

Locoregional Treatment of Breast Cancer

Session 6: Growth Areas in IO

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Disclosures

- Consultant — Hologic, Inc.

Outline

- Justification for locoregional treatment of breast cancer
- Approach
- Cryo-immune effects
- Remaining issues

Justification for Locoregional Treatment of Primary Breast Cancer

- Increase in screening – increase in incidence of breast cancer < 2 cm
- Evolution of breast cancer surgery – similar recurrence rates, improved cosmesis
- Evolution in assessment of margins – “tumor on ink” for invasive cancer, 2 mm for DCIS

Why Ablation?

- Less invasive than surgery
- Less morbidity
- Less mortality
- Better cosmesis

Cryoablation – ACOSOG Z-1072

- Multicenter phase II trial
- 87 cancers treated with cryoablation followed by surgery
- 100% of patients with tumors less than 1 cm in size treated with cryoablation had no residual invasive cancer on pathologic examination of the specimen

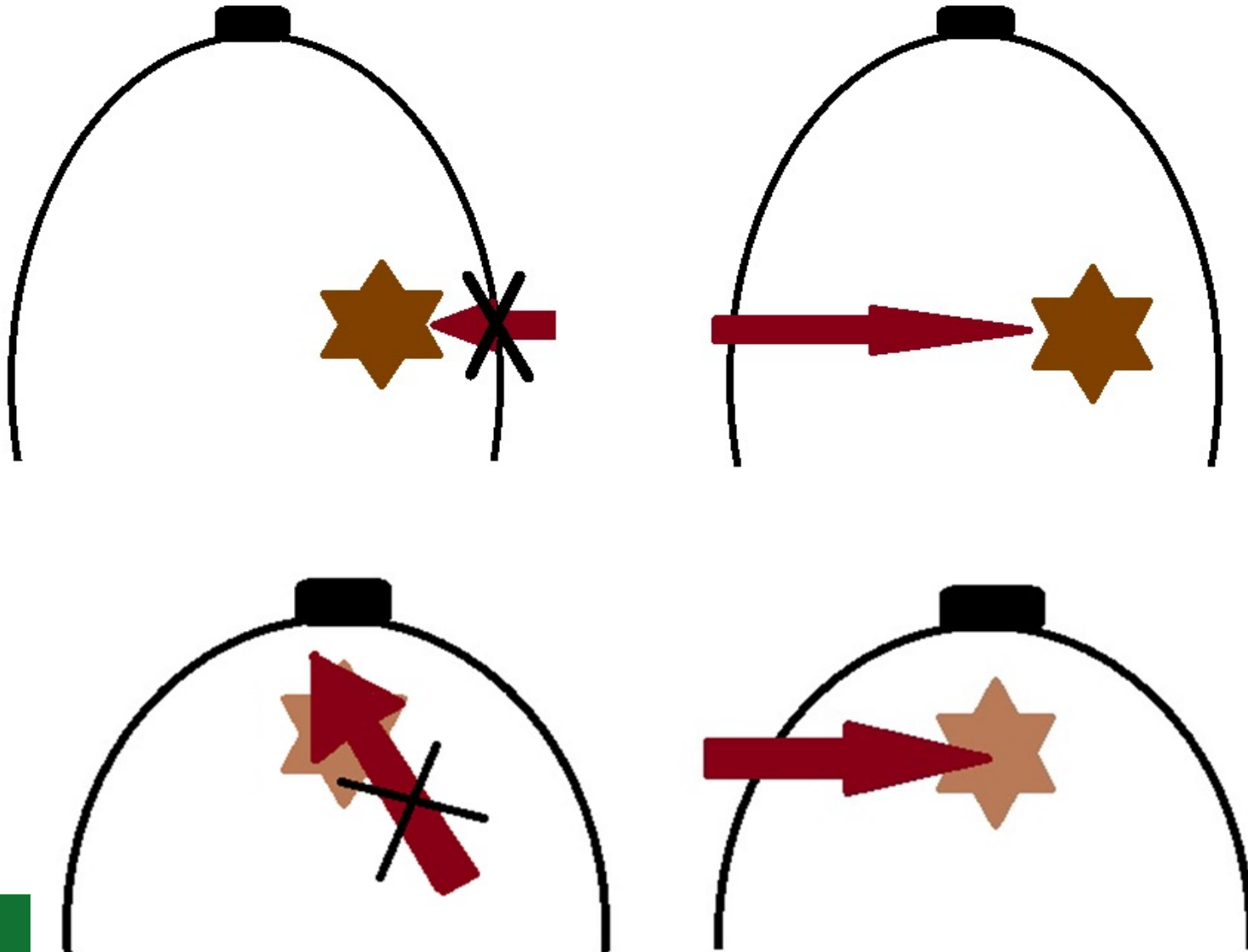
Littrup, et al. 2009

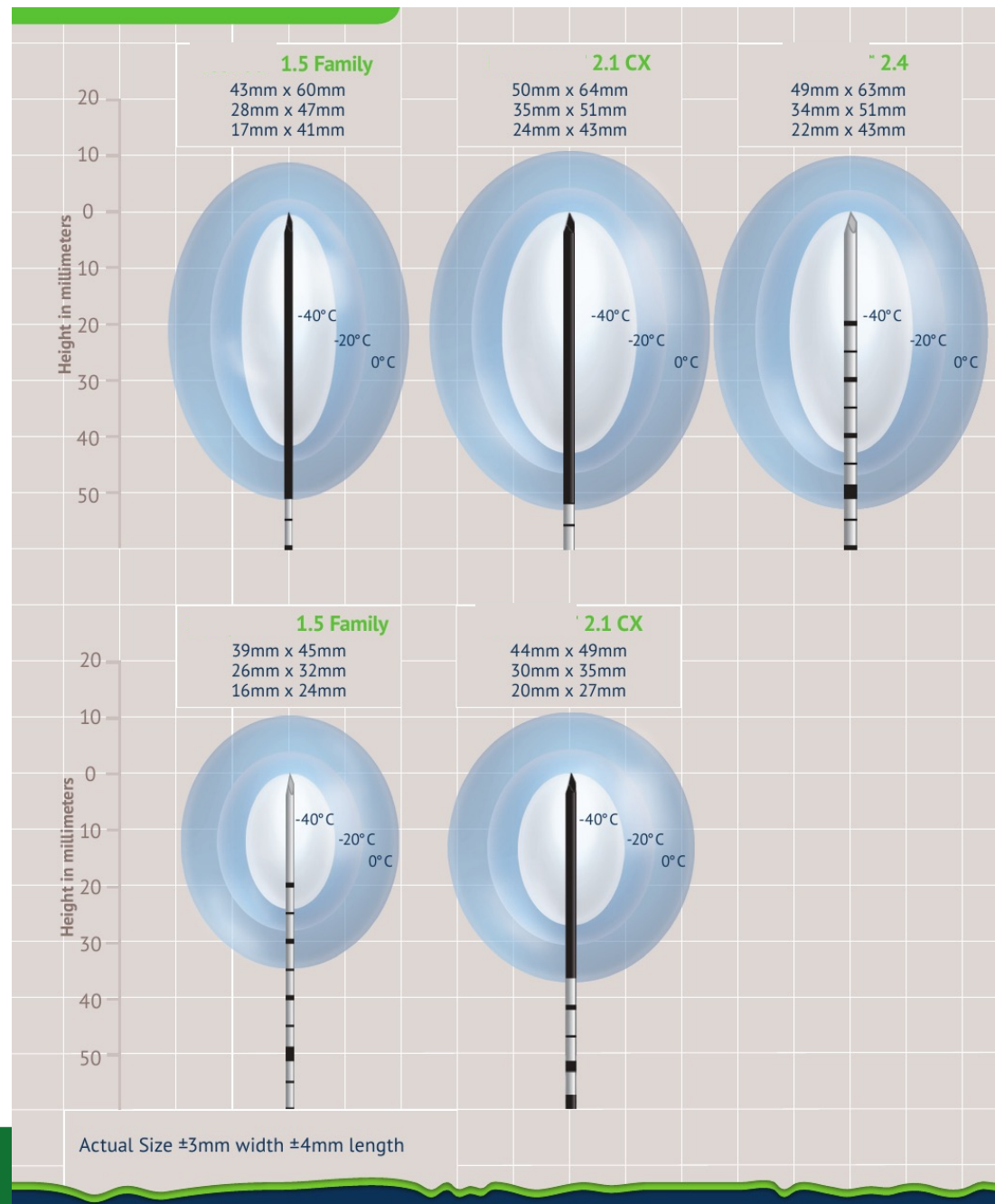
- Tumors ranging from 0.5-5.8 cm (average 1.7 cm \pm 1.2)
- Treated with multiprobe cryoablation
- Biopsies performed at the margins of the cryoablation site immediately after cryoablation and at follow-up
- No local recurrences at an average follow-up of 18 months

Choosing the right lesion

- Small, ideally $< 1\text{-}2$ cm
- No extensive intraductal component
- Not too close to the skin, ideally $> 0.5\text{-}1$ cm

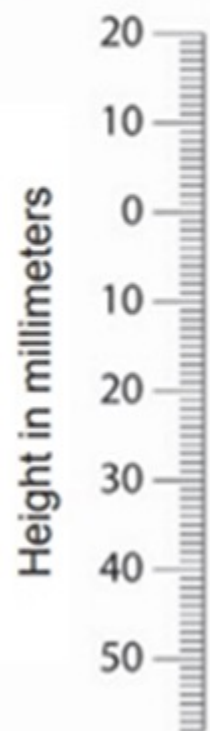
Planning





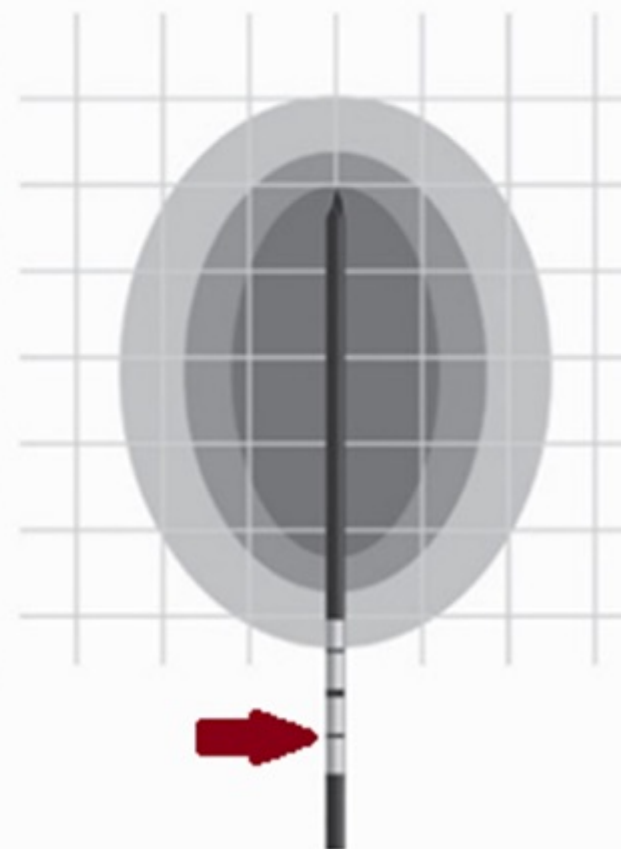
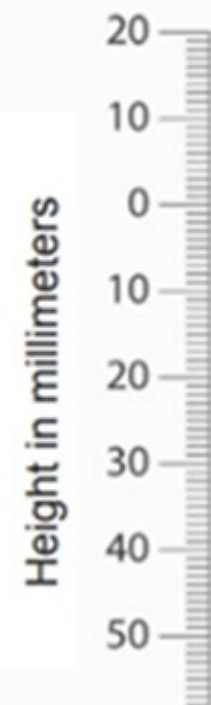
0° C
-20° C
-40° C

