

Optoacoustic imaging features correlate with breast cancer clinicopathological prognostic factors

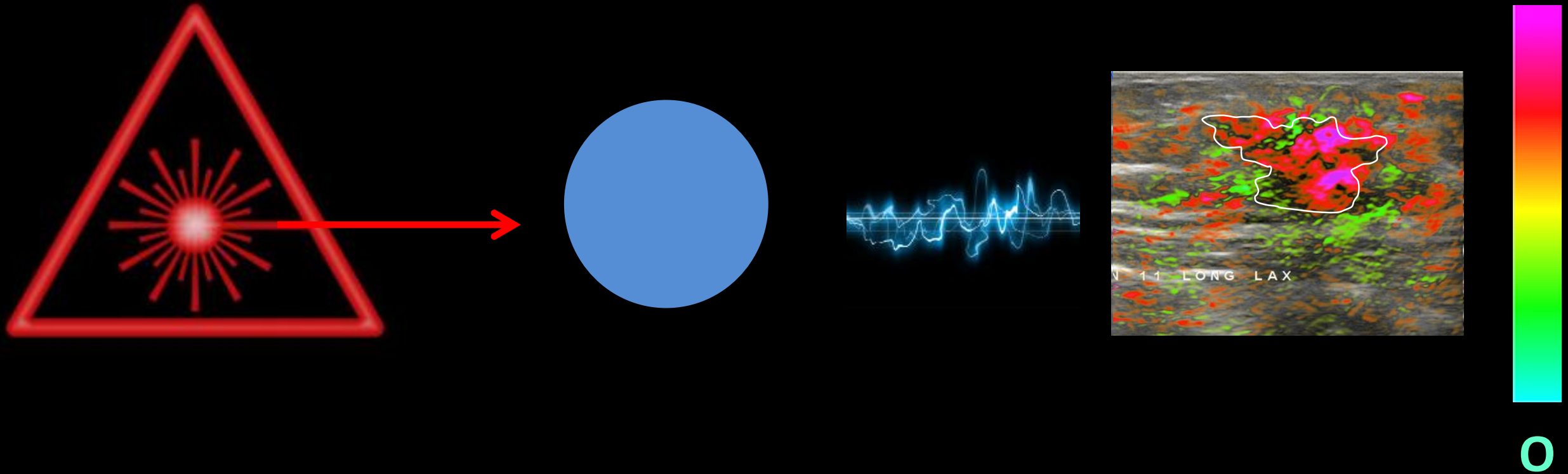
B. Dogan, G. Menezes, R. Butler, E. Neuschler, P. Lavin, R. Aitchison, L.F. Tucker, P. Otto, S. Grobmyer;

Conflicts of interest



- **B. Dogan:** None. **G. Menezes:** Employee; Part-time employment contract at Seno Medical Instruments. **R. Butler:** None. **E. Neuschler:** None. **P. Lavin:** Consultant; Research contract with Seno Medical Instruments to provide study design and analysis services. **R. Aitchison:** Consultant; Research contract with Seno Medical Instruments to provide study design and analysis services. **L.F. Tucker:** None. **P. Otto:** None. **S. Grobmyer:** Advisory Board; Member of the Medical Advisory Board at Seno Medical Instruments.

How does OA work?



Aim of the study

- To identify the potential role of OA/US as an indicator for breast cancer prognostic markers of Grade, Ki-67 and axillary lymph node metastases.

- Prospective, multicenter, observational study.
- We analyzed the data retrospectively to determine the relationship between OA/US and prognostic markers of breast cancer.
- ANOVA tests were used to identify the relationship between OA/US features, prognostic factors and metastatic lymph node groups. Spearman correlation was used to test correlation of continuous variables.

Methods

Results

- 1690 patients with 1757 breast masses were included in this study (between 2012 and 2015).
- 678 were malignant.
- 653 invasive cancers were identified.
- 163 (25%) Grade 1, 287 (44%) Grade 2, 193 (30%) Grade 3 carcinomas and 10 (1%) missing.
- 384 Lymph nodes available: 278 (72%) Negative, 86 (22%) 1 or 2 positive and 20 (6%) were 3 or more positive.
- Ki-67 available in 519 cases.

