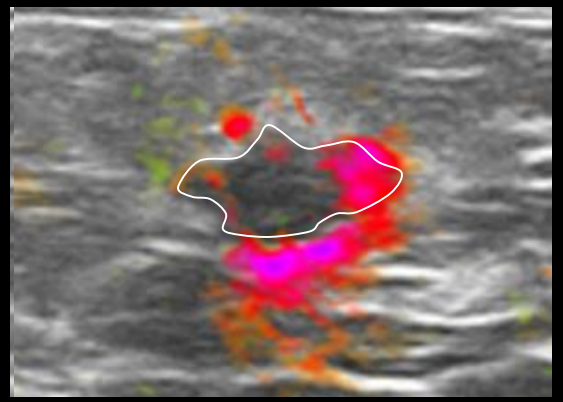

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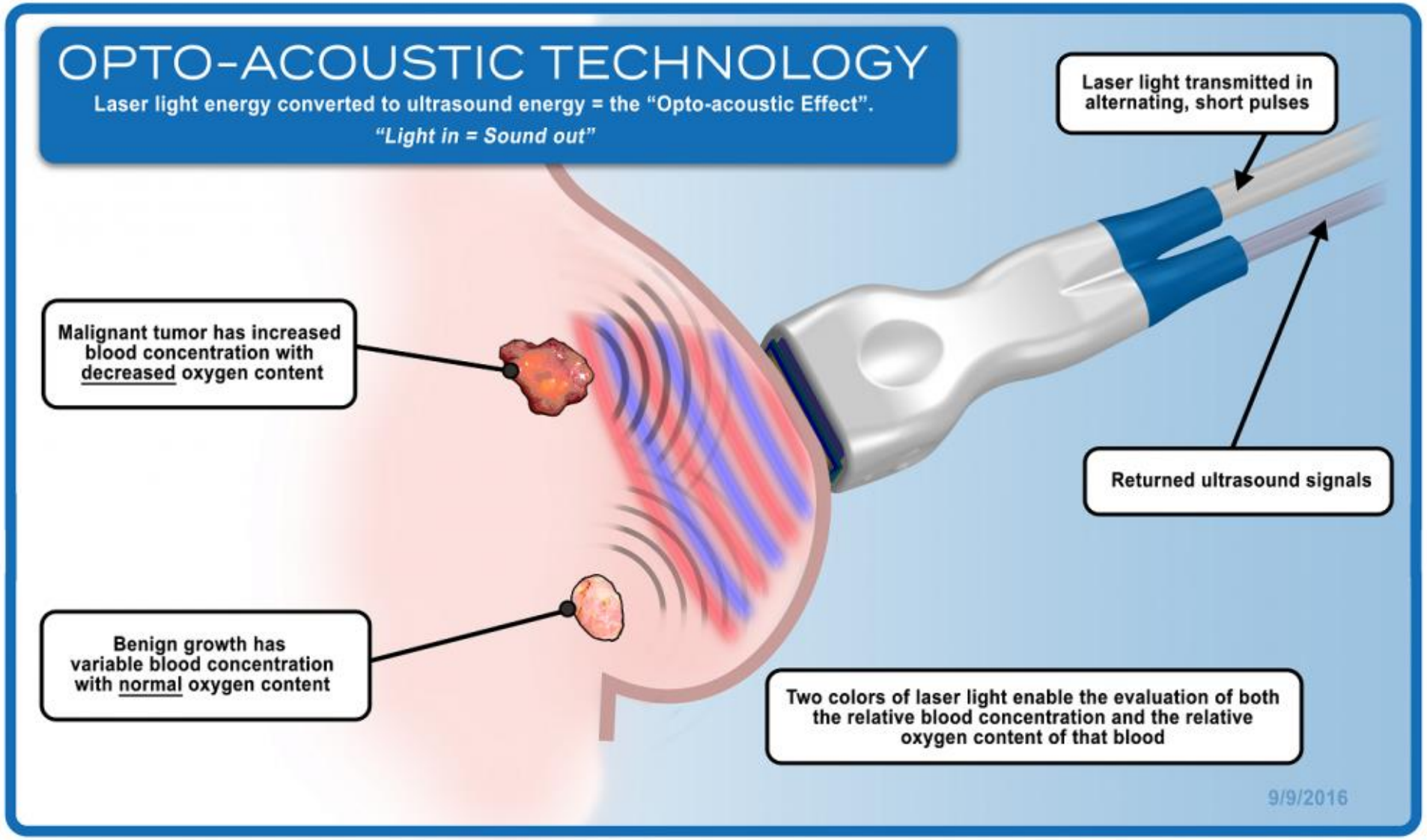
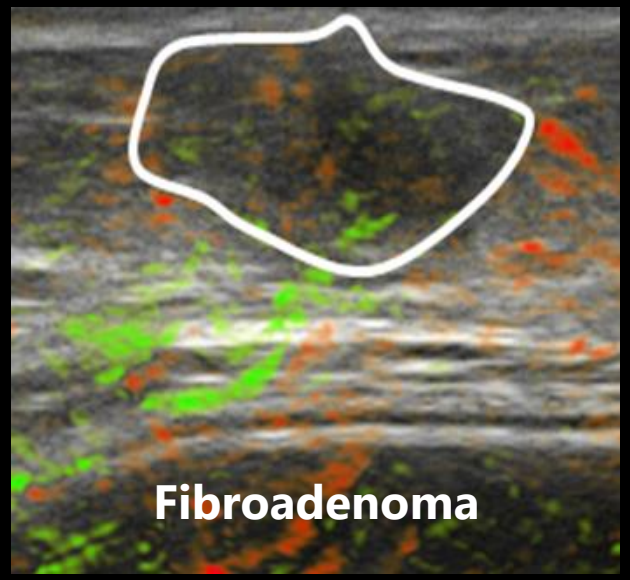
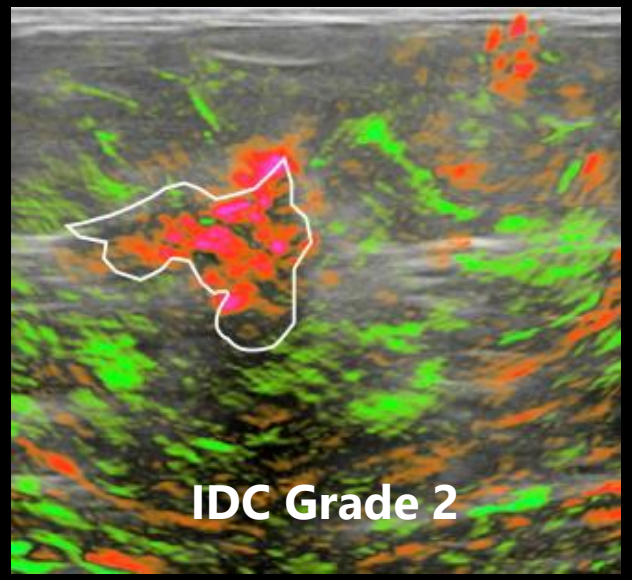


Optoacoustic Imaging





MAESTRO - Primary Objectives

- To assess OA/US's ability to correctly downgrade benign masses classified as BI-RADS 4a and 4b to BI-RADS 3 or 2.

- Sensitivity, specificity, PPV, NPV, positive likelihood ratio (PLR) and negative likelihood ratio (NLR) of CDU and OA/US.

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Why BI-RADS 4a and 4b?