44 mm x 49 mm
30 mm x 35 mm
20 mm x 27 mm

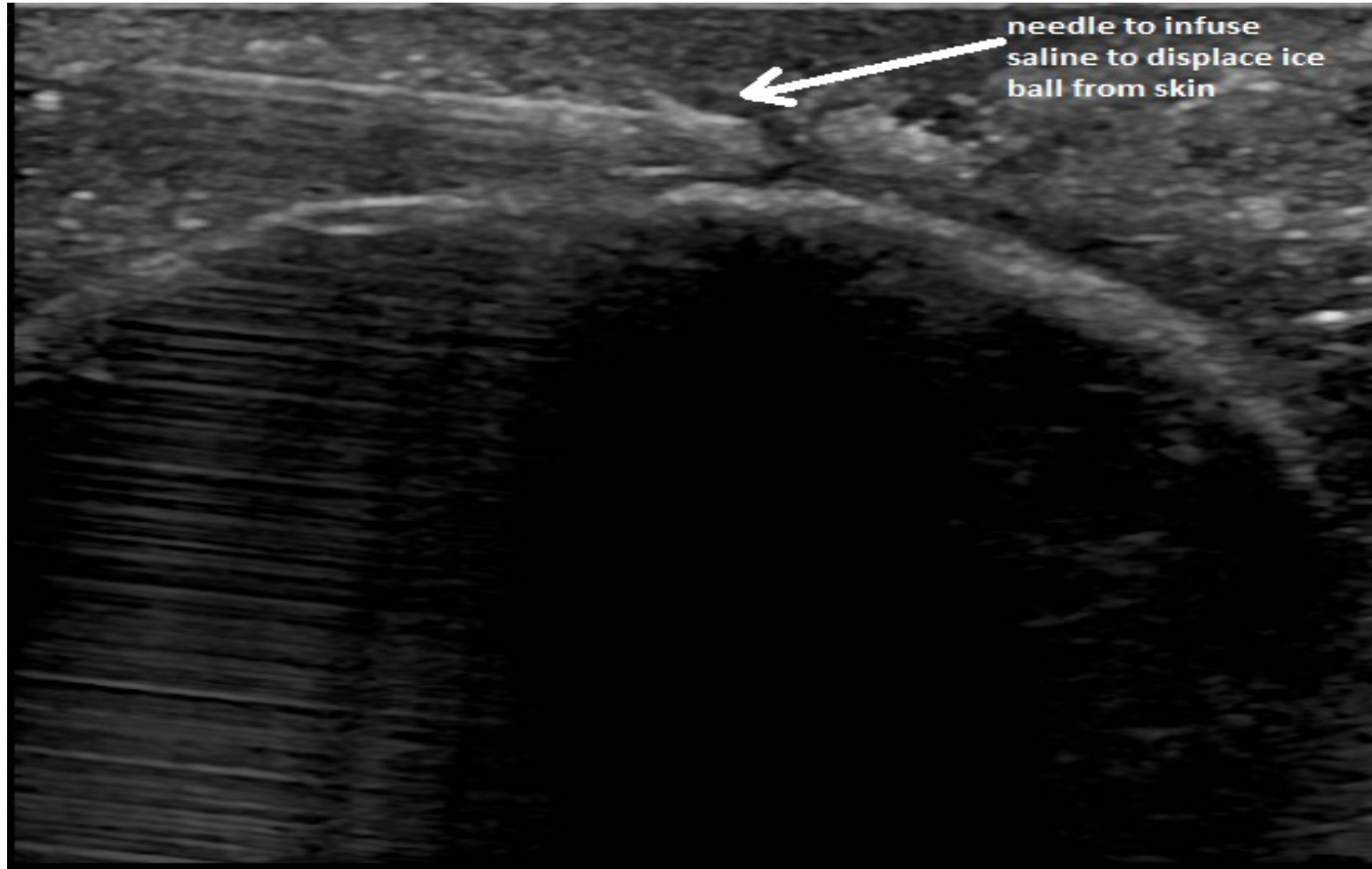


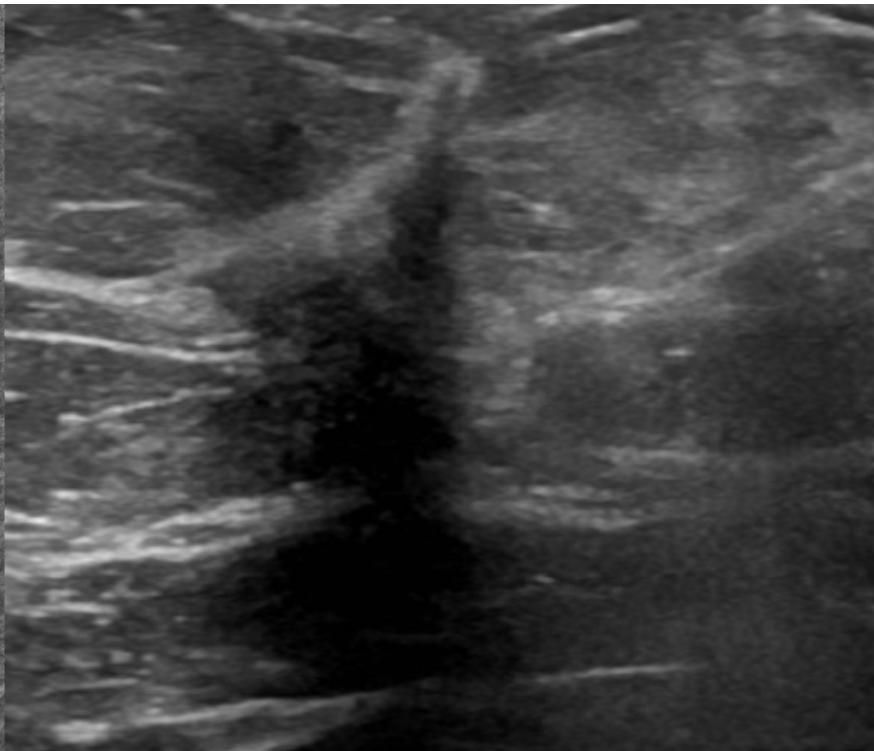
0° C
-20° C
-40° C

50 mm x 64 mm
35 mm x 51 mm
24 mm x 43 mm

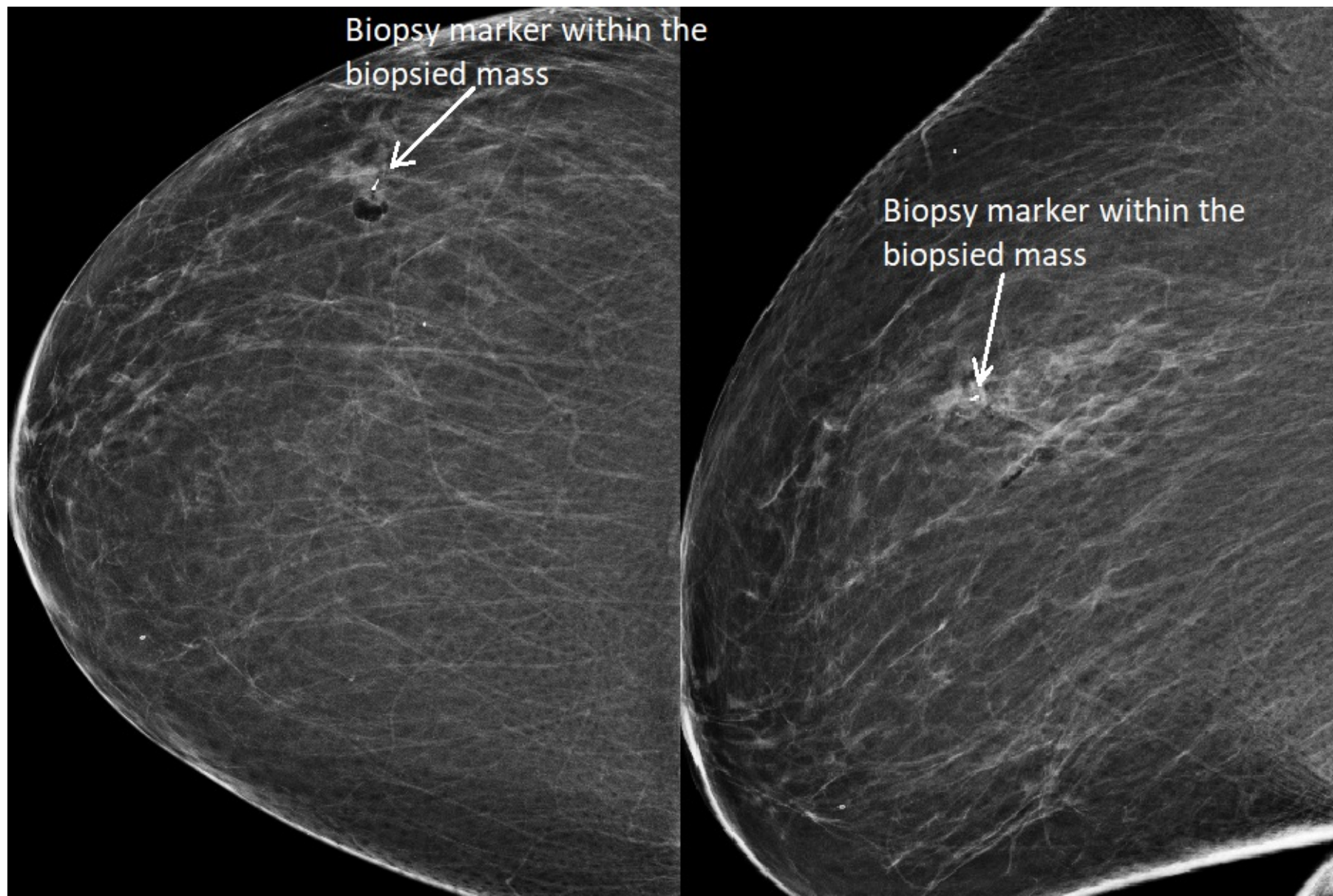


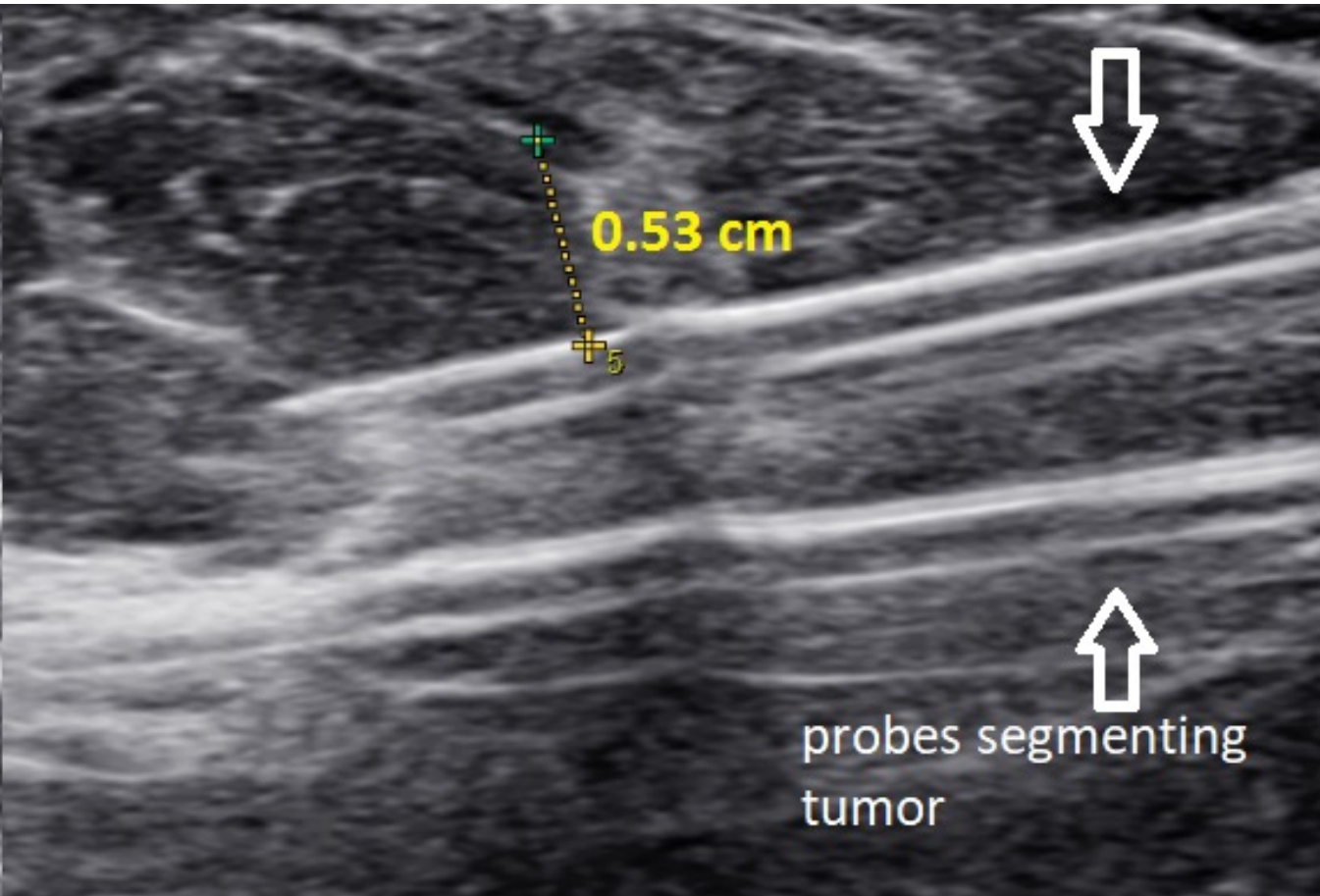
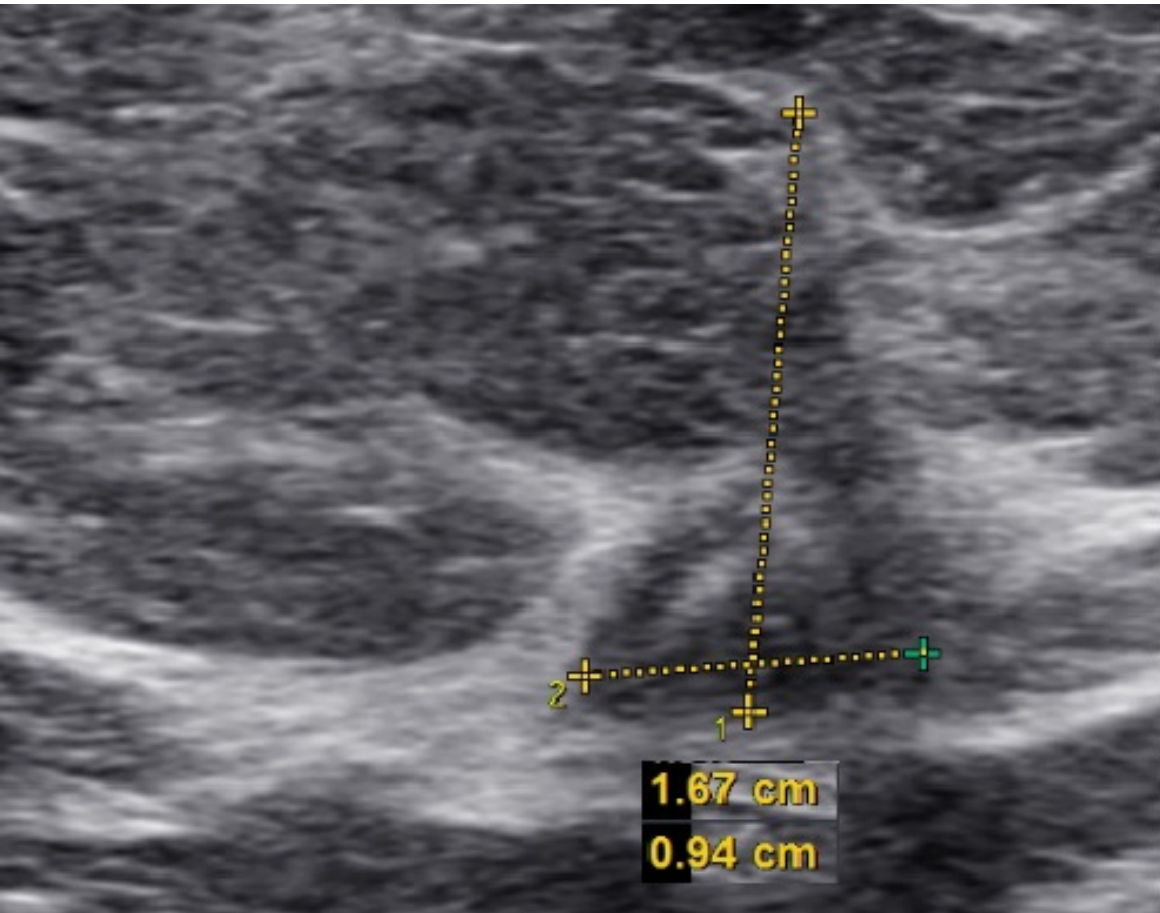
Protecting the skin