Results OA/US - Grades

| | Grade 1 vs. Grade 3 p-values | Grade 1 vs. Grade 2 p-values | Grade 2 vs. Grade 3 p-values | Grade 1 vs. Grades 2+3 p-values | Grade 2 vs. Grades 1+3 p-values | Grade 3 vs. Grades 1+2 p-values |
|--|------------------------------------|------------------------------------|------------------------------------|---------------------------------------|---------------------------------------|---------------------------------------|
| OA/US Total Internal Scores | 0.006 | 0.102 | 0.117 | 0.019 | 0.943 | 0.021 |
| OA/US Total External Scores | 0.019 | 0.753 | 0.003 | 0.367 | 0.041 | 0.002 |
| OA/US Ratio Total Internal/Total External | 3.3237×10^{-9} | 0.051 | 6.8679×10^{-7} | 0.000051 | 0.040 | 1.2229×10^{-9} |

Results OA/US - Grades

| | Grade 1 vs. Grade 3 p-values | Grade 1 vs. Grade 2 p-values | Grade 2 vs. Grade 3 p-values | Grade 1 vs. Grades 2+3 p-values | Grade 2 vs. Grades 1+3 p-values | Grade 3 vs. Grades 1+2 p-values |
|--|---|---|---|--|--|--|
| OA/US Total Internal Scores | 0.006 | 0.102 | 0.117 | 0.019 | 0.943 | 0.021 |
| OA/US Total External Scores | 0.019 | 0.753 | 0.003 | 0.367 | 0.041 | 0.002 |
| OA/US Ratio Total Internal/Total External | 3.3237 x10⁻⁹ | 0.051 | 6.8679 x10⁻⁷ | 0.000051 | 0.040 | 1.2229 x10⁻⁹ |

Results OA/US - Grades

| | Grade 1 vs. Grade 3 p-values | Grade 1 vs. Grade 2 p-values | Grade 2 vs. Grade 3 p-values | Grade 1 vs. Grades 2+3 p-values | Grade 2 vs. Grades 1+3 p-values | Grade 3 vs. Grades 1+2 p-values |
|--|------------------------------------|------------------------------------|------------------------------------|---------------------------------------|---------------------------------------|---------------------------------------|
| OA/US Total Internal Scores | 0.006 | 0.102 | 0.117 | 0.019 | 0.943 | 0.021 |
| OA/US Total External Scores | 0.019 | 0.753 | 0.003 | 0.367 | 0.041 | 0.002 |
| OA/US Ratio Total Internal/Total External | 3.3237×10^{-9} | 0.051 | 6.8679×10^{-7} | 0.000051 | 0.040 | 1.2229×10^{-9} |

Results OA/US - Grades

| | Grade 1 vs. Grade 3 p-values | Grade 1 vs. Grade 2 p-values | Grade 2 vs. Grade 3 p-values | Grade 1 vs. Grades 2+3 p-values | Grade 2 vs. Grades 1+3 p-values | Grade 3 vs. Grades 1+2 p-values |
|--|------------------------------------|------------------------------------|------------------------------------|---------------------------------------|---------------------------------------|---------------------------------------|
| OA/US Total Internal Scores | 0.006 | 0.102 | 0.117 | 0.019 | 0.943 | 0.021 |
| OA/US Total External Scores | 0.019 | 0.753 | 0.003 | 0.367 | 0.041 | 0.002 |
| OA/US Ratio Total Internal/Total External | 3.3237×10^{-9} | 0.051 | 6.8679×10^{-7} | 0.000051 | 0.040 | 1.2229×10^{-9} |