Category	Definition	Probability of Malignancy
0	Needs additional imaging evaluation	NA
1	Normal mammography – back to screening program	0%
2	Benign findings – back to screening program	0%
3	Probably benign – 6-month interval follow-up	≤ 2%
4	Suspicious abnormality – tissue diagnosis (biopsy)	4a. Low POM (>2% to ≤ 10%) 4b. Moderate POM (>10% to ≤ 50%) 4c. High POM (> 50% to < 95%)
5	Highly suggestive of malignancy – tissue diagnosis (biopsy)	≥ 95%
6	Known biopsy-proven malignancy	NA

Study Design

- **Prospective, multicenter, and observational study.**

- **Based on images obtained with OA/US, investigators estimated the probability of malignancy (POM) on a scale from 0% to 100% and, when appropriate, adjusted the BI-RADS classification.**

Study Design

- Five OA features were scored (downgrade or upgrade the lesion classification).
- 140 benign and 70 malignant masses were projected.
- Power>80% (2% Type I error).
- Sensitivity and specificity for CDU and OA were calculated. PLR and NLR were also calculated.

Results: BI-RADS classification of benign lesions according to CDU and OA (n=146)

	CDU BI-RADS	
OA BI-RADS	4a (N=119)	4b (N=27)
2	8 (6.7%)	0
3	49 (41.2%)	3 (11.1%)
4a	44 (37.0%)	3 (11.1%)
4b	18 (15.1%)	11 (40.7%)
4c	0	9 (33.3%)
5	0	1 (3.7%)
Downgrade CDU BI-RADs (4a, 4b) to OA BI-RADs (2, 3):		
Downgrade [n/N (%)]	60/146 (41.1%)	
96% CI	(32.7, 49.4)	
P-value [null hypothesis is ≤ 15%]	< 0.0001	

Results: BI-RADS classification of malignant lesions according to CDU and OA (n=67)

	CDU BI-RADS	
OA BI-RADS	4a (N=7)	4b (N=60)
2	1 (14.3%)	0
3	1 (14.3%)	1 (1.7%)
4a	4 (57.1%)	6 (10.0%)
4b	1 (14.3%)	21 (35.0%)
4c	0	30 (50.0%)
5	0	2 (3.3%)
Downgrade CDU BI-RADs (4a, 4b) to OA BI-RADs (2, 3):		
Downgrade [n/N (%)]	3/67 (4.5%)	
96% CI	(0.9, 13.0)	
p-value [null hypothesis is ≥ 10%]	0.0872	

Results

- CDU sensitivity $= \frac{TP}{TP+FN} = \frac{67}{67} = 100\%$
- CDU Specificity $= \frac{TN}{TN+FP} = \frac{0}{146} = 0\%$
- OA sensitivity $= \frac{TP}{TP+FN} = \frac{64}{67} = 95.5\%$
- OA Specificity $= \frac{TN}{TN+FP} = \frac{60}{146} = 41.1\%$
- OA without the estimator : PPV was 42.7% and NPV was 95.2%. PLR was 1.61 and NLR was 0.11

Discussion

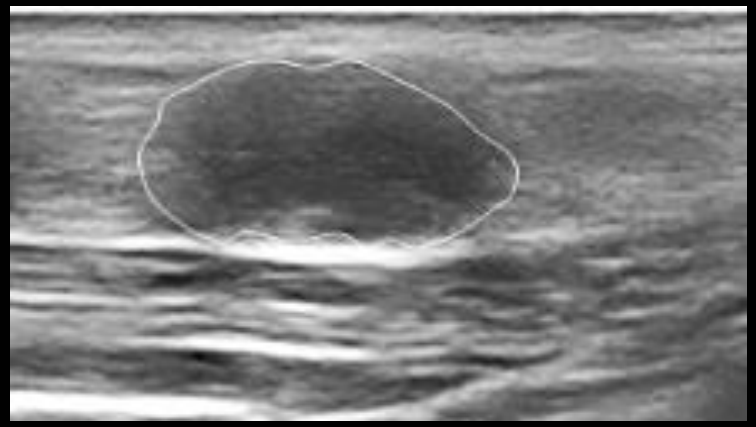
- NLR of 0.11 - post-test probability lower than the pre-test probability.
- BI-RADS 3 (benign) has a very low POM (≤ 2%).
- The POM of BI-RADS 4a varies from >2% to ≤10%.
- A NLR of 0.11 shows that a pre-test probability at the upper end of a 4a lesion (≈10%) can be reduced to a post-test probability of 1.1% by a negative OA examination, allowing the lesion to be downgraded from BI-RADS 4a to 3.