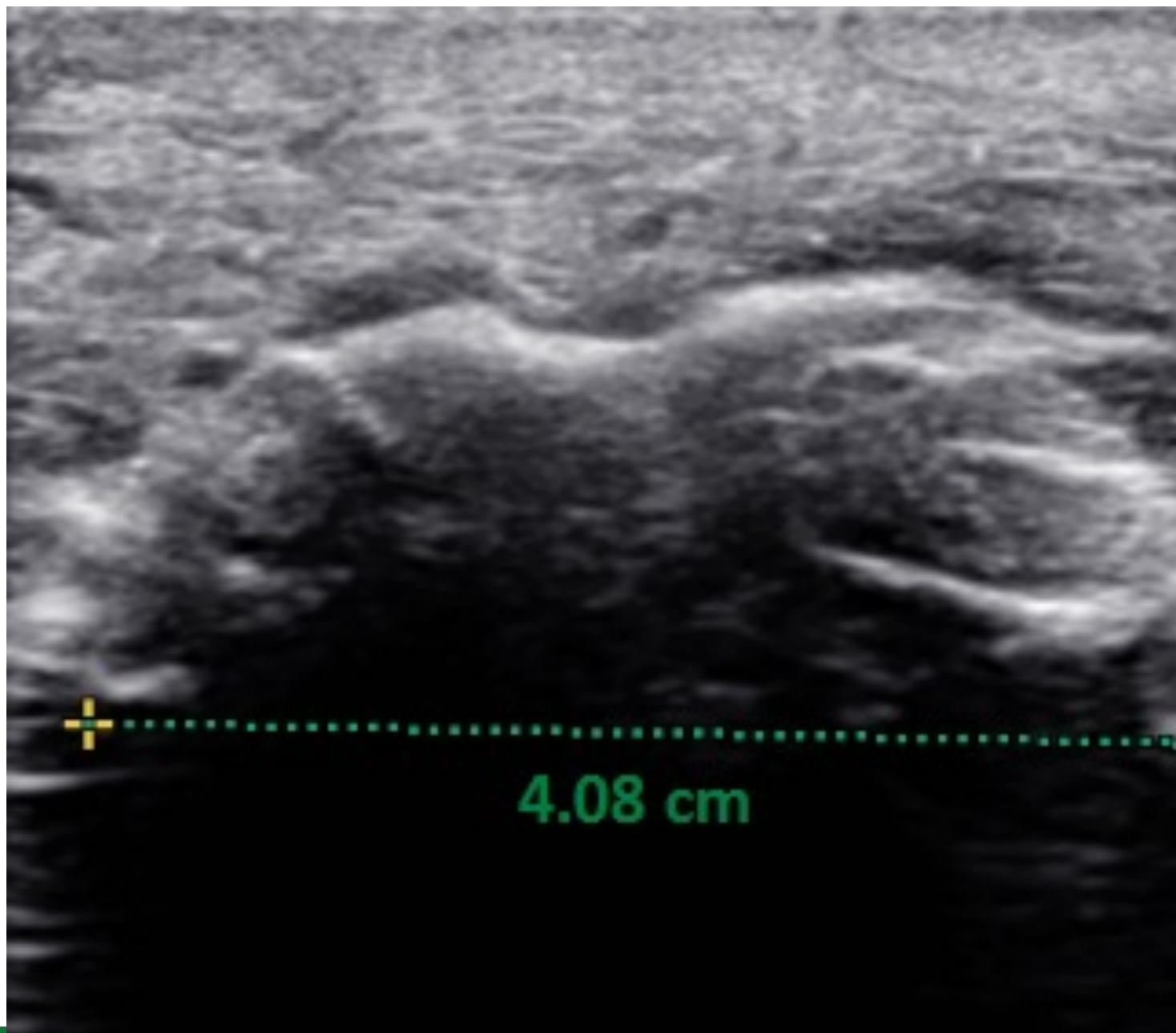


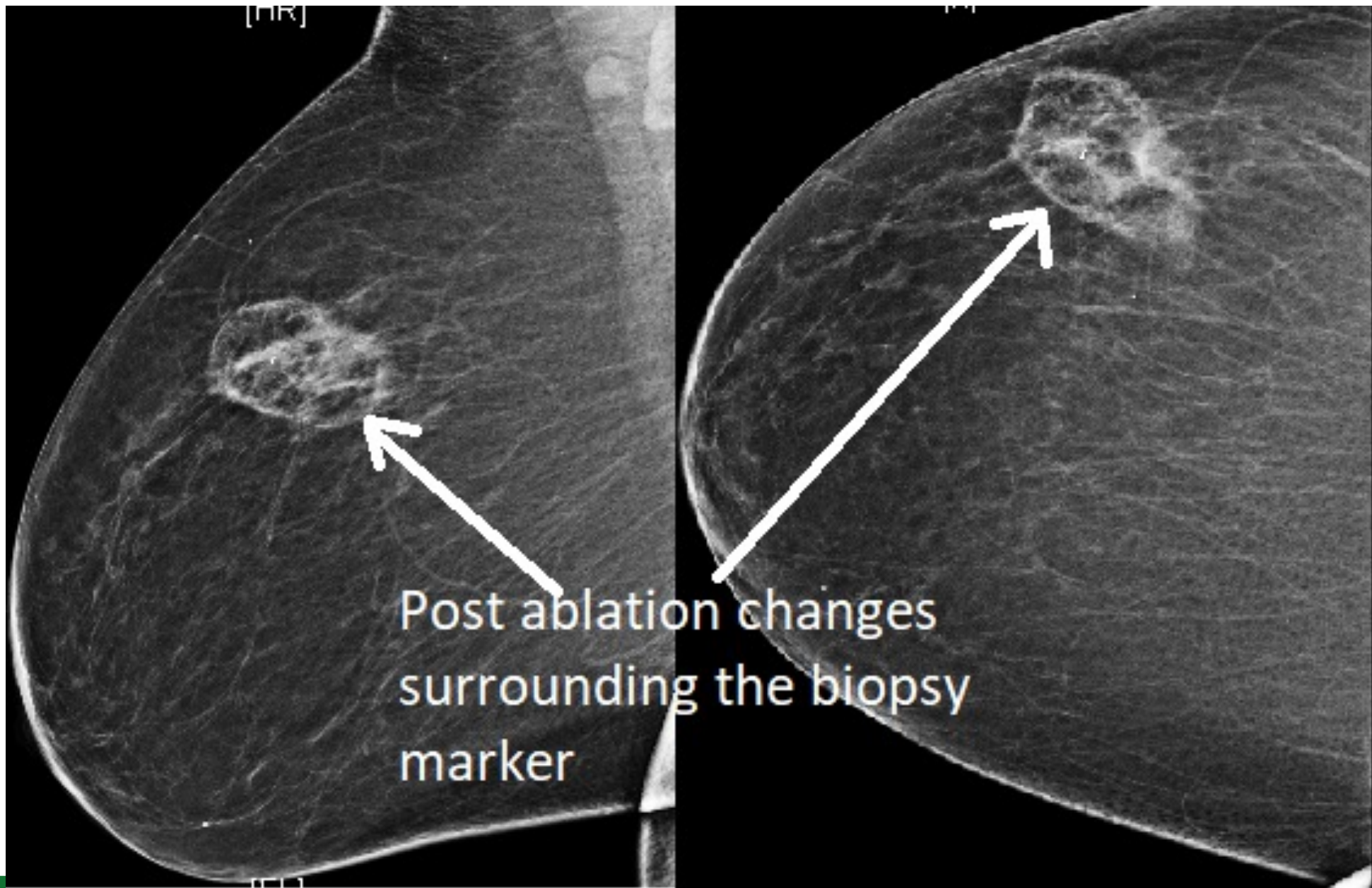


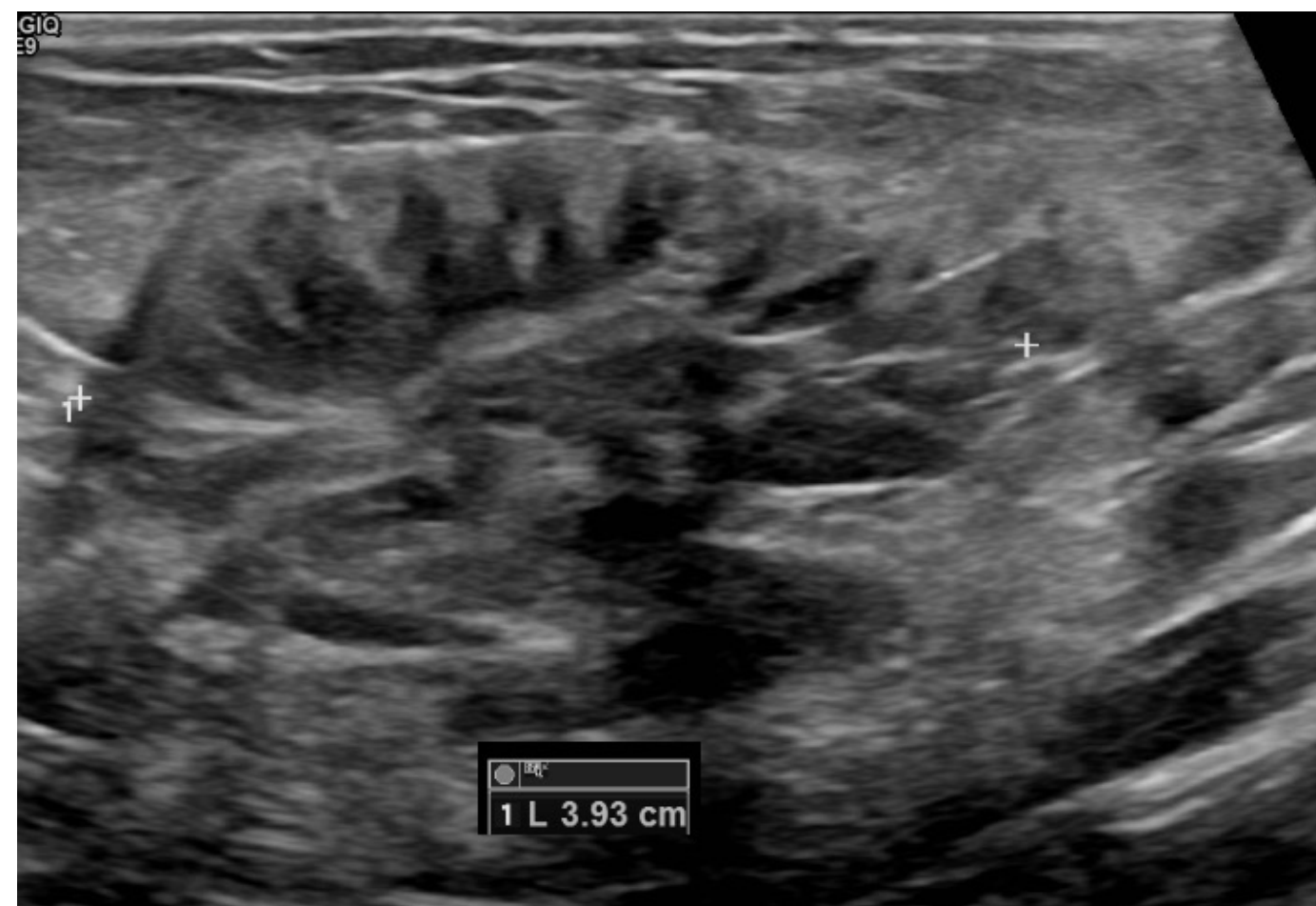
A-RAD RT BREAST 10:00 6 CM FN

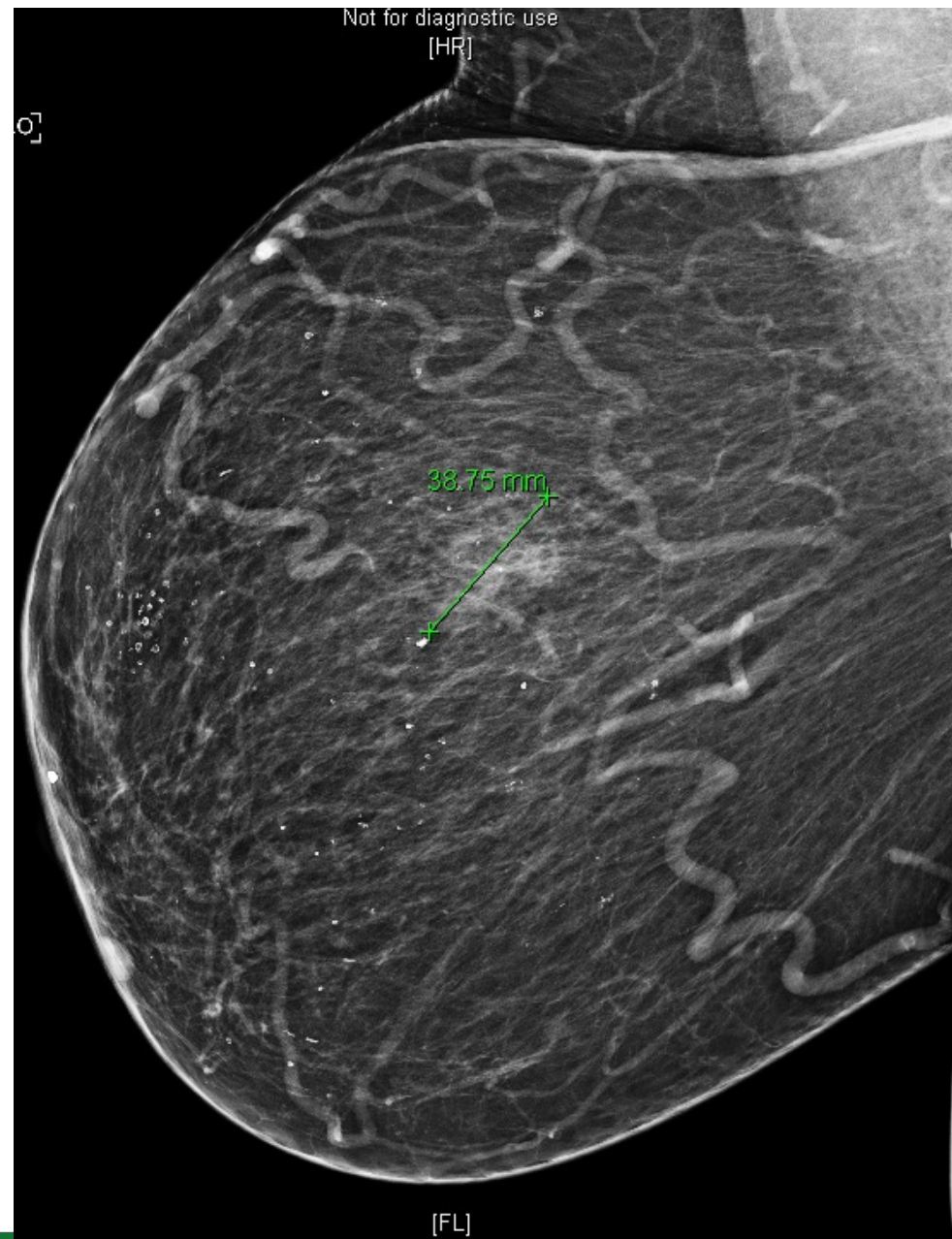
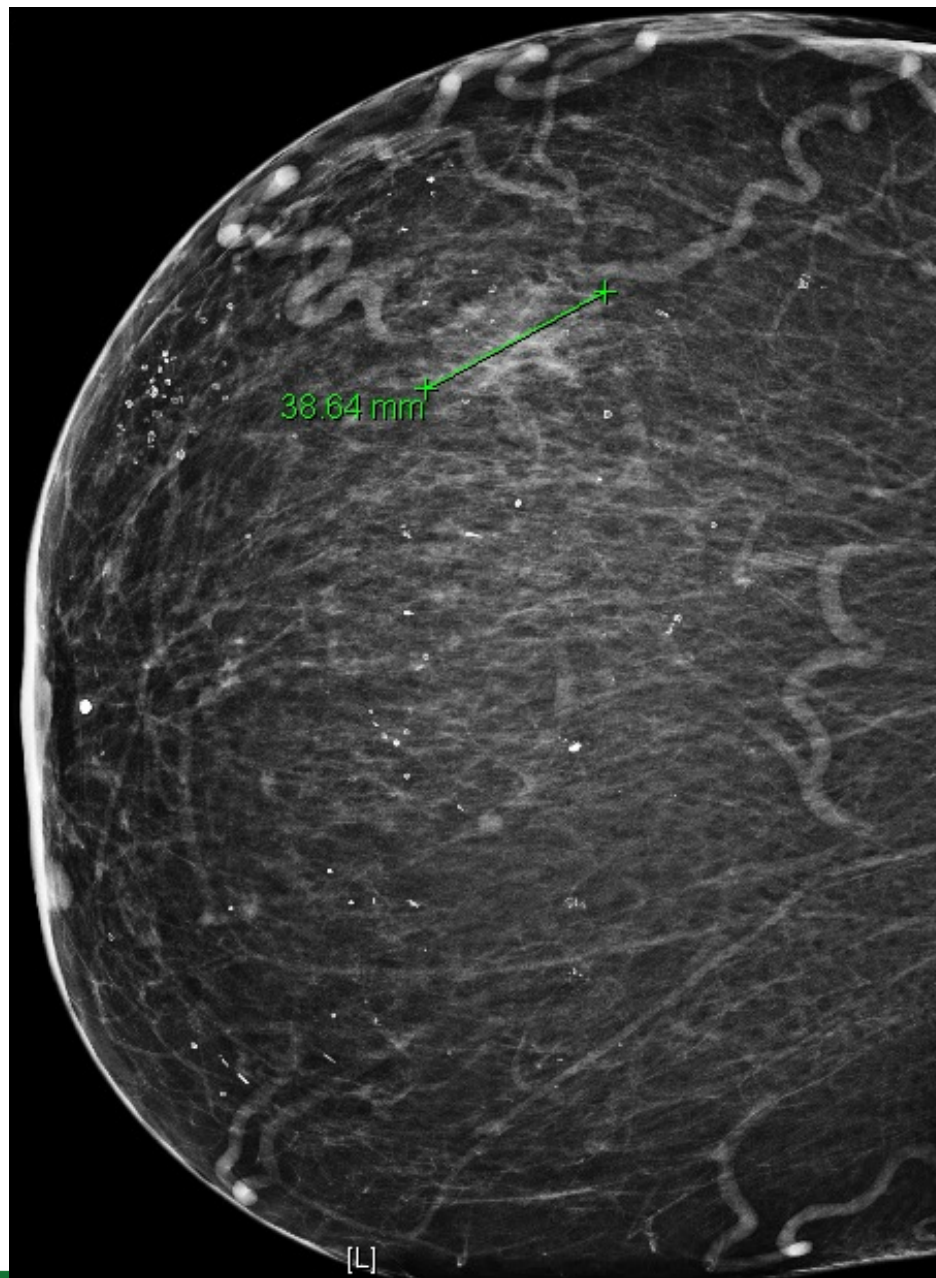




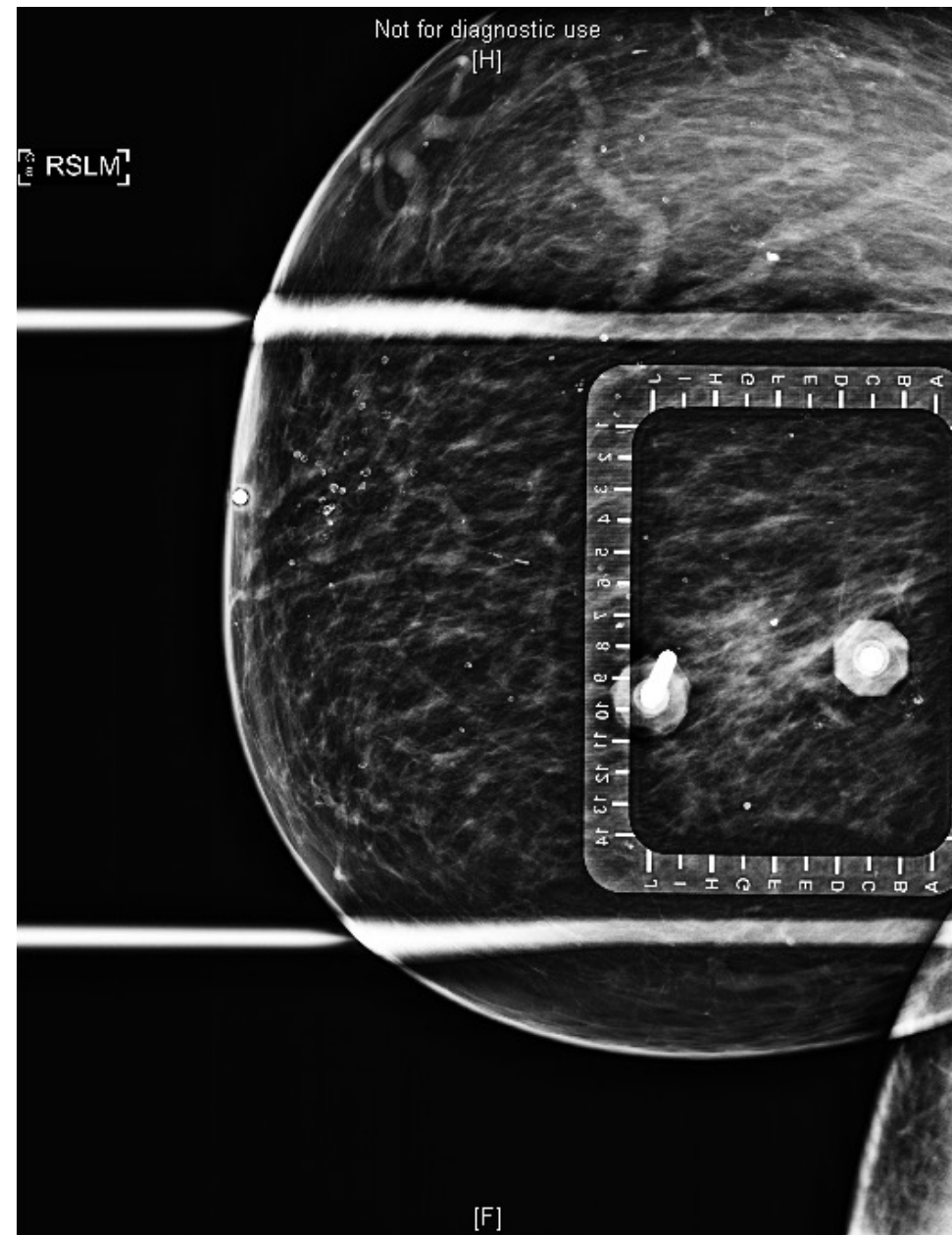
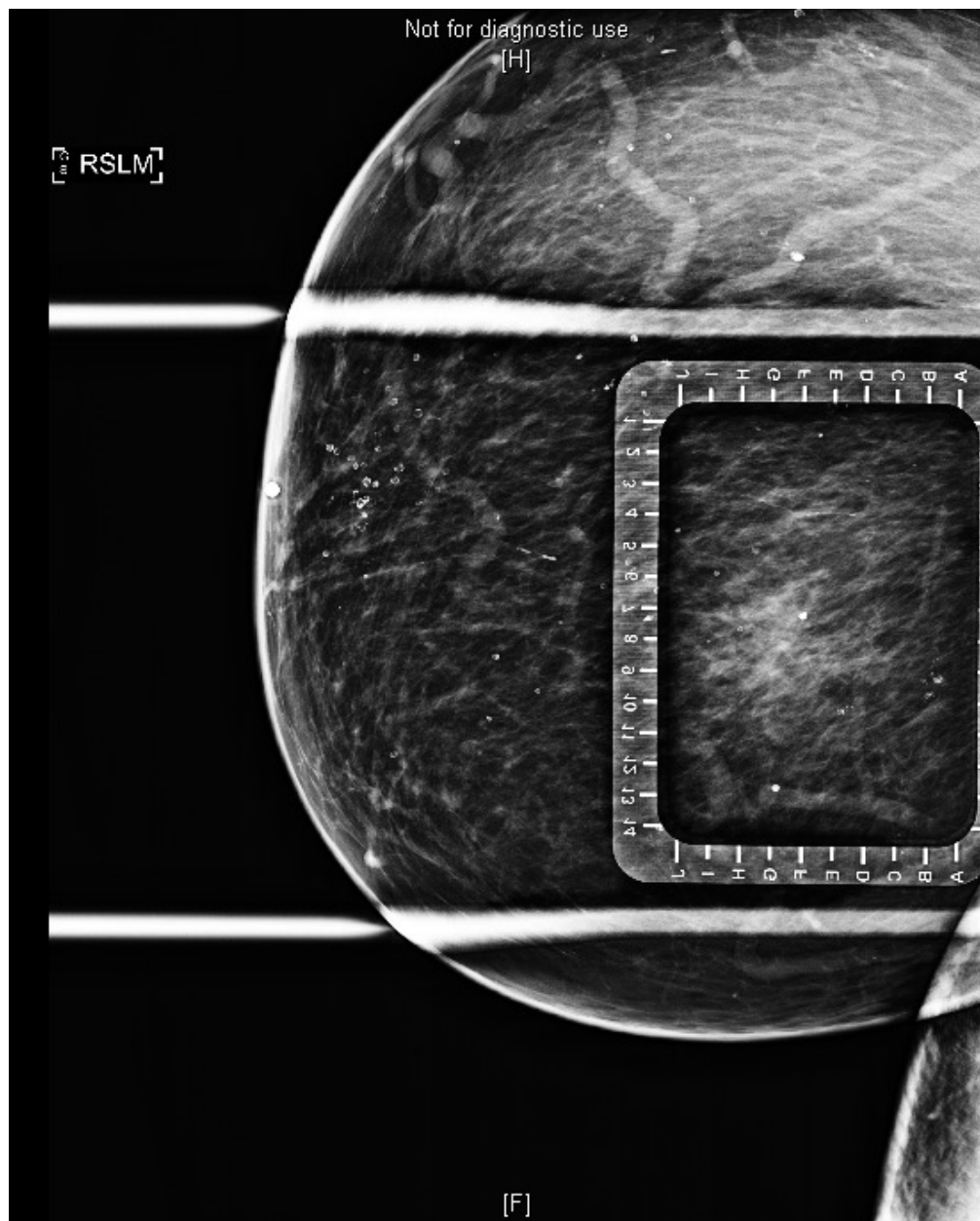