Results OA/US - Grades

| | Internal OA/US Features | External OA/US Features | Ratio Total Internal/Total External Features |
|---------|--|--|--|
| GRADE 1 | 8.37 SD 2.78 95% CI 7.94 – 8.81 | 7.57 SD 2.16 95% CI 7.23 – 7.90 | 1.13 SD 0.42 95% CI 1.07 – 1.20 |
| GRADE 2 | 8.81 SD 2.67 95% CI 8.50 – 9.12 | 7.63 SD 2.10 95% CI 7.38 – 7.87 | 1.20 SD 0.41 95% CI 1.16 – 1.25 |
| GRADE 3 | 9.11 SD 2.78 95% CI 8.72 – 9.51 | 7.11 SD 2.14 95% CI 6.81 – 7.41 | 1.31 SD 0.35 95% CI 1.26 – 1.36 |


Results OA/US - Grades

| | Internal OA/US Features | External OA/US Features | Ratio Total Internal/Total External Features |
|----------------|---------------------------------------|---------------------------------------|--|
| GRADE 1 | 8.37 SD 2.78 95% CI 7.94 – 8.81 | 7.57 SD 2.16 95% CI 7.23 – 7.90 | 1.13 SD 0.42 95% CI 1.07 – 1.20 |
| GRADE 2 | 8.81 SD 2.67 95% CI 8.50 – 9.12 | 7.63 SD 2.10 95% CI 7.38 – 7.87 | 1.20 SD 0.41 95% CI 1.16 – 1.25 |
| GRADE 3 | 9.11 SD 2.78 95% CI 8.72 – 9.51 | 7.11 SD 2.14 95% CI 6.81 – 7.41 | 1.31 SD 0.35 95% CI 1.26 – 1.36 |



Results OA/US - Grades

| | Internal OA/US Features | External OA/US Features | Ratio Total Internal/Total External Features |
|---------|--|--|--|
| GRADE 1 | <p>8.37 SD 2.78 95% CI 7.94 – 8.81</p> | <p>7.57 SD 2.16 95% CI 7.23 – 7.90</p> | <p>1.13 SD 0.42 95% CI 1.07 – 1.20</p> |
| GRADE 2 | <p>8.81 SD 2.67 95% CI 8.50 – 9.12</p> | <p>7.63 SD 2.10 95% CI 7.38 – 7.87</p> | <p>1.20 SD 0.41 95% CI 1.16 – 1.25</p> |
| GRADE 3 | <p>9.11 SD 2.78 95% CI 8.72 – 9.51</p> | <p>7.11 SD 2.14 95% CI 6.81 – 7.41</p> | <p>1.31 SD 0.35 95% CI 1.26 – 1.36</p> |




Results OA/US - Grades

| | Internal OA/US Features | External OA/US Features | Ratio Total Internal/Total External Features |
|----------------|--|--|--|
| GRADE 1 | 8.37 SD 2.78 95% CI 7.94 – 8.81  | 7.57 SD 2.16 95% CI 7.23 – 7.90 | 1.13 SD 0.42 95% CI 1.07 – 1.20 |
| GRADE 2 | 8.81 SD 2.67 95% CI 8.50 – 9.12 | 7.63 SD 2.10 95% CI 7.38 – 7.87 | 1.20 SD 0.41 95% CI 1.16 – 1.25 |
| GRADE 3 | 9.11 SD 2.78 95% CI 8.72 – 9.51 | 7.11 SD 2.14 95% CI 6.81 – 7.41 | 1.31 SD 0.35 95% CI 1.26 – 1.36 |





Results OA/US - Grades

| | Internal OA/US Features | External OA/US Features | Ratio Total Internal/Total External Features |
|----------------|--|---------------------------------------|--|
| GRADE 1 | 8.37 SD 2.78 95% CI 7.94 – 8.81  | 7.57 SD 2.16 95% CI 7.23 – 7.90 | 1.13 SD 0.42 95% CI 1.07 – 1.20 |
| GRADE 2 | 8.81 SD 2.67 95% CI 8.50 – 9.12 | 7.63 SD 2.10 95% CI 7.38 – 7.87 | 1.20 SD 0.41 95% CI 1.16 – 1.25 |
| GRADE 3 | 9.11 SD 2.78 95% CI 8.72 – 9.51  | 7.11 SD 2.14 95% CI 6.81 – 7.41 | 1.31 SD 0.35 95% CI 1.26 – 1.36 |