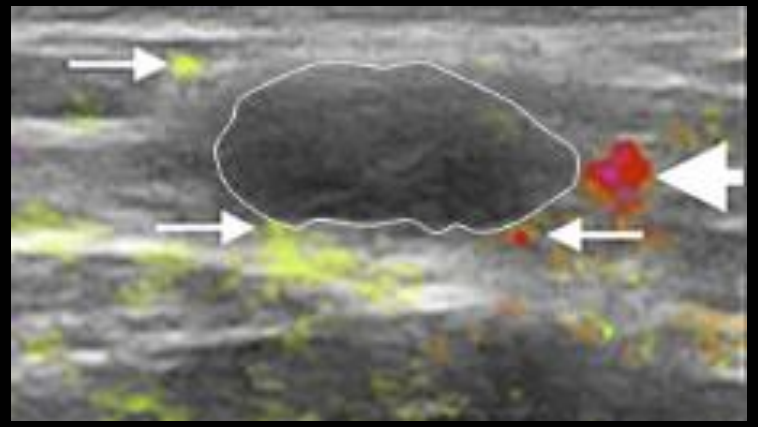
Discussion

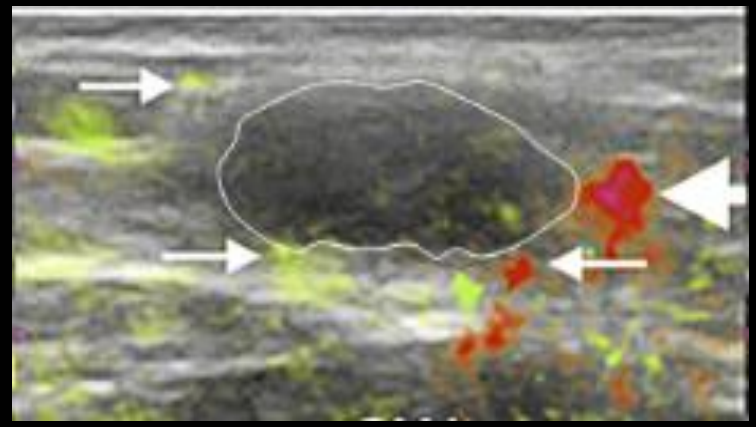
- BI-RADS lexicon: Categories 1 or 2 are typically benign (virtually 0% chance of malignancy).
- In 8 cases benign masses were downgraded from BI-RADS 4a to BI-RADS 2.
- The lower end of BI-RADS 4a range (≈2%) can be reduced to a post-test probability of only 0.22%.
- The PPV of category 4b varies from from >10% to ≤50%.
- Considering category 4b, a mass with a pre-test probability of 15.6% could be downgraded to BI-RADS 3 (2 categories downgrade). However, lesions with a higher probability of malignancy cannot be downgraded without increasing the FN rates.

Conclusions

- **41.1%** of benign masses could be **downgraded** in BIRADS category using OA/US.