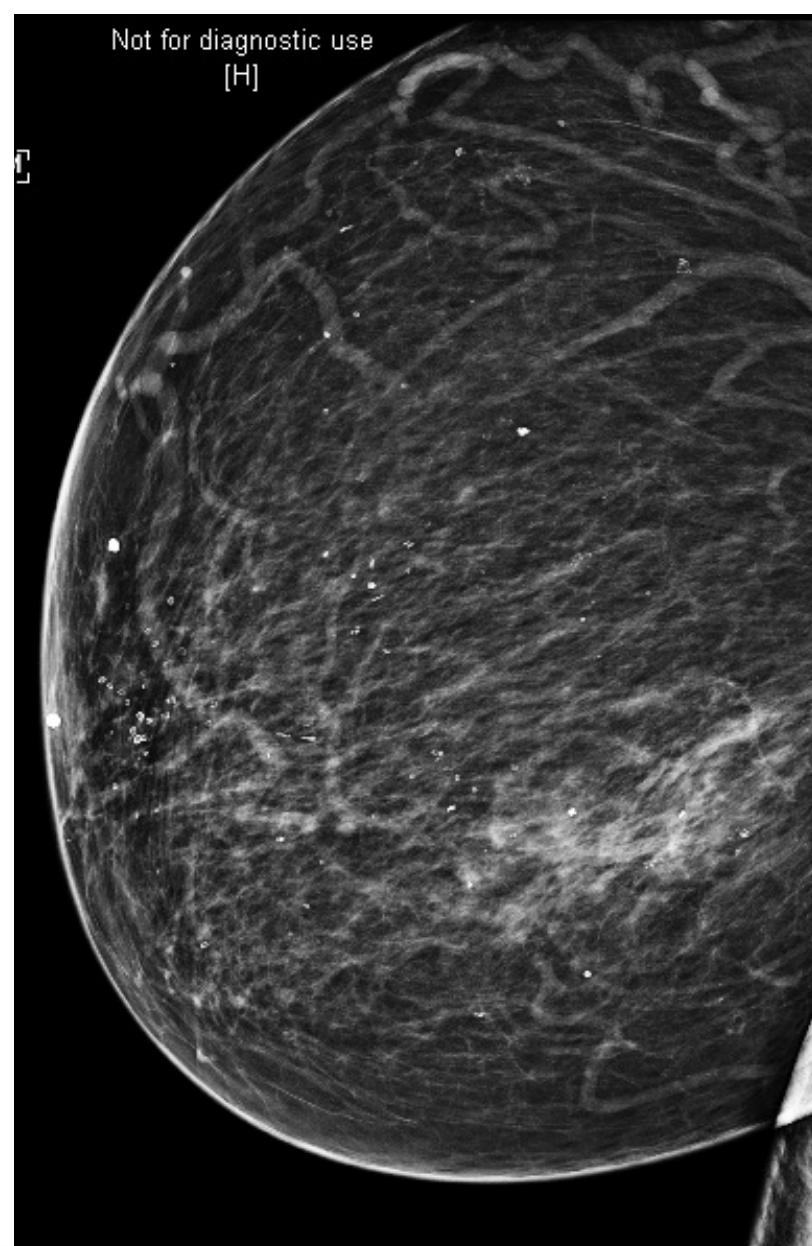
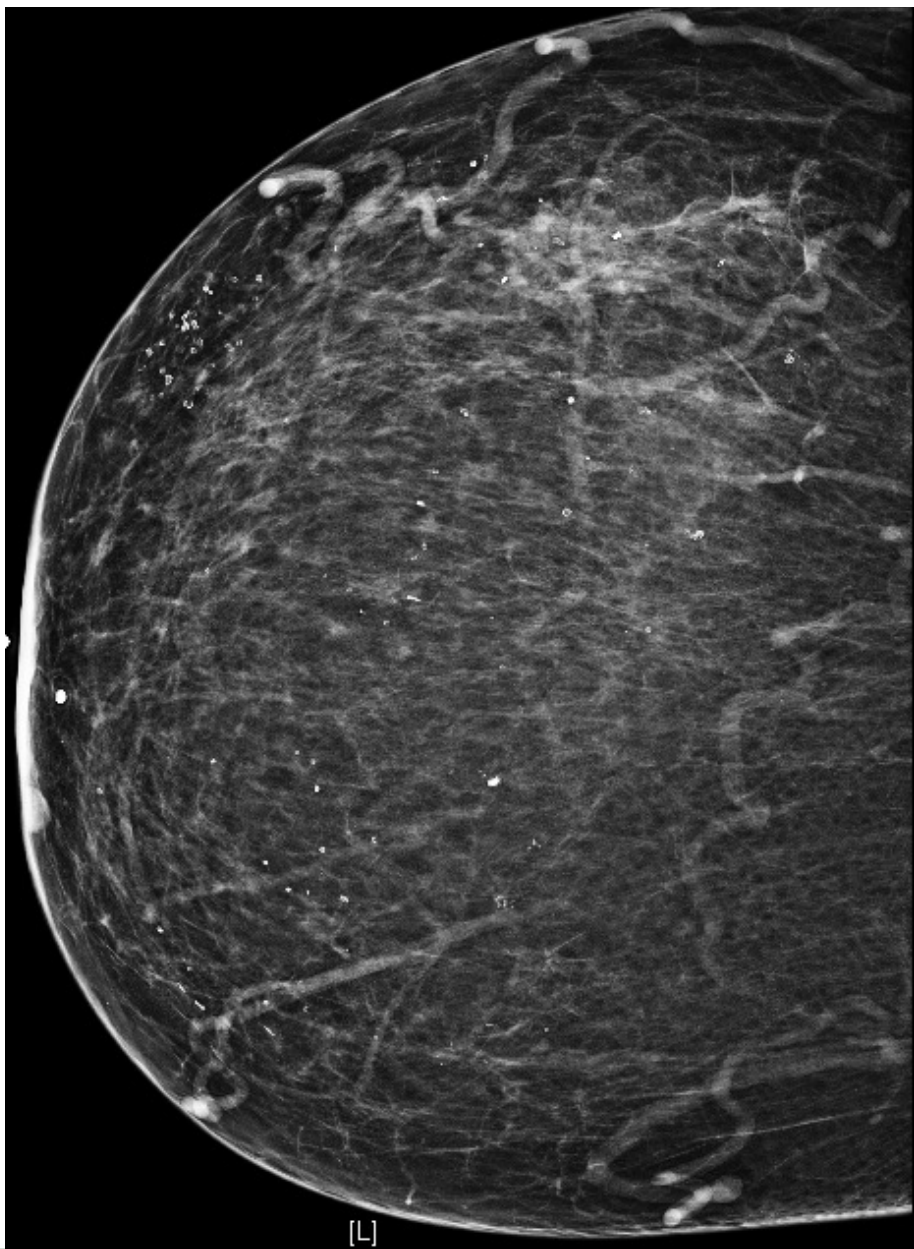










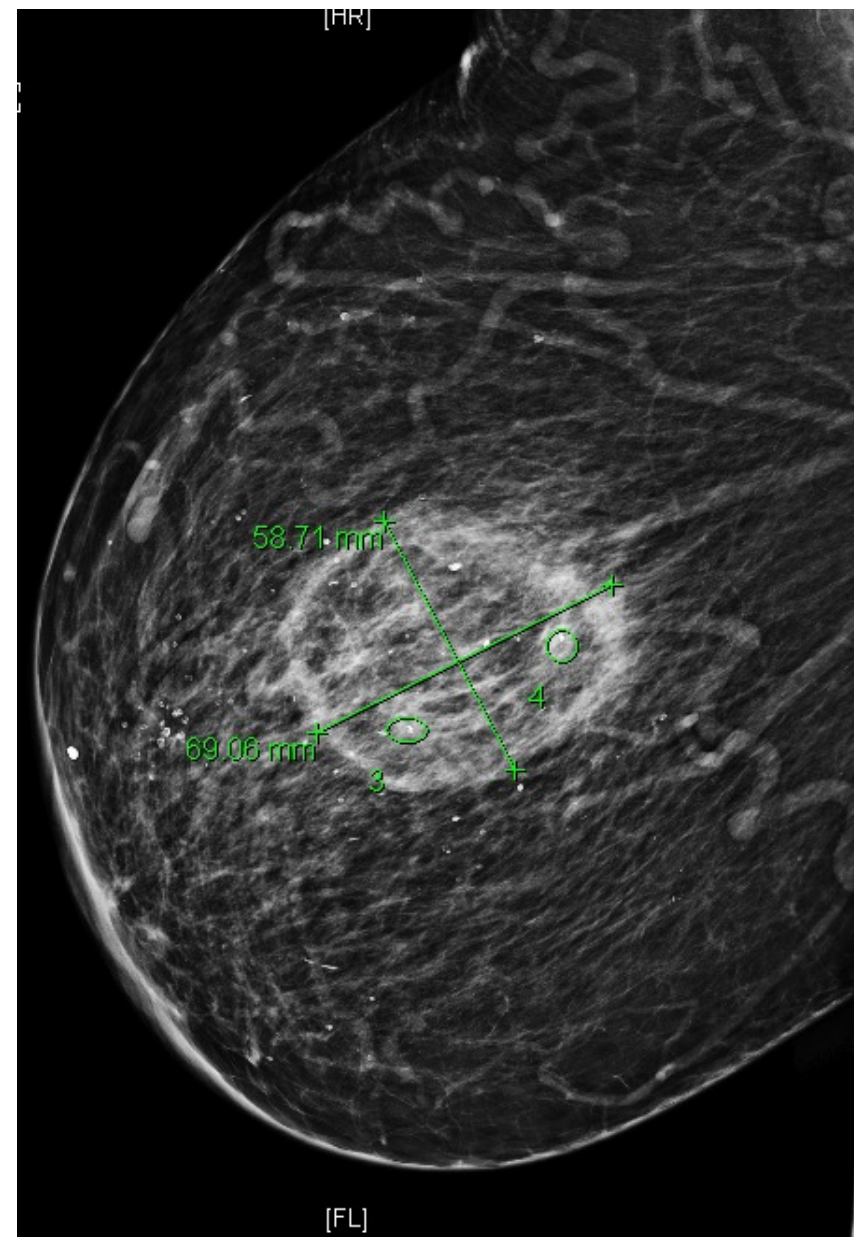
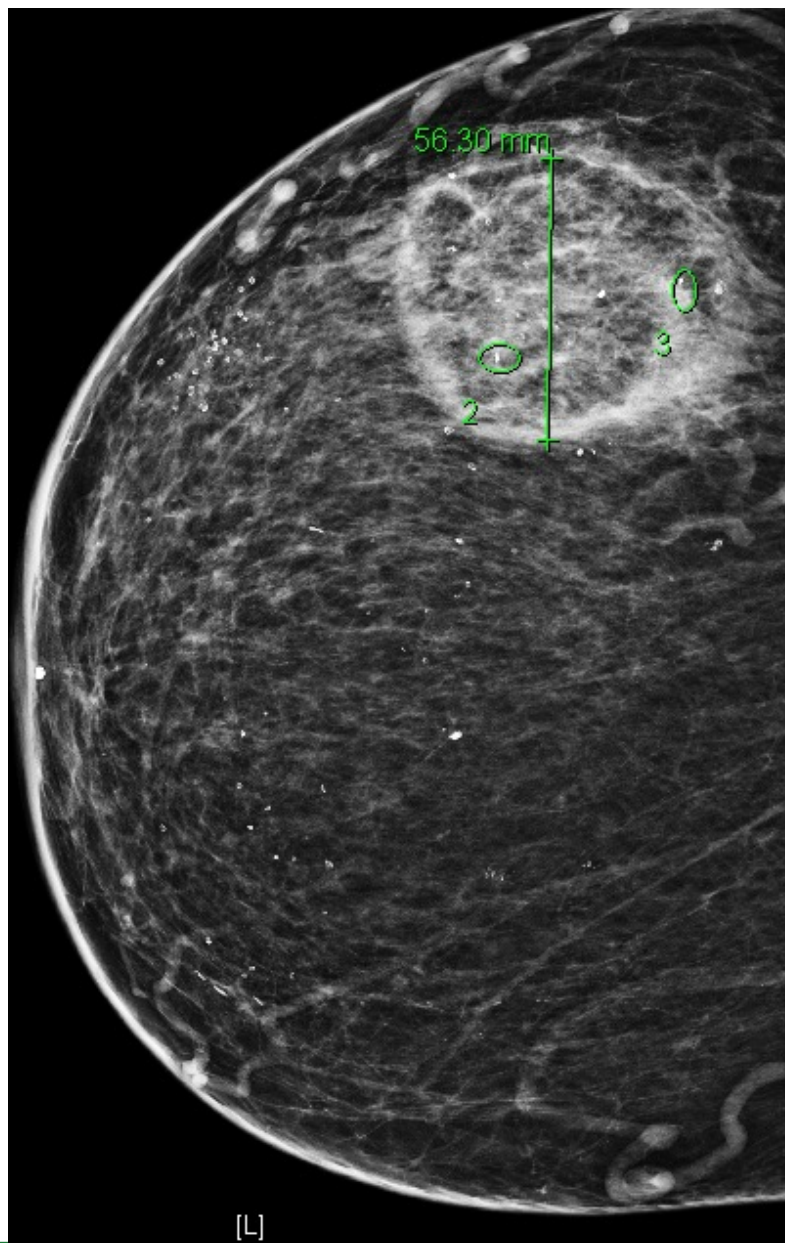


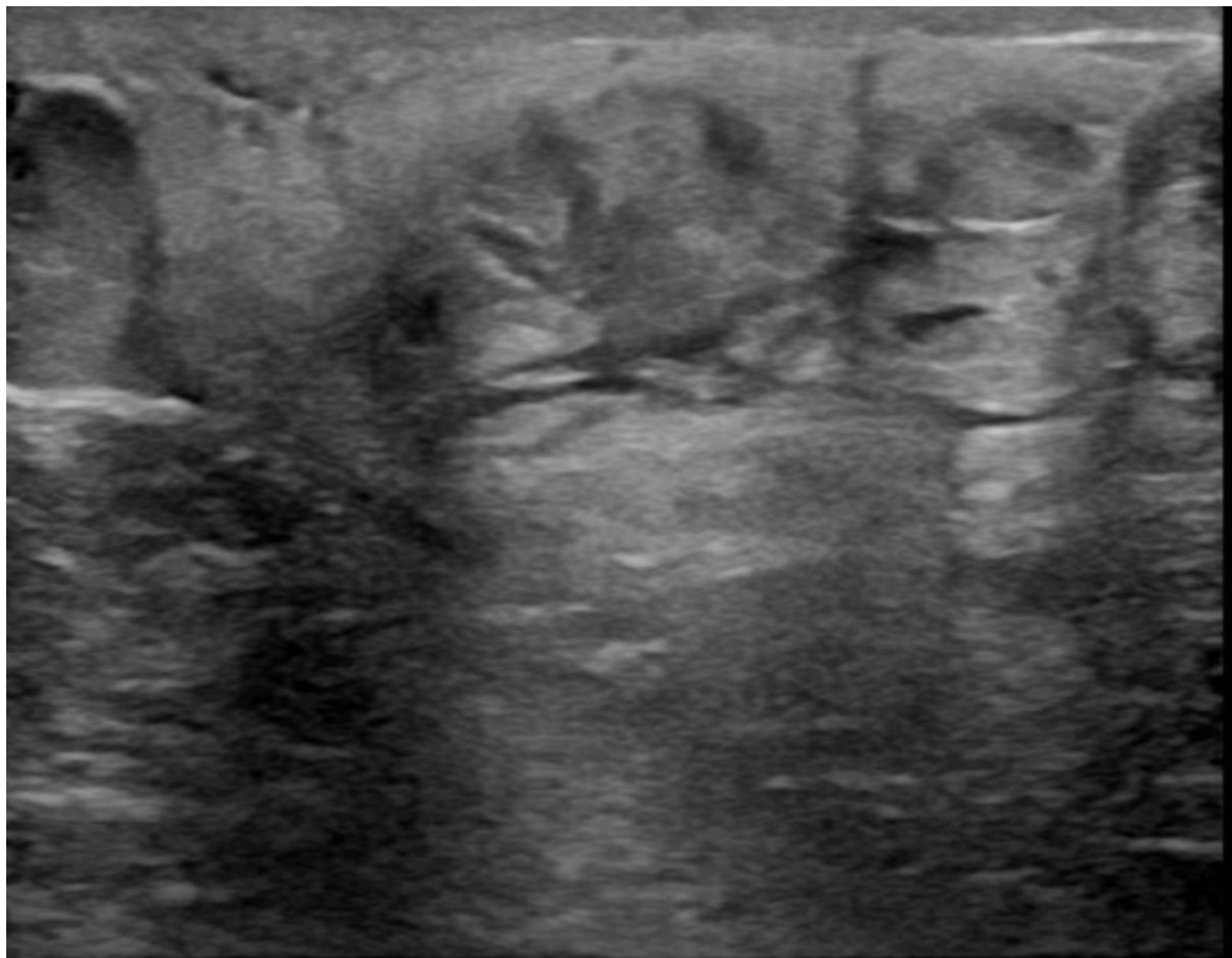
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LS7