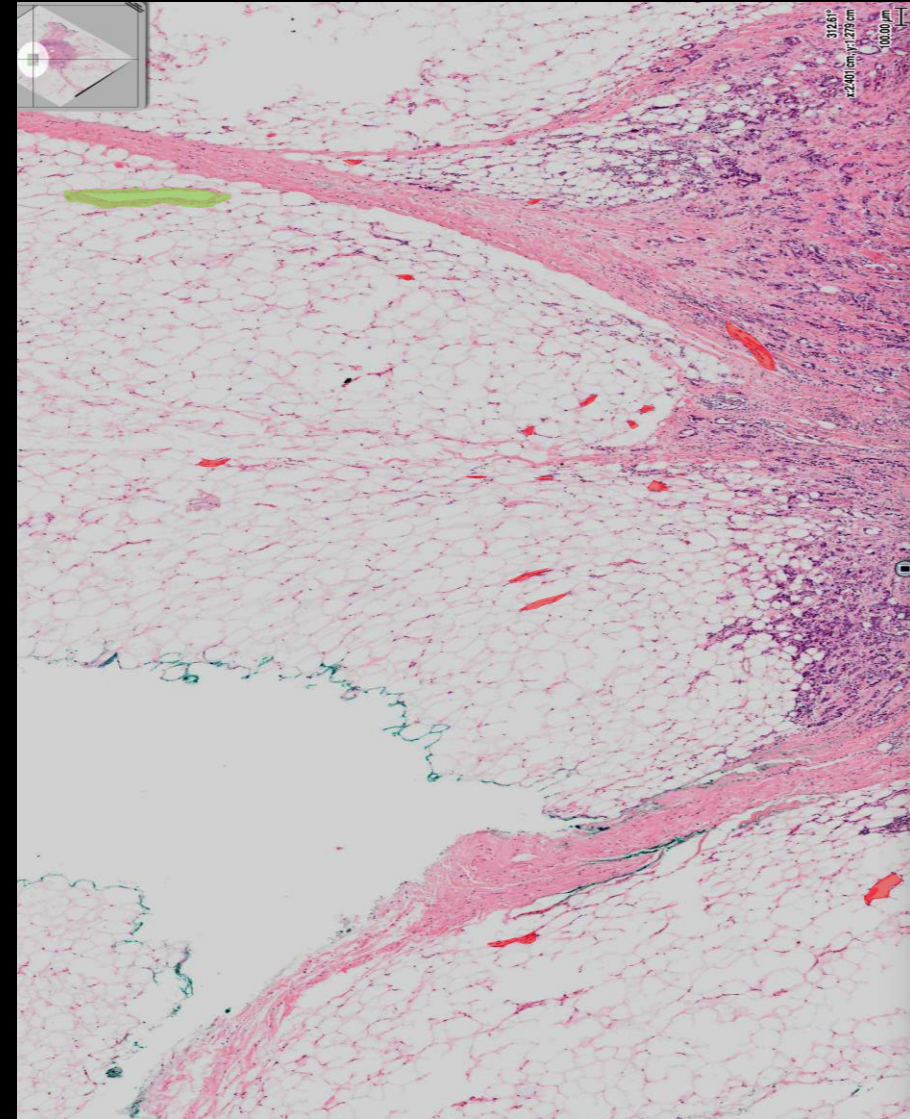
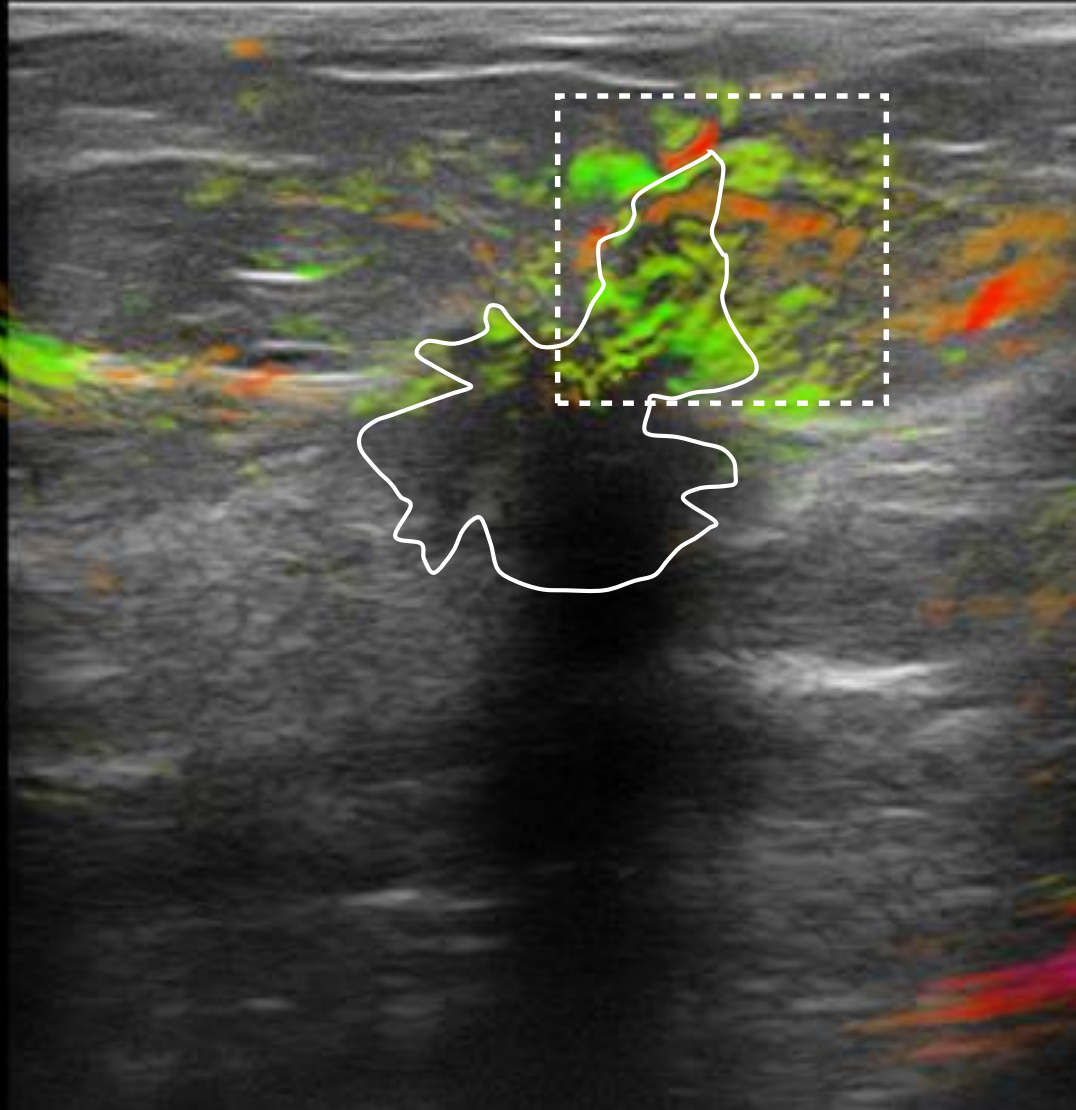
Results OA/US - Grades

| | Internal OA/US Features | External OA/US Features | Ratio Total Internal/Total External Features |
|----------------|--|--|--|
| GRADE 1 | <p>8.37 SD 2.78 95% CI 7.94 – 8.81</p>  | <p>7.57 SD 2.16 95% CI 7.23 – 7.90</p>  | <p>1.13 SD 0.42 95% CI 1.07 – 1.20</p> |
| GRADE 2 | <p>8.81 SD 2.67 95% CI 8.50 – 9.12</p> | <p>7.63 SD 2.10 95% CI 7.38 – 7.87</p> | <p>1.20 SD 0.41 95% CI 1.16 – 1.25</p> |
| GRADE 3 | <p>9.11 SD 2.78 95% CI 8.72 – 9.51</p>  | <p>7.11 SD 2.14 95% CI 6.81 – 7.41</p> | <p>1.31 SD 0.35 95% CI 1.26 – 1.36</p> |