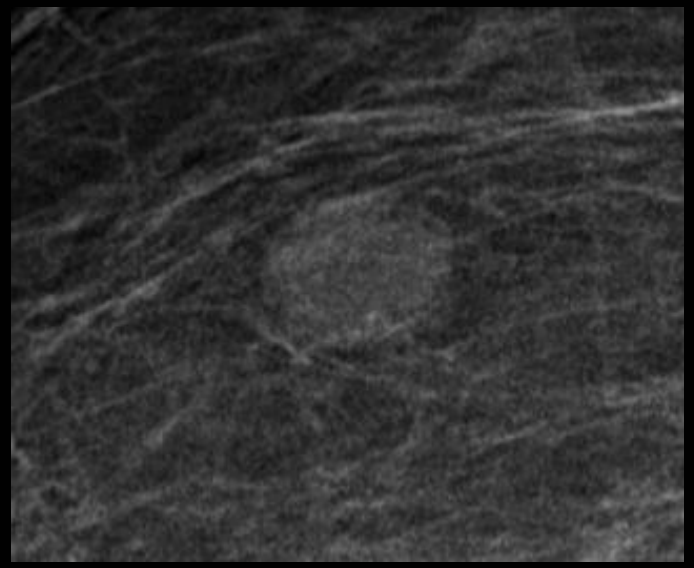


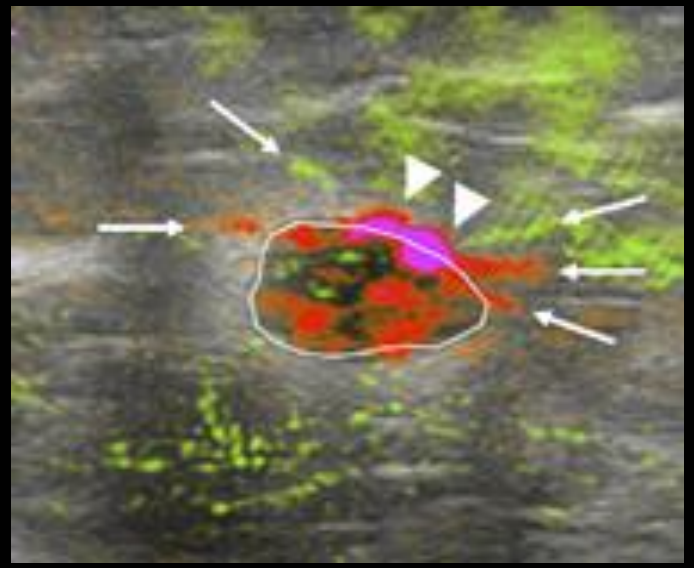




Conclusions

- **49.2%** of malignant masses could be **upgraded** with OA/US.