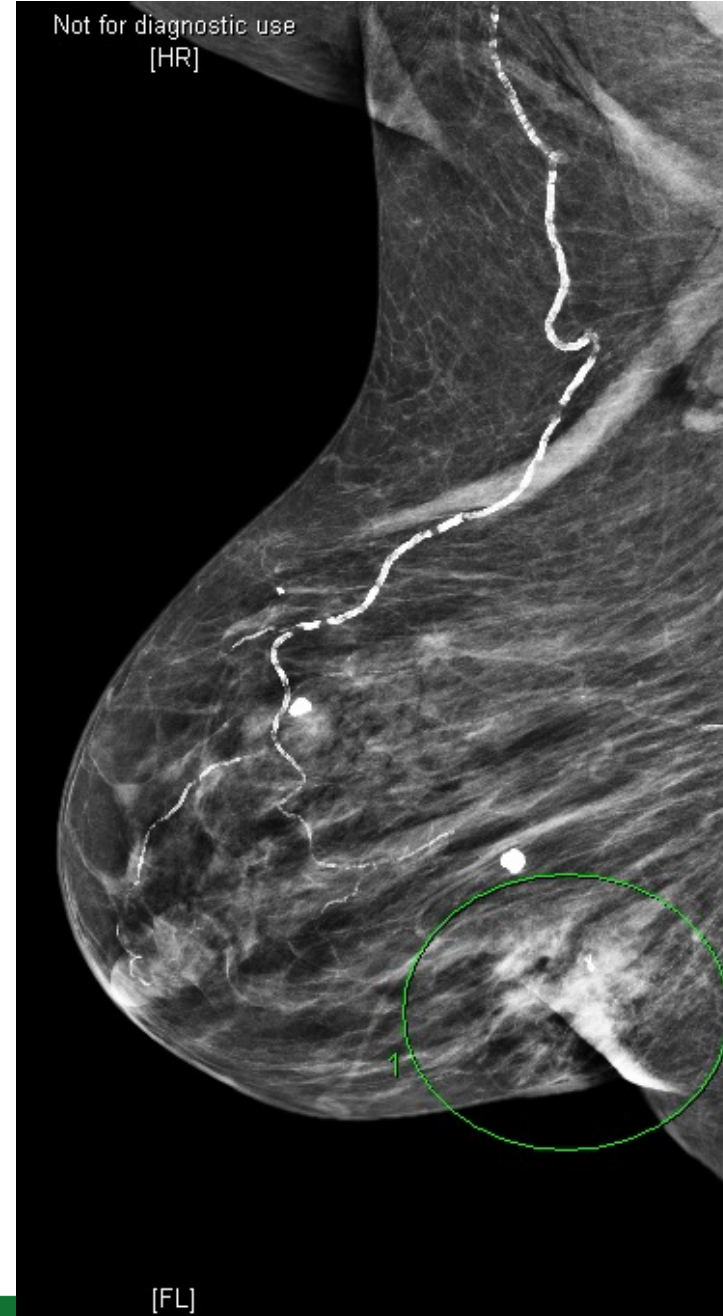


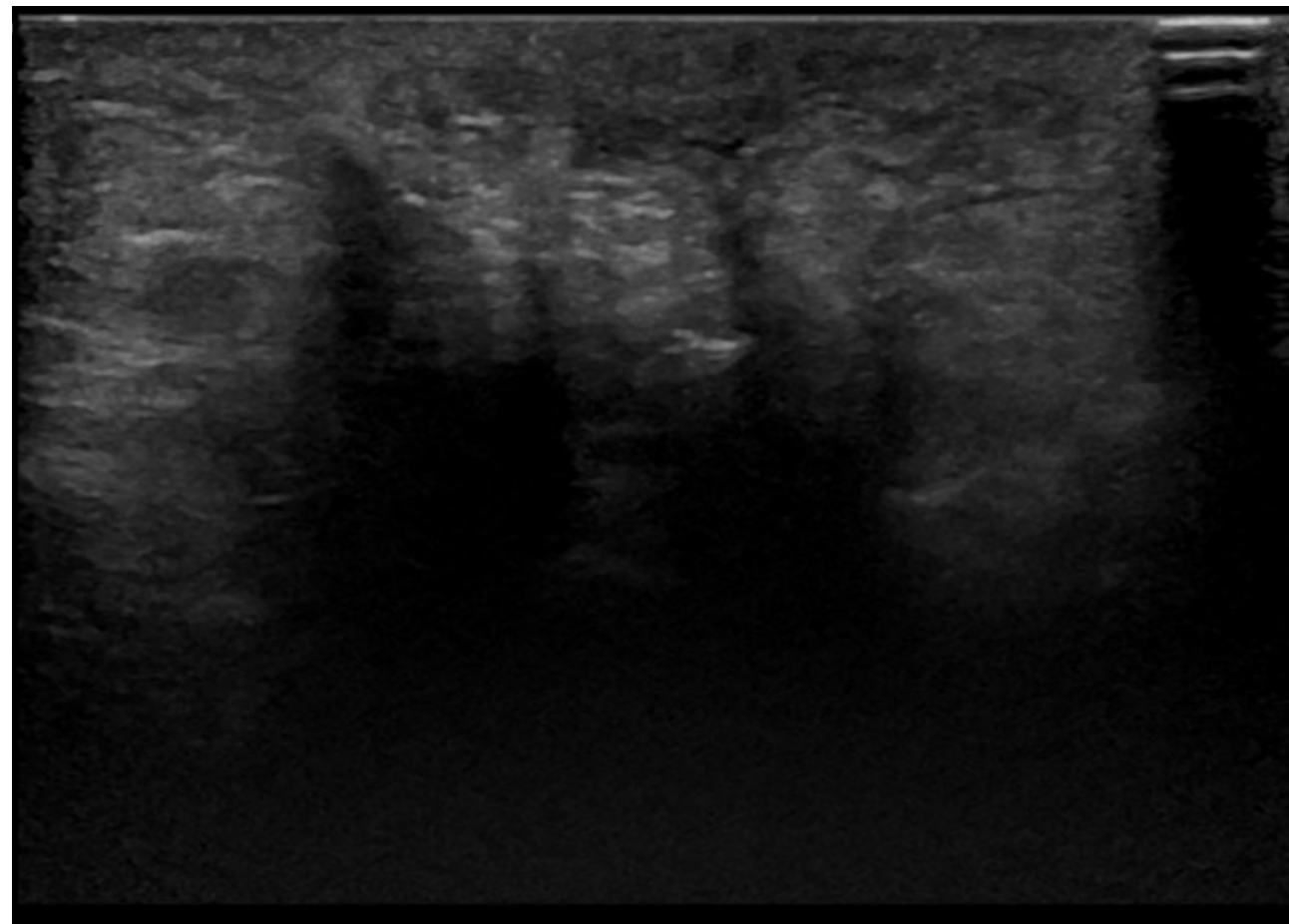
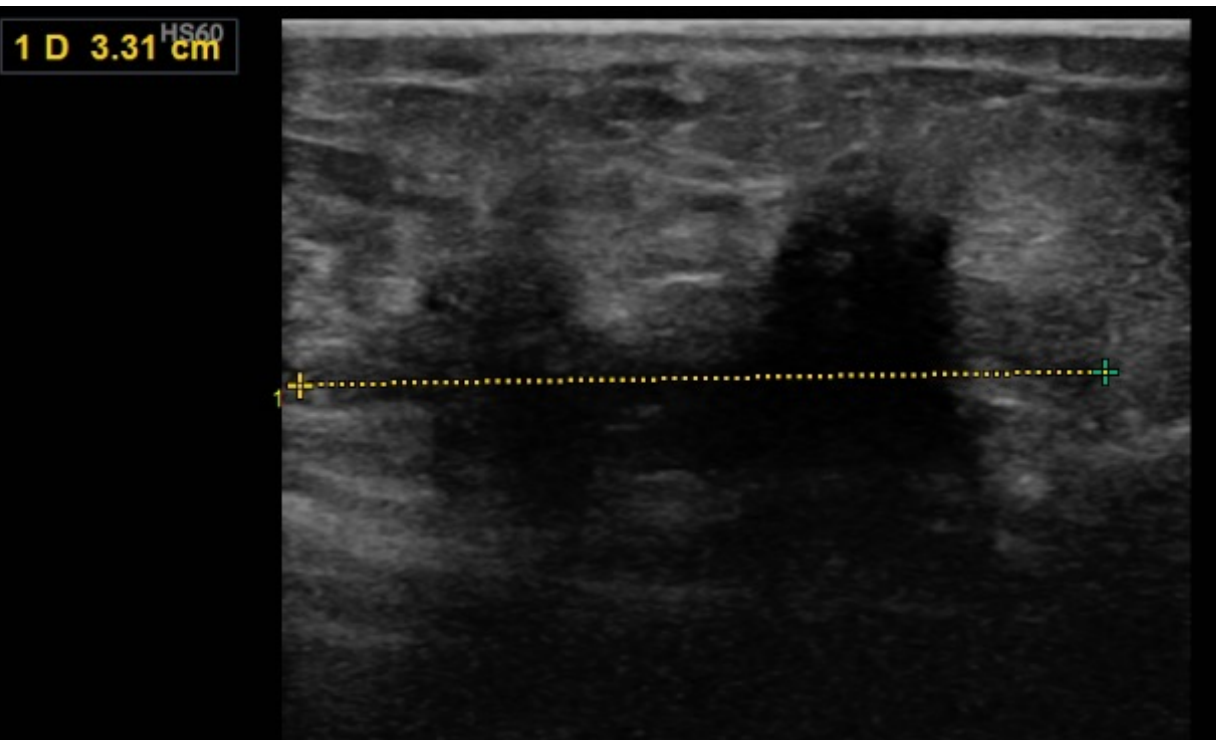
1 L 5.33 cm

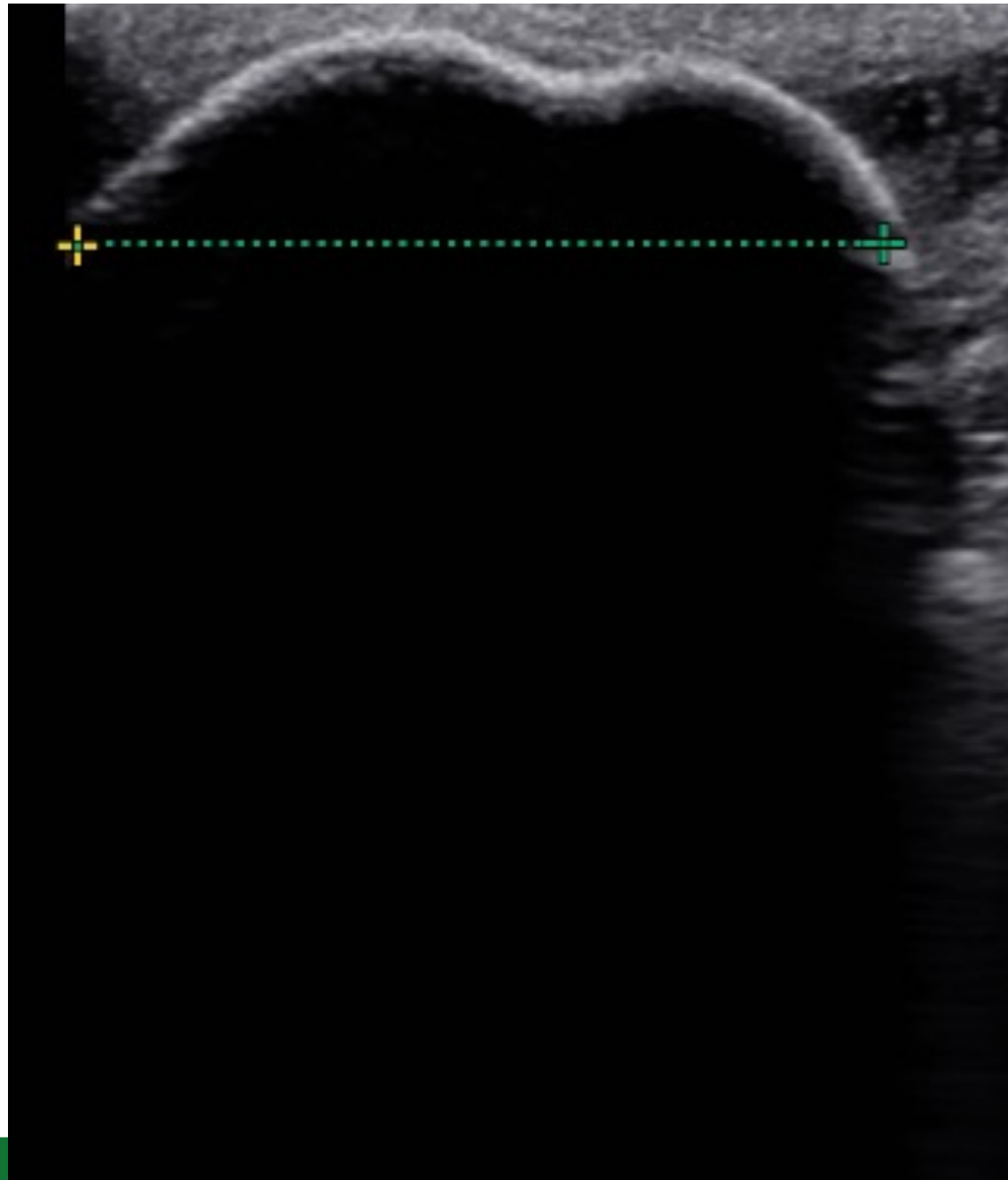


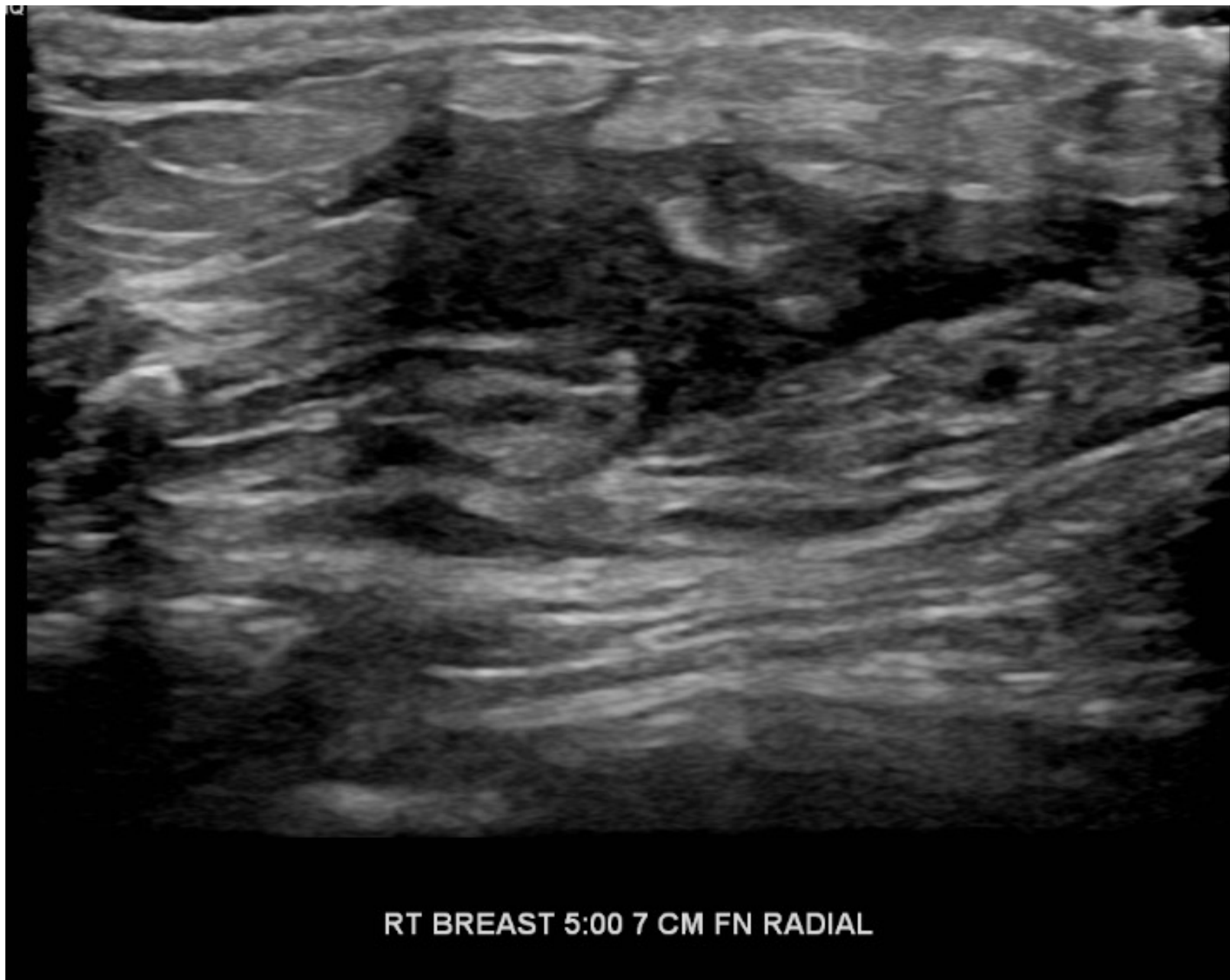


RT BREAST 7 00 9 CM FN LONG CINE

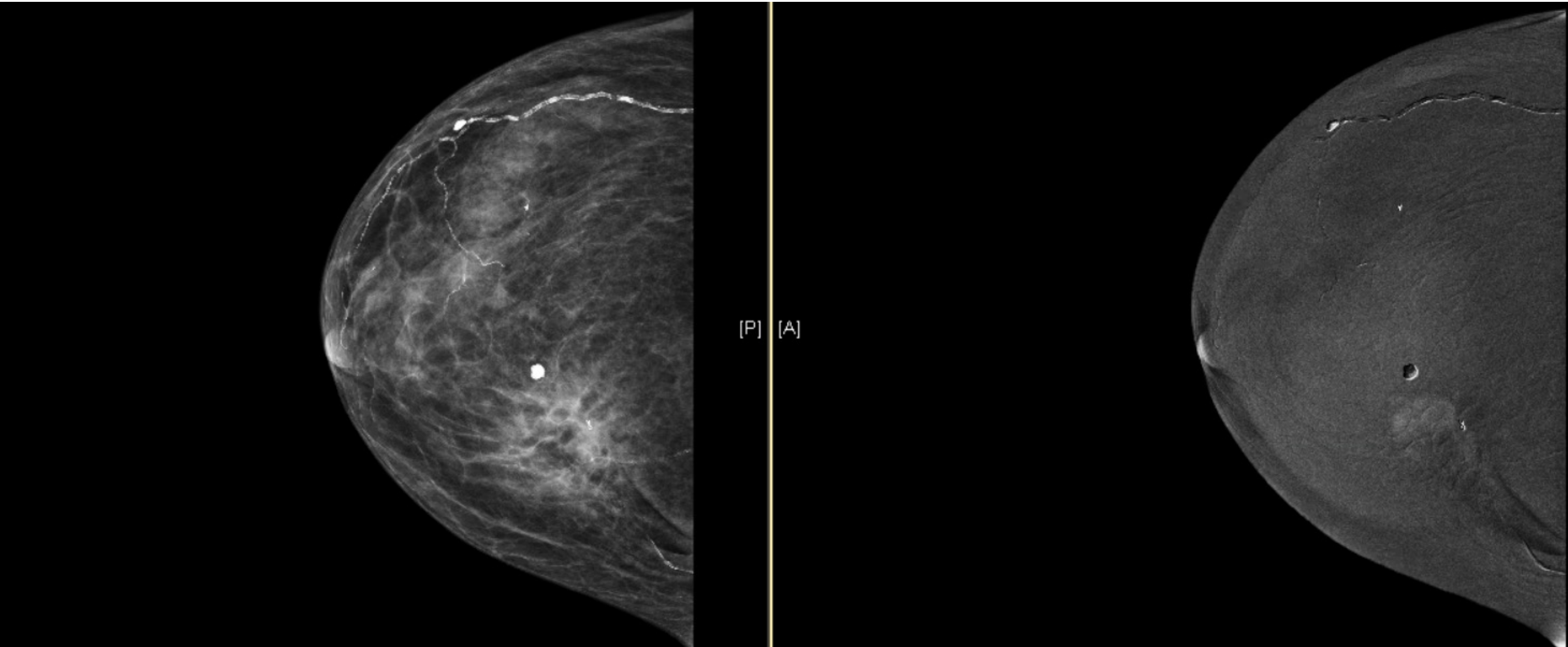


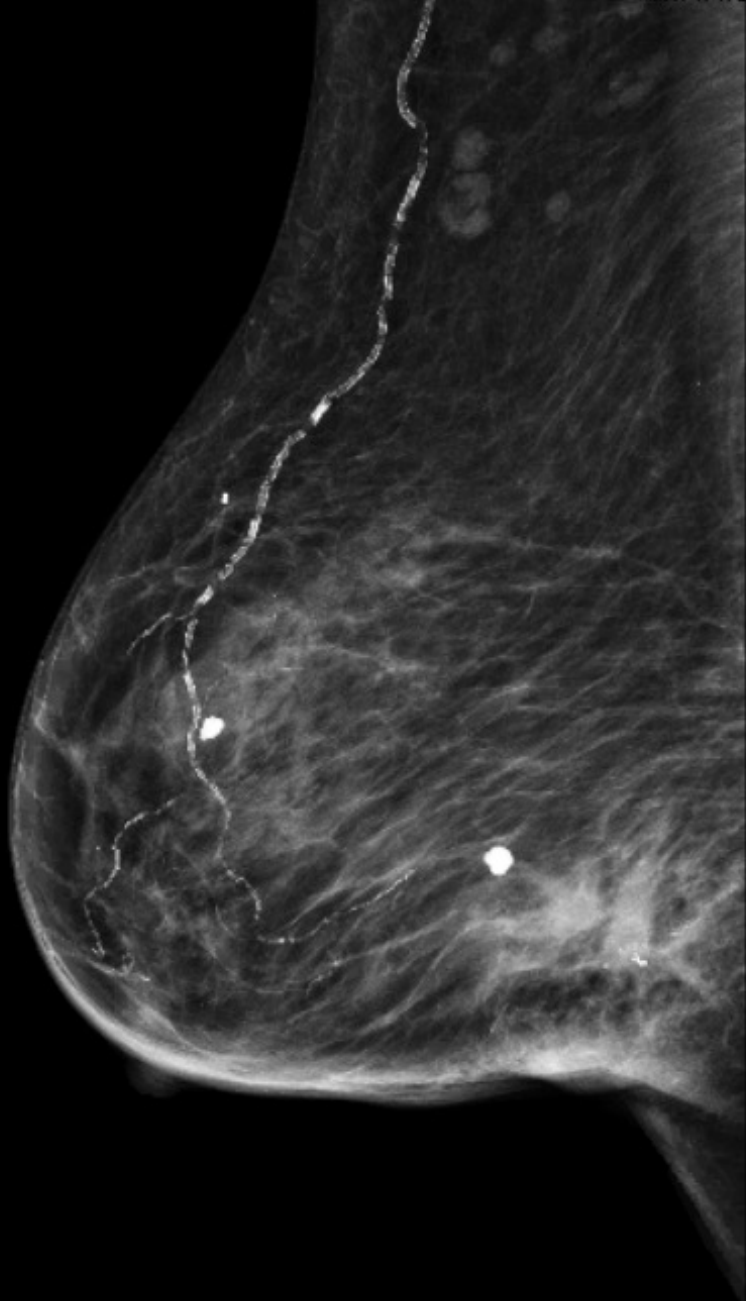




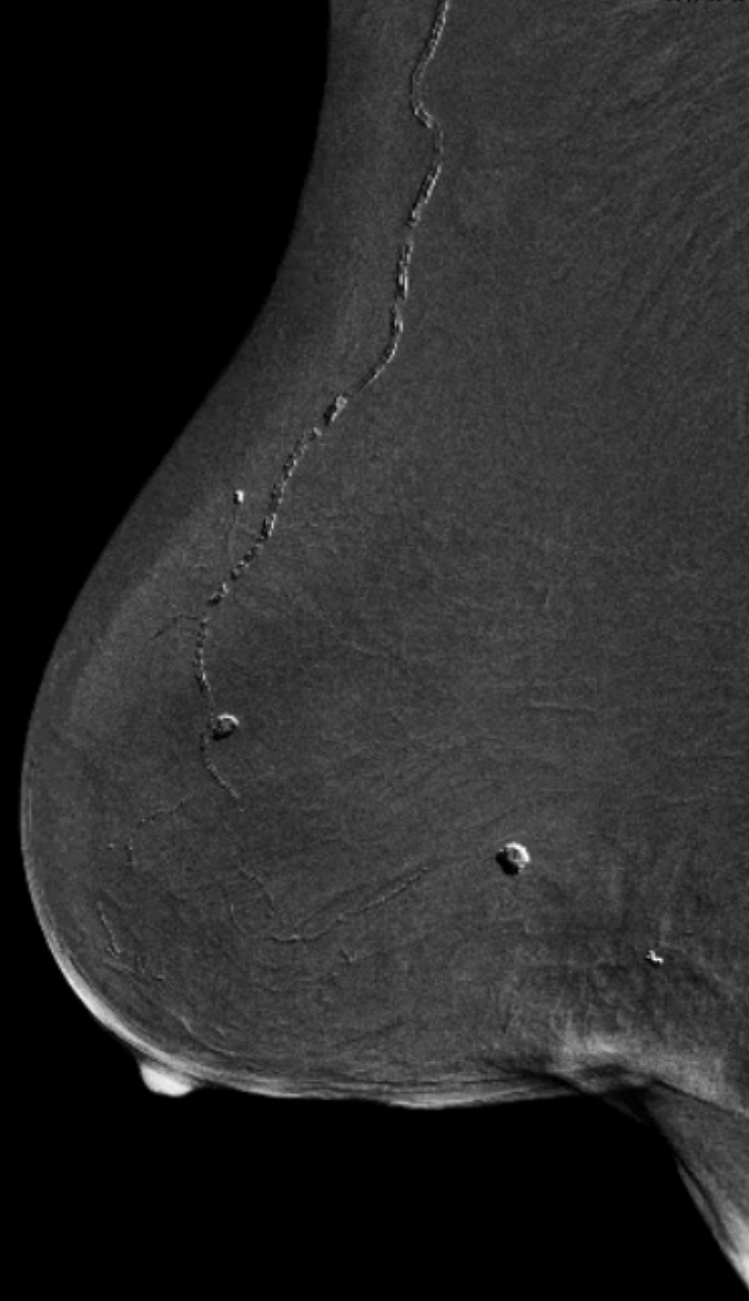


RT BREAST 5:00 7 CM FN RADIAL





[P] [A]

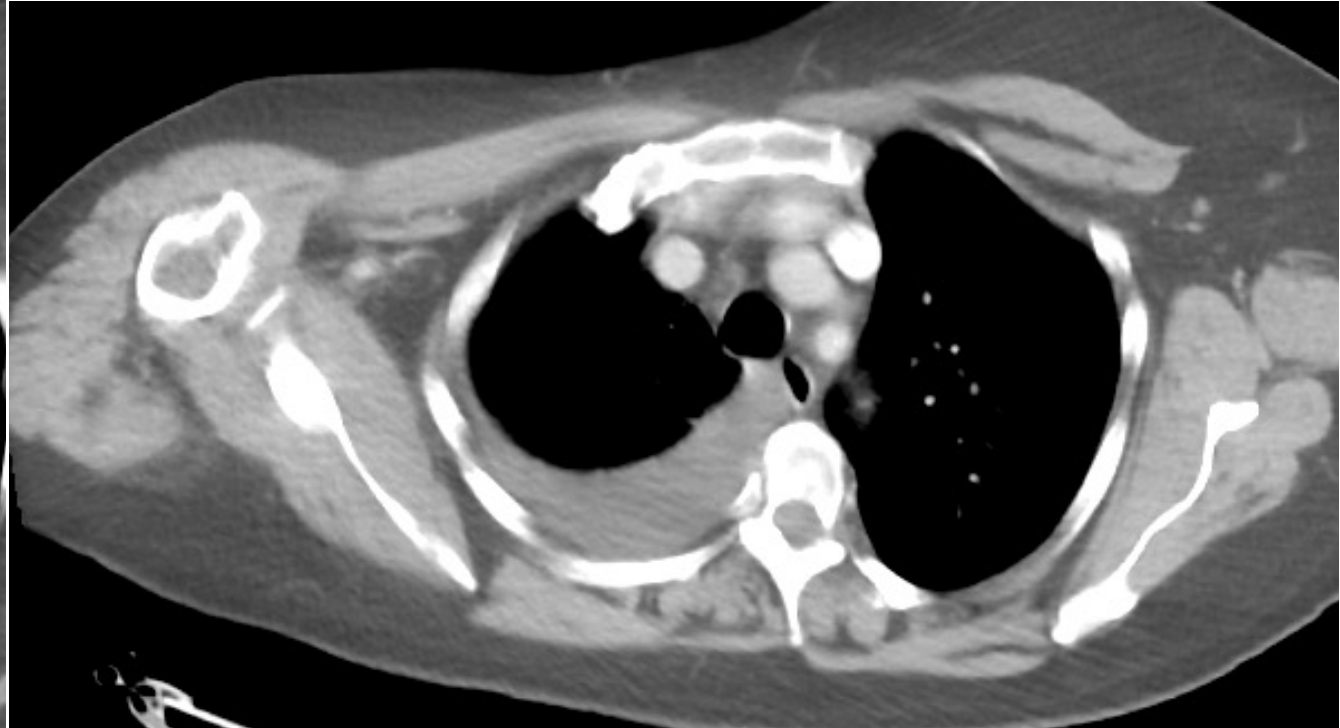
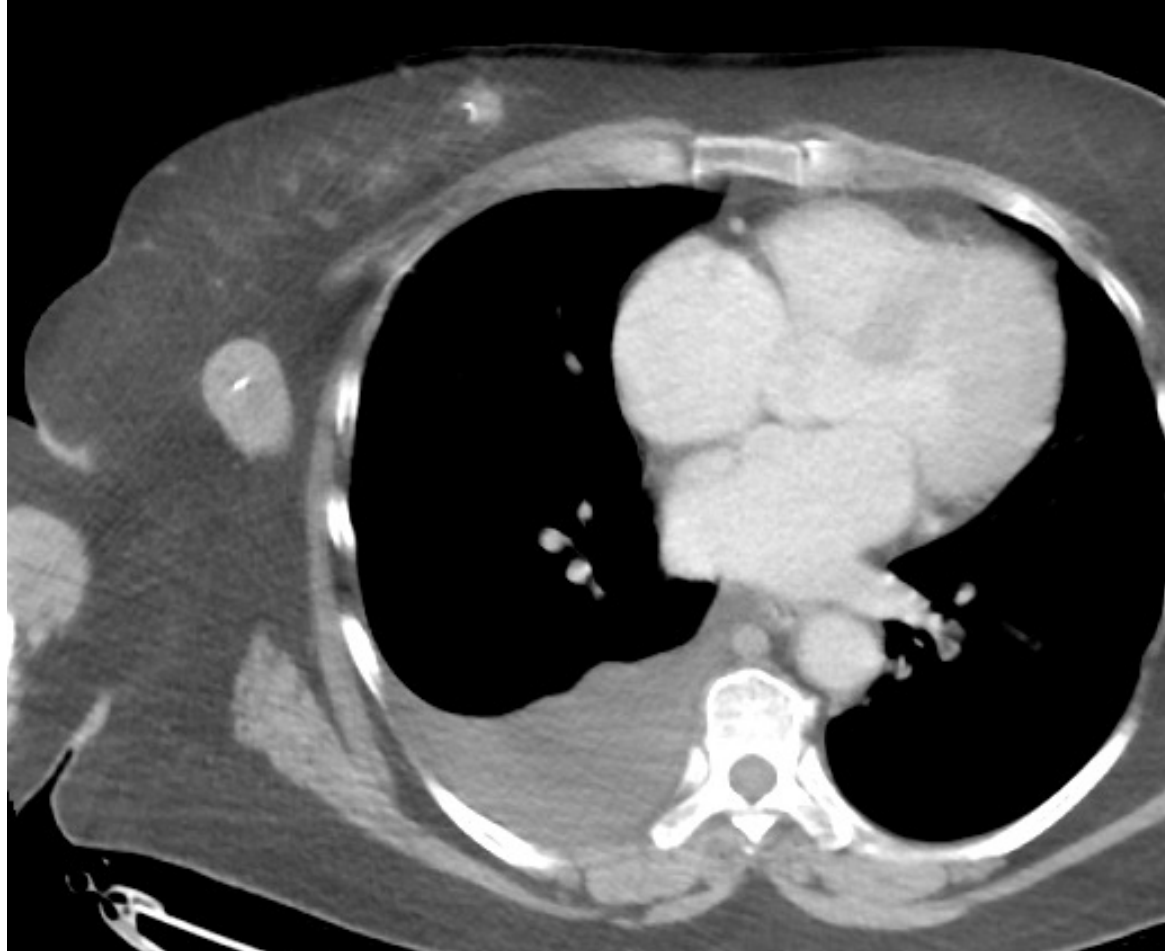


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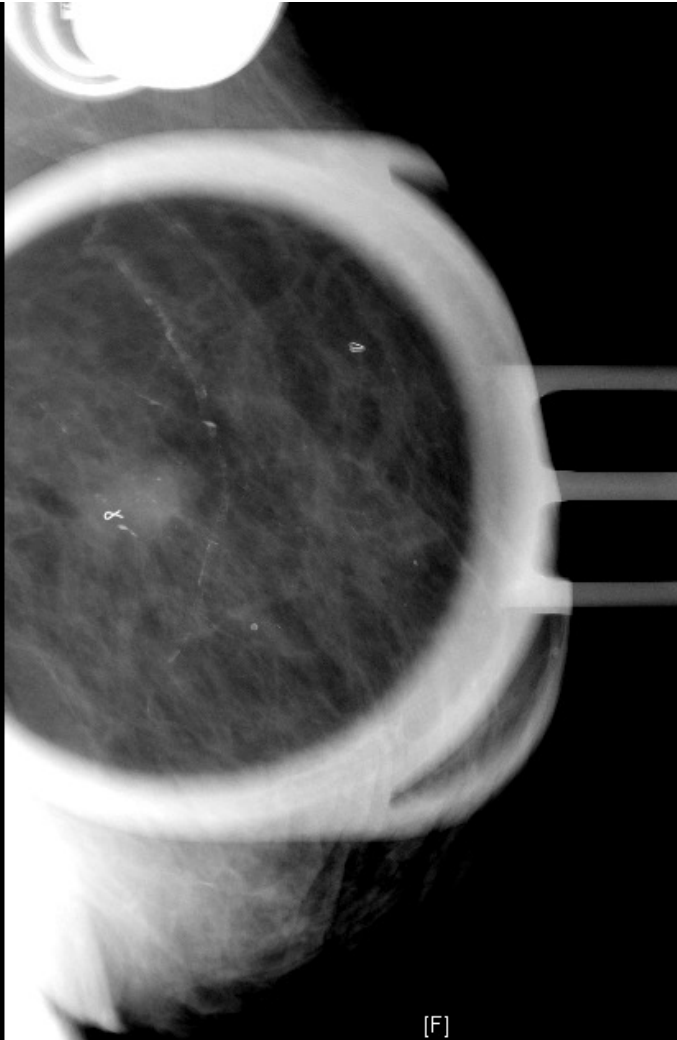
Treating Axillary Lymphadenopathy

- *Stretch* justification: ACOSOG Z0011 (Alliance) Randomized Clinical Trial
- 891 women with median follow-up of 9.3 years, clinical T1 or T2 invasive breast cancer, no palpable axillary adenopathy, and 1 or 2 sentinel lymph nodes containing metastases
- 10-year regional recurrence did not differ significantly between the 2 groups
- Therefore, microscopic disease left behind does not change outcome
 - So, I treat the abnormal lymph nodes I see if possible
 - My goal is control in a nonsurgical candidate

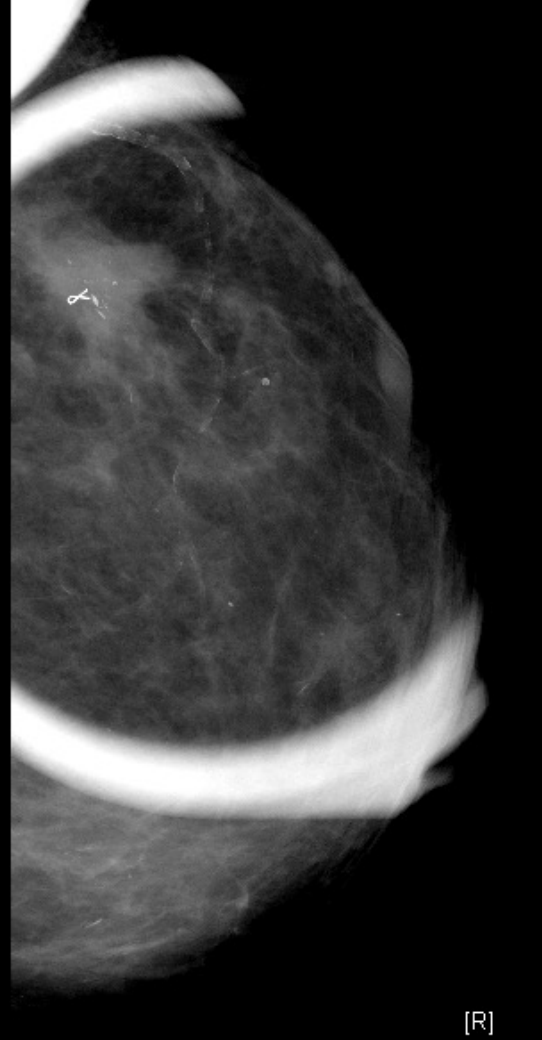
Assess Distance from Brachial Plexus with CT Scan