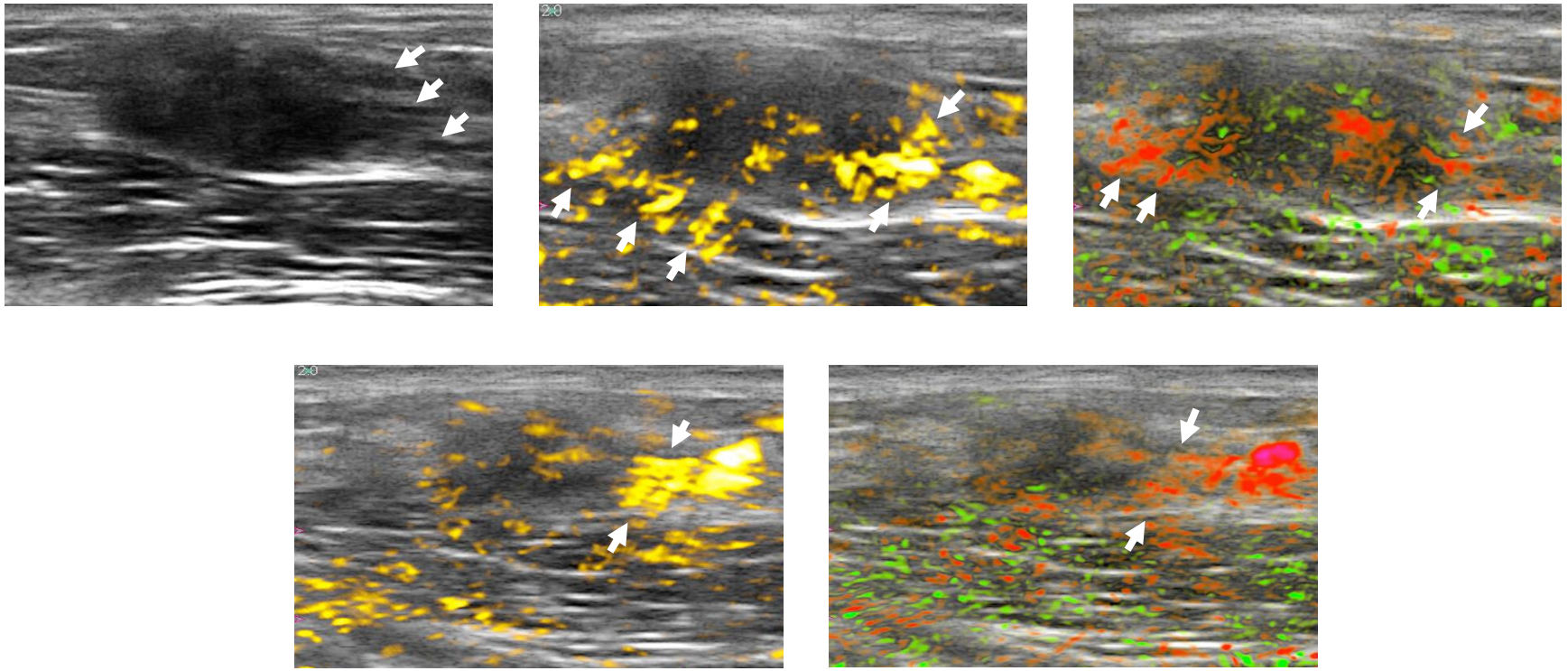




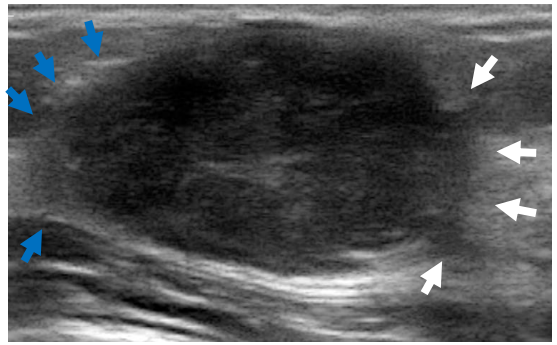
Conclusions - Implications for patient care

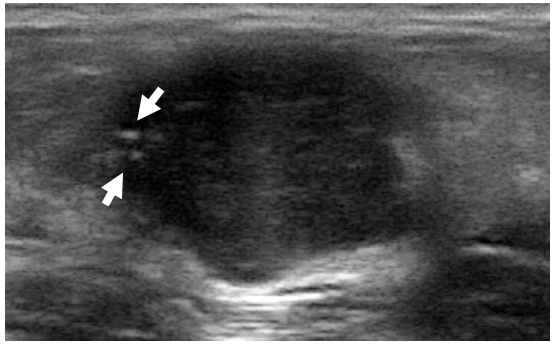
- OA improves the distinction between benign and malignant masses compared to CDU alone.
- Benign masses classified as BI-RADS 4a can be downgraded to BI-RADS 3 or 2, potentially minimizing negative biopsies and short interval follow-up imaging exams.
- Potential to lower overall costs related to interventional procedures and short-interval follow-up imaging studies.
- Limitations: 3 false-negatives.