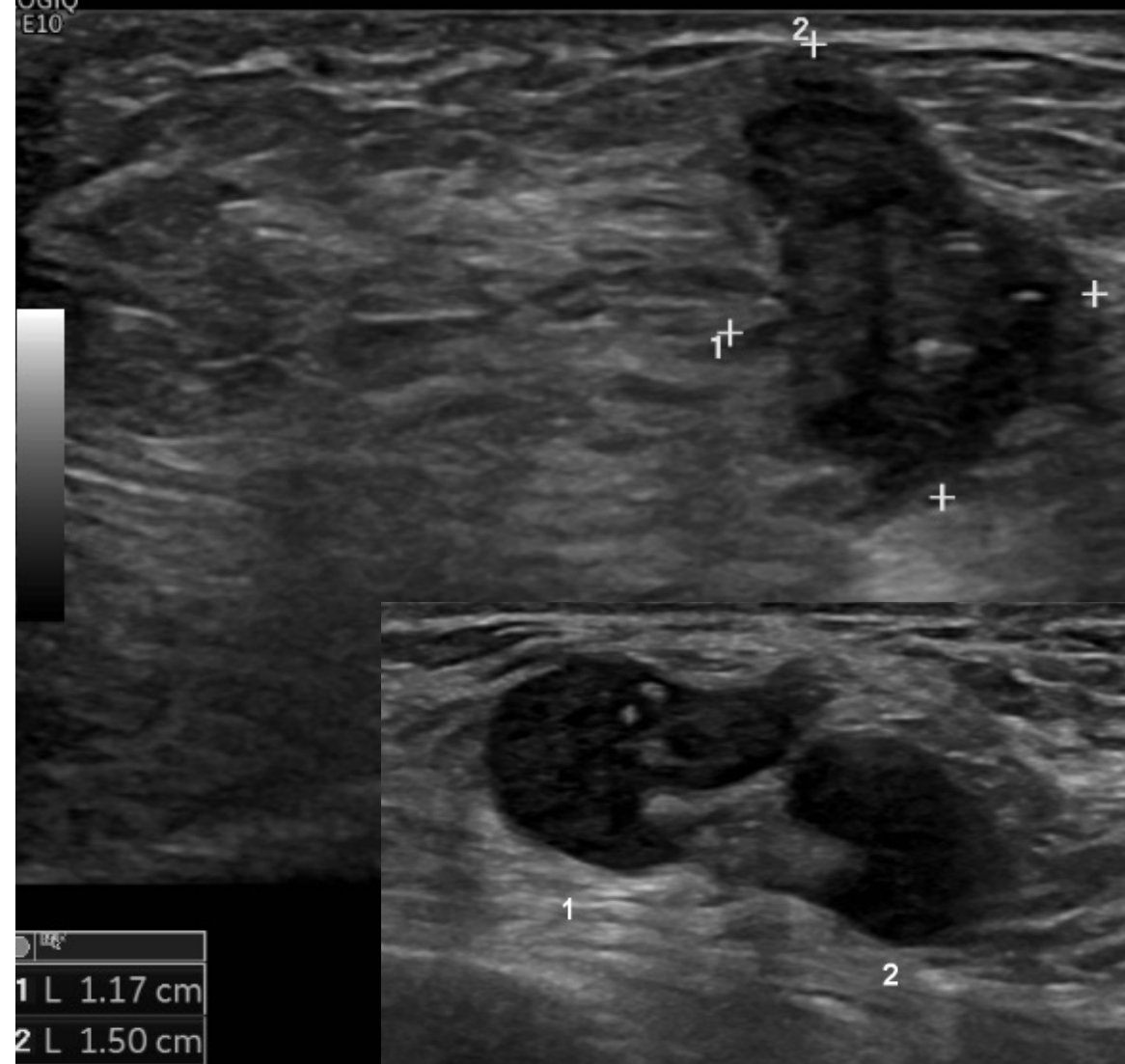
93 y/o Female, Nonsurgical Candidate



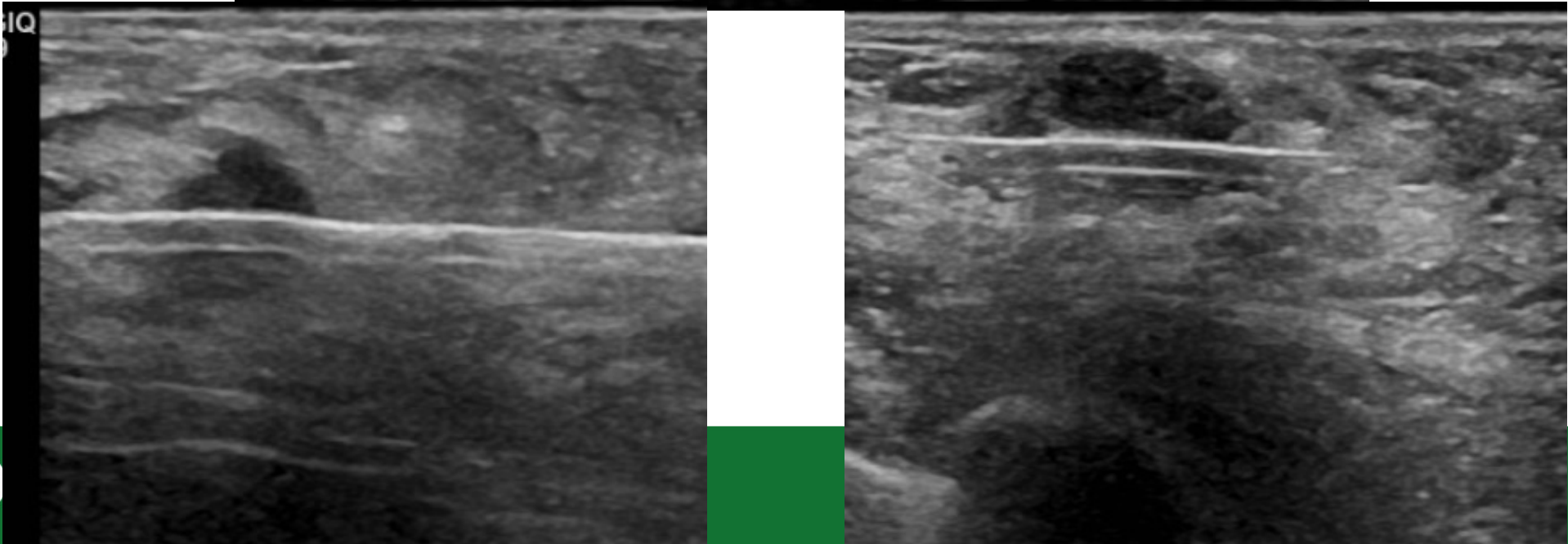
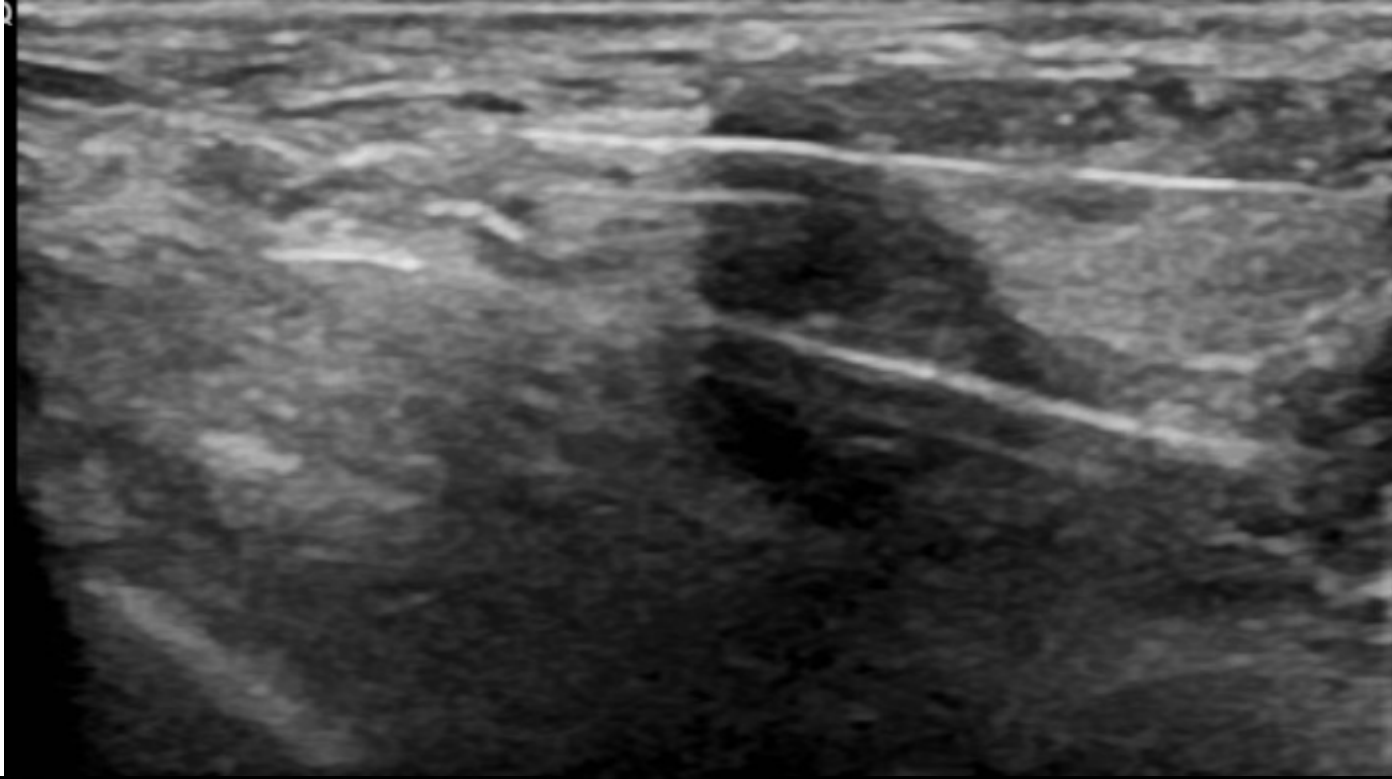
[F]



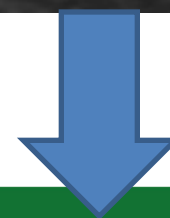
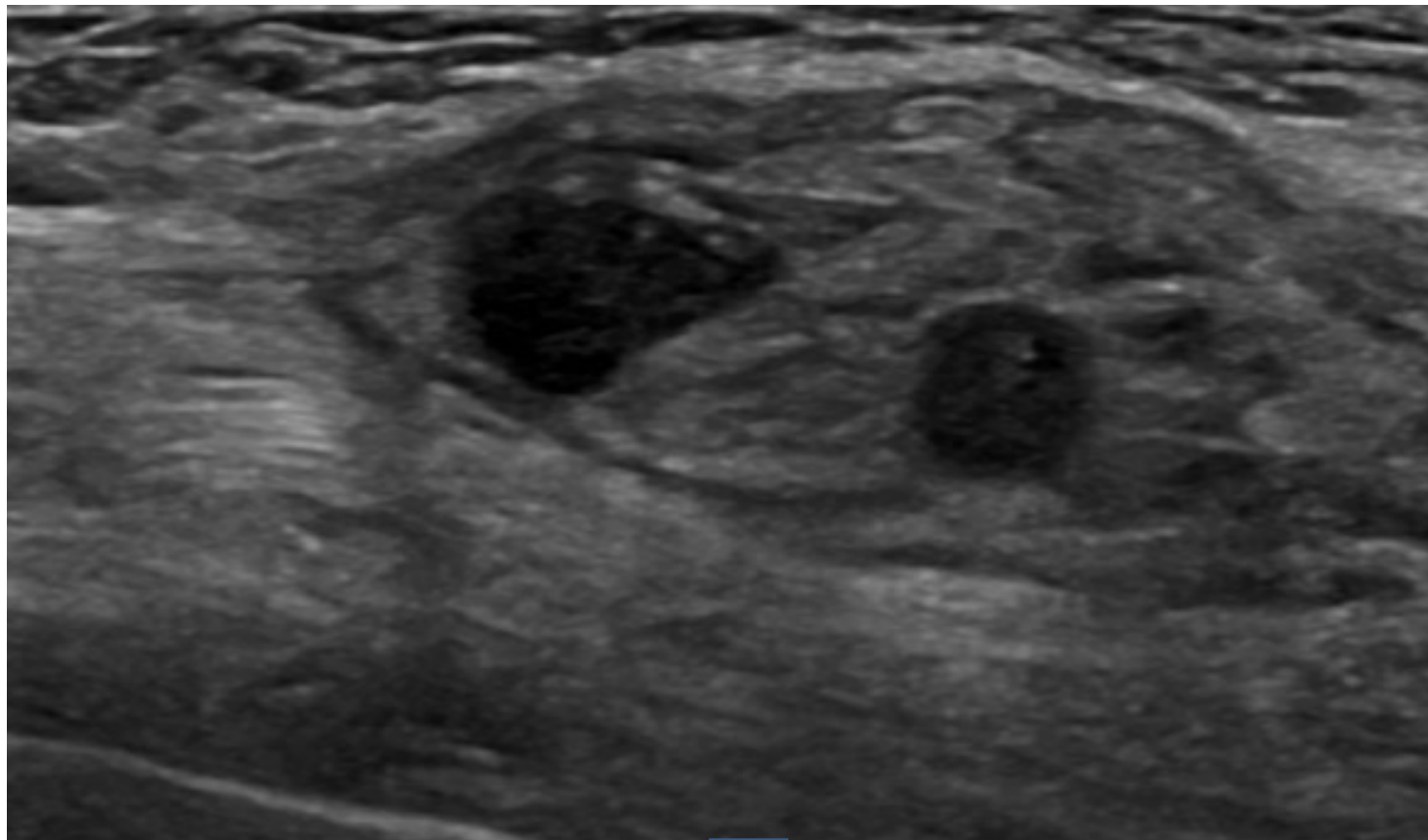
[R]



LT AXILLA 1:00 10 CMFN RADIAL



3-Months Post Ultrasound



Lymph nodes no longer seen at 9 months post

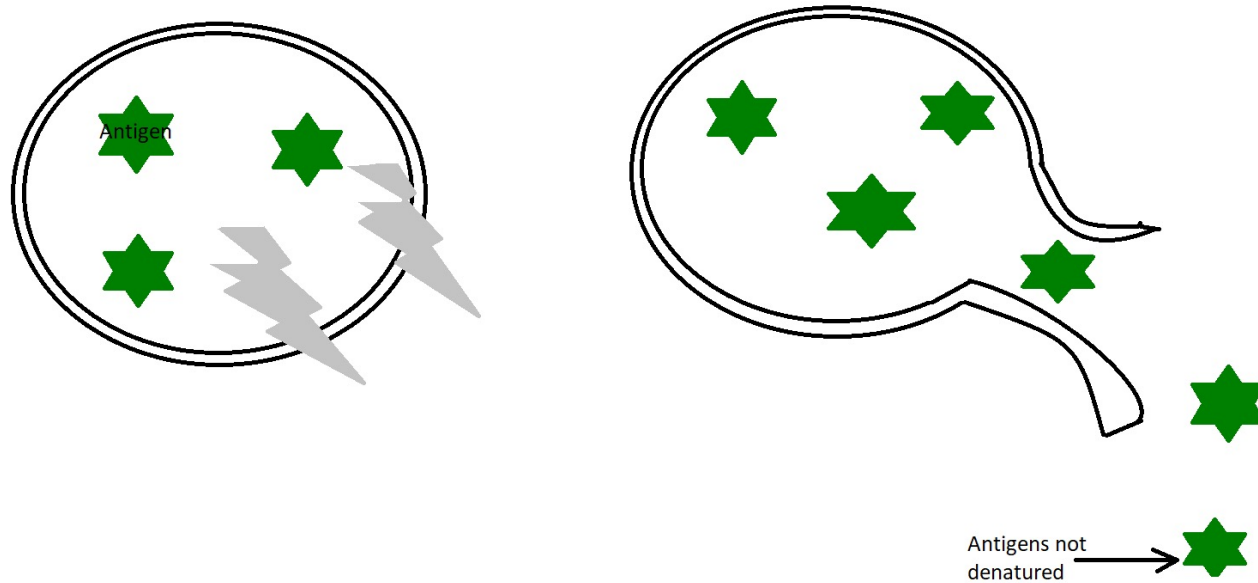
Cryo-Immuno Effects

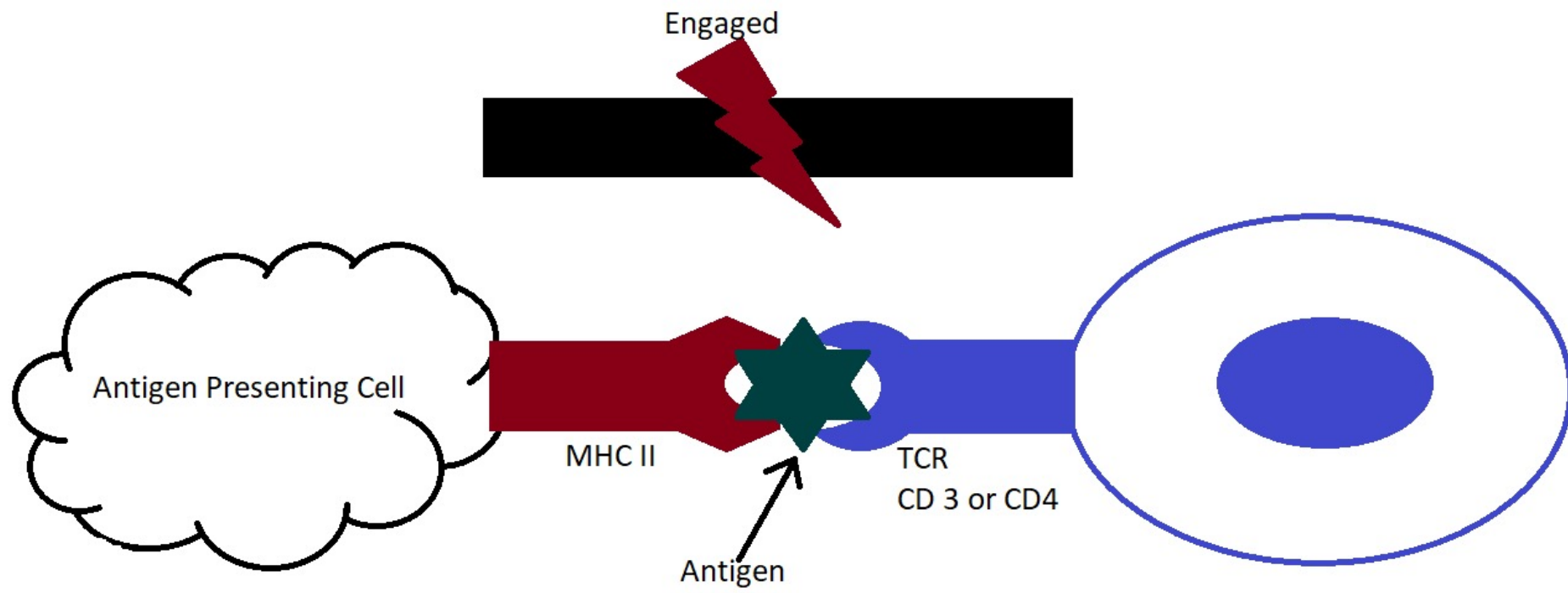
Pre-clinical trials, Sabel 2006

- BALB/c mice with MT-901 mammary adenocarcinoma tumors underwent cryoablation, resection or no treatment, and tumor draining lymph nodes were harvested
- Cryoablation resulted in significant increase in the fraction of tumor-specific T-cells
- Significant decrease of pulmonary metastases in mice undergoing cryoablation compared with surgical excision

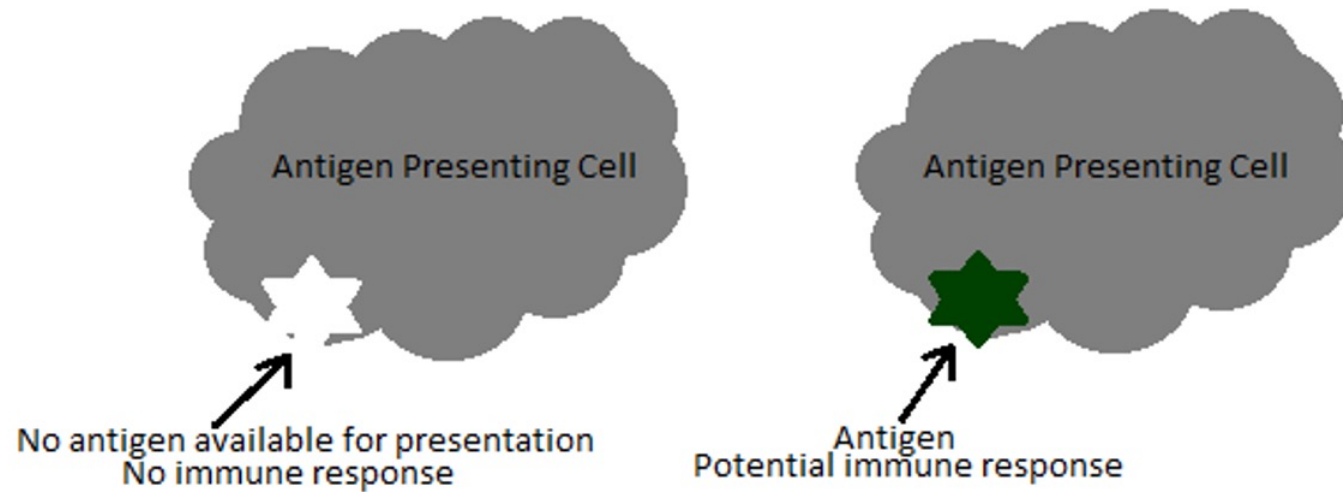
Cryo-Immuno Effects

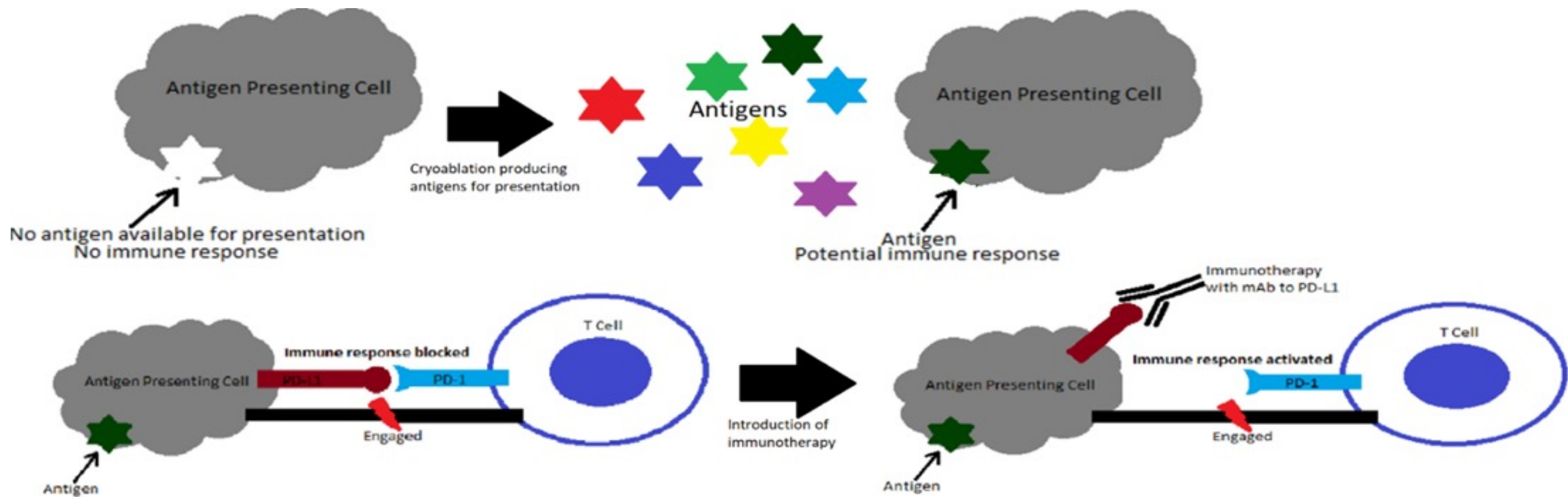
- Preserved proteins released from cryoablation serve as antigens





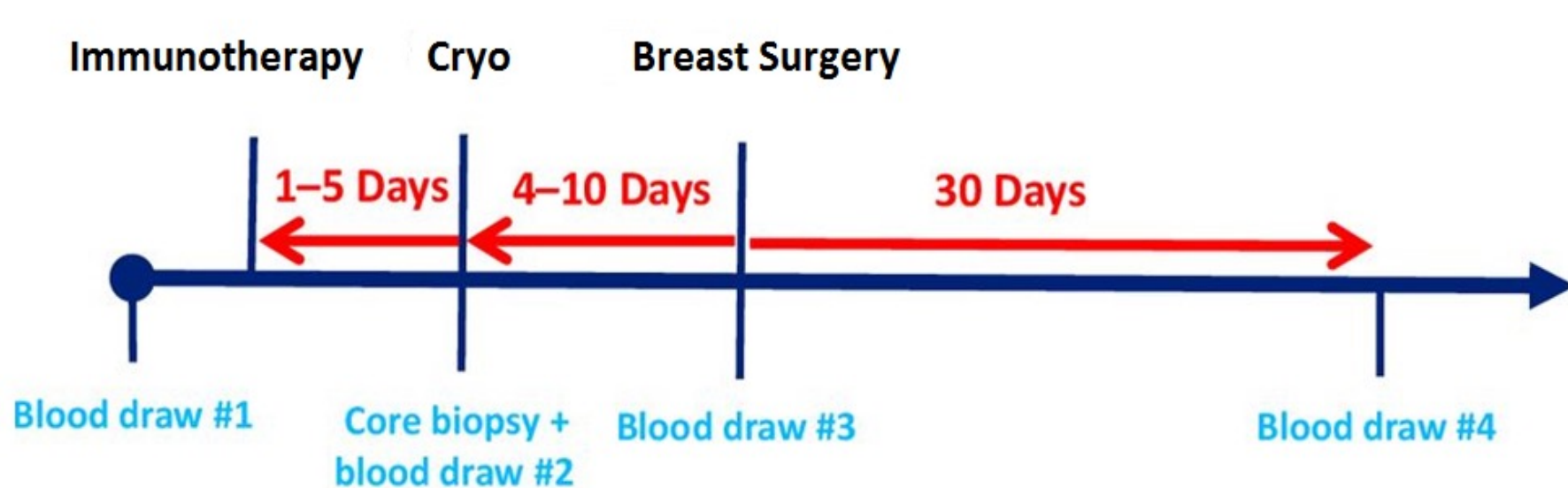
Cryo-Immune Effects



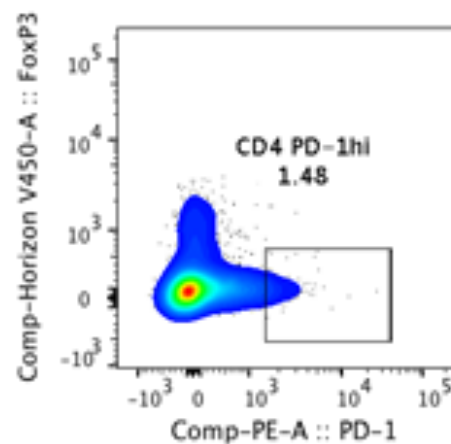


Research

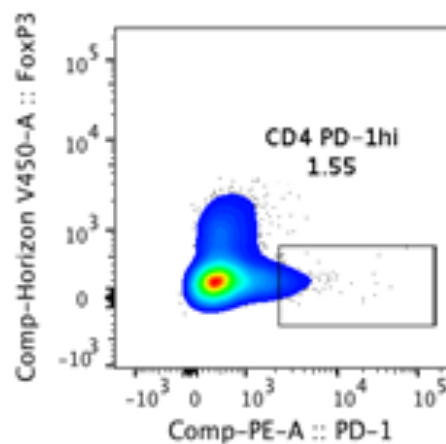
- Cryoablation and ipilimumab/nivolumab in early-stage operative breast cancer



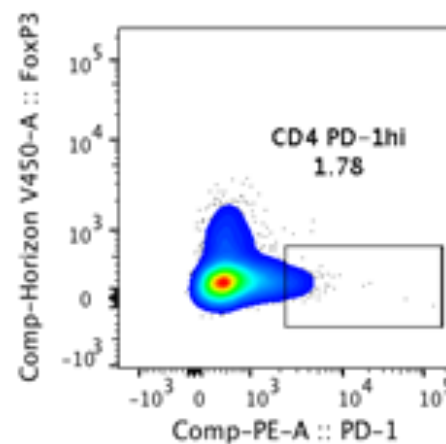
Cryoablation



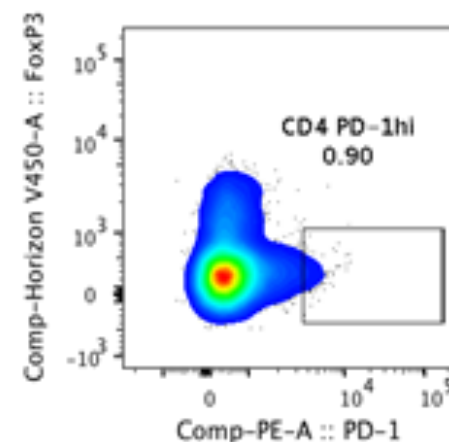
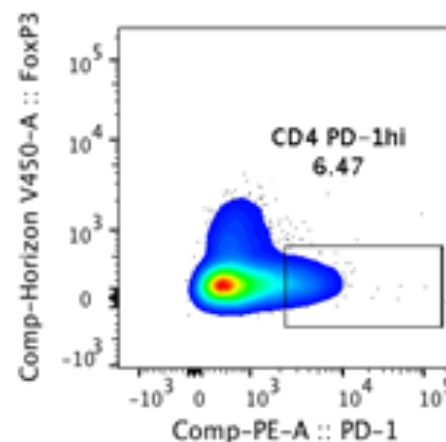
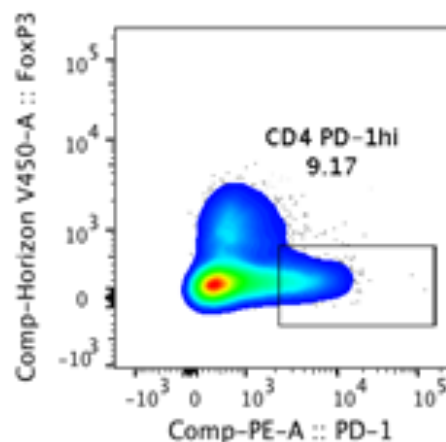
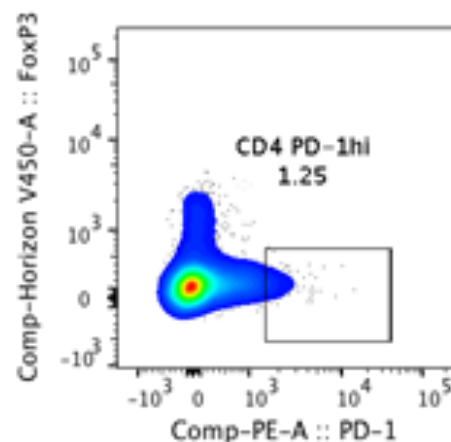
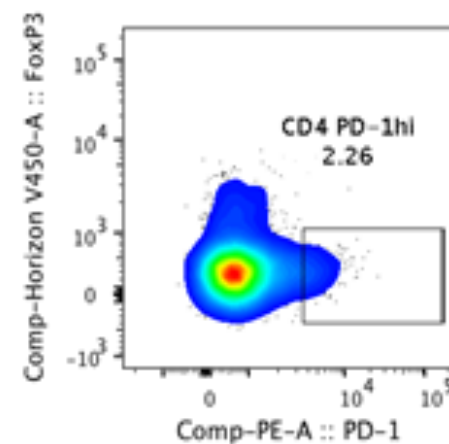
Ipilimumab

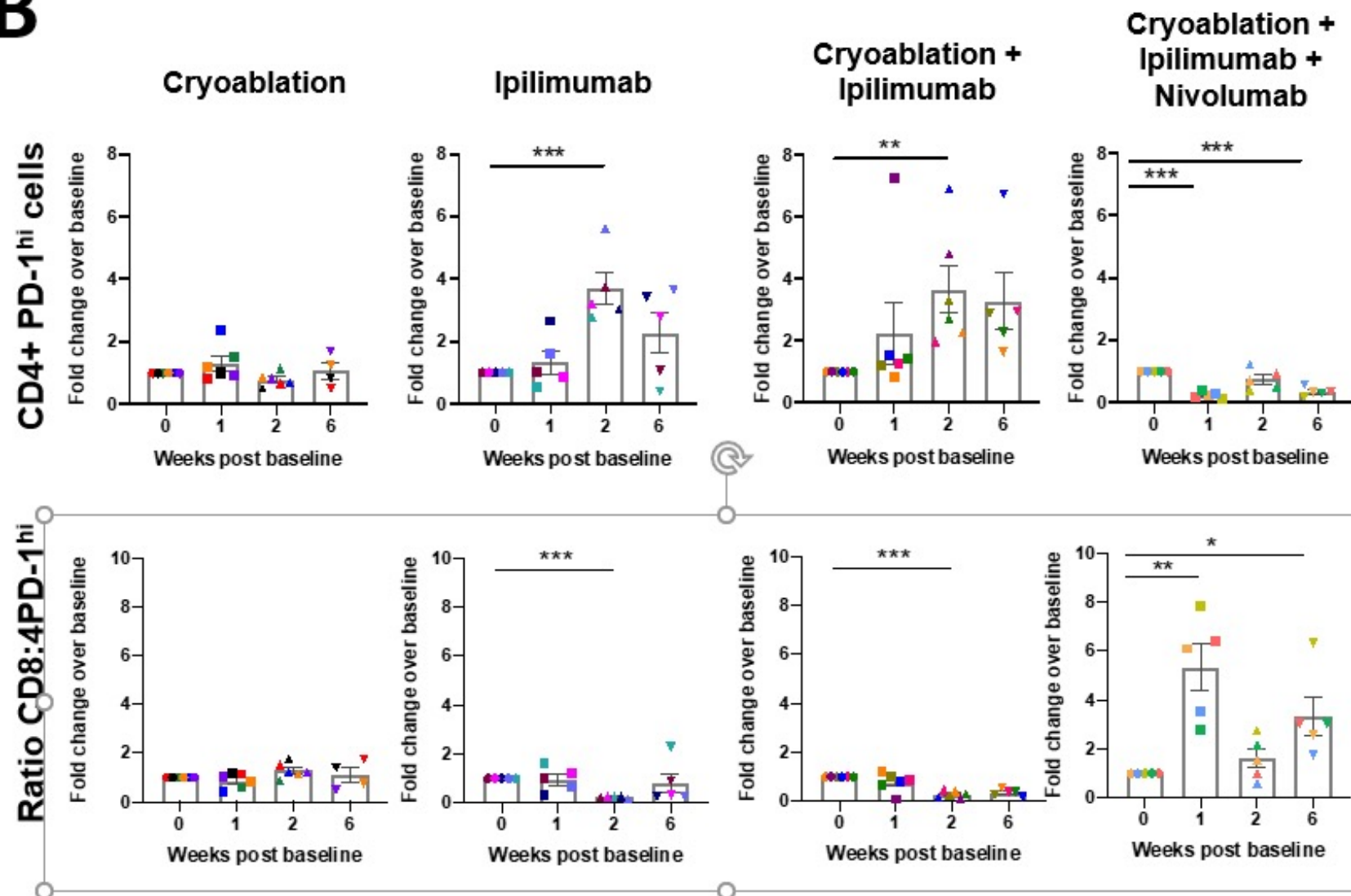


Cryoablation +
Ipilimumab



Cryoablation +
Ipilimumab +
Nivolumab



B

Differences in Hyperthermic vs. Hypothermic ablation

- RFA and MWA
 - Shorter treatment times
 - Can burn the skin and **pectoralis muscle**
 - Need for sedation
 - Proteins denatured
- Cryoablation
 - Longer treatment times
 - Can burn the skin, **typically not the pectoralis muscle**
 - No need for sedation, ice ball is analgesic
 - Proteins not denatured

Remaining Issues to Think About

- What should we do about the axilla?
- Reliability of imaging (contrast-enhanced MRI or mammography)

Conclusion

- Justification for locoregional treatment of breast cancer
- Approach
- Cryo-immune effects
- Remaining issues