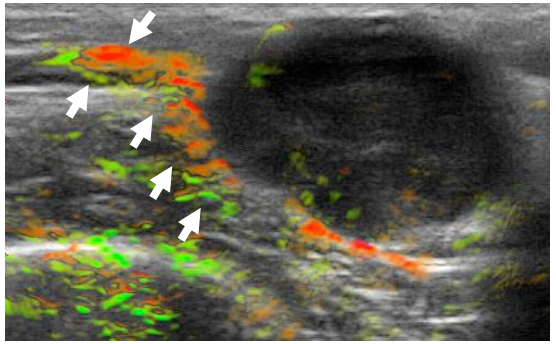
First false-negative mass: an IDC grade 1 which was downgraded from BI-RADS 4b to BI-RADS 2

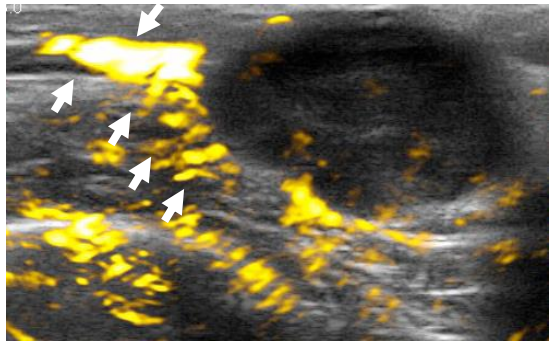


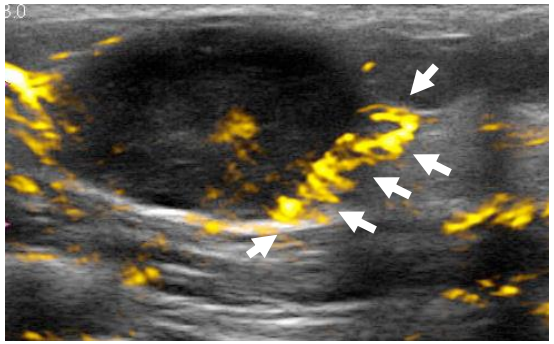
Second false-negative mass: an IDC grade 3 which was downgraded from BI-RADS 4a to BI-RADS 2



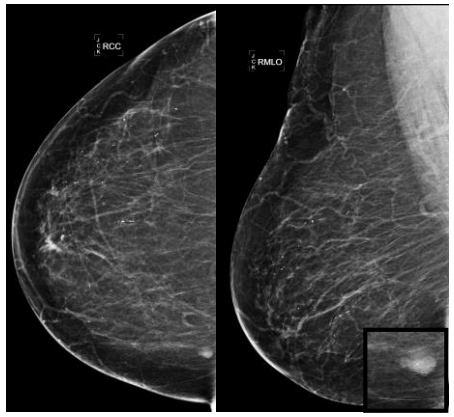


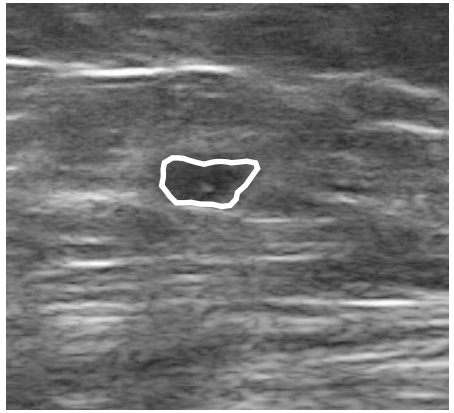


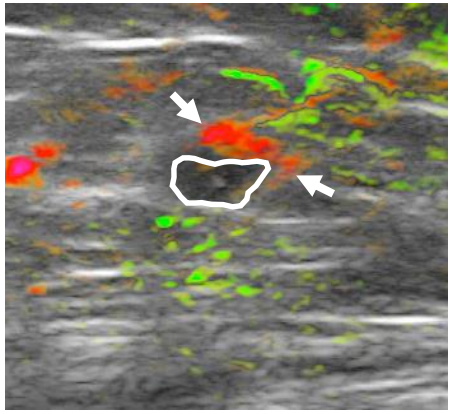


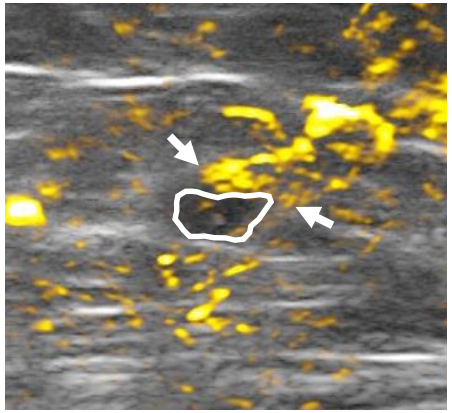


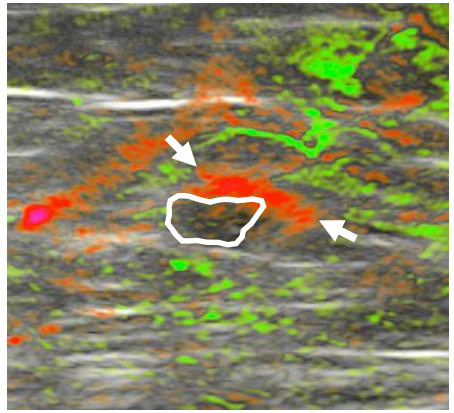
Third false-negative mass: an ILC grade 2 (alveolar variant) which was downgraded from BI-RADS 4a to BI-RADS 3









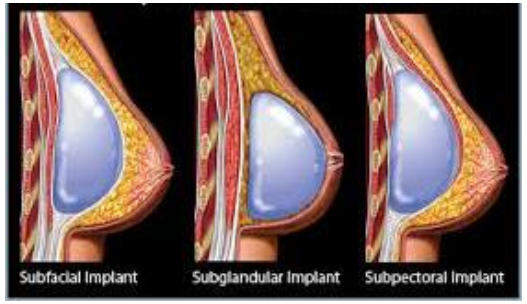


Inclusion Criteria

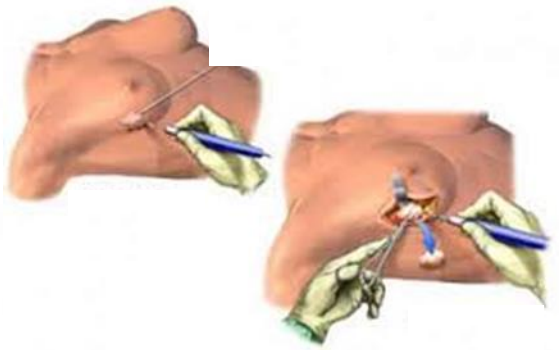
- Females ≥ 18 years.
- Have a suspicious finding classified by CDU as BI-RADS 4a or 4b.
- Have received recommendation for an image-guided biopsy.

Exclusion Criteria

- Has a condition that could interfere with the intended field of view (breast implants or tattoos).



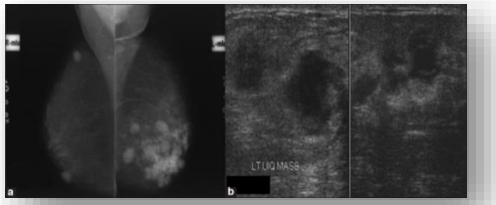
- Prior surgery within the same quadrant as the mass to be biopsied.



- Have had prior excisional biopsy within the vicinity of the suspicious mass within the past 18 months.

Exclusion Criteria

- More than 3 masses recommended for biopsy.
- Mass to be biopsied is greater than 3.0 cm in maximum diameter.
- Patient currently has mastitis.
- Patient is pregnant or lactating or planning to become pregnant during study participation.



Likelihood Ratios

- Likelihood ratios are important to assess the value of performing a diagnostic test.
- $PLR = \frac{sensitivity}{1 - specificity}$
- $NLR = \frac{1 - sensitivity}{specificity}$
- The larger the PLR, the greater the likelihood of disease; the smaller the NLR, the lesser the likelihood of disease.
- These rates are less likely to change with the prevalence of the disorder.
- To use this measure a nomogram (estimators) should be employed or pre-test probabilities should be converted into Odds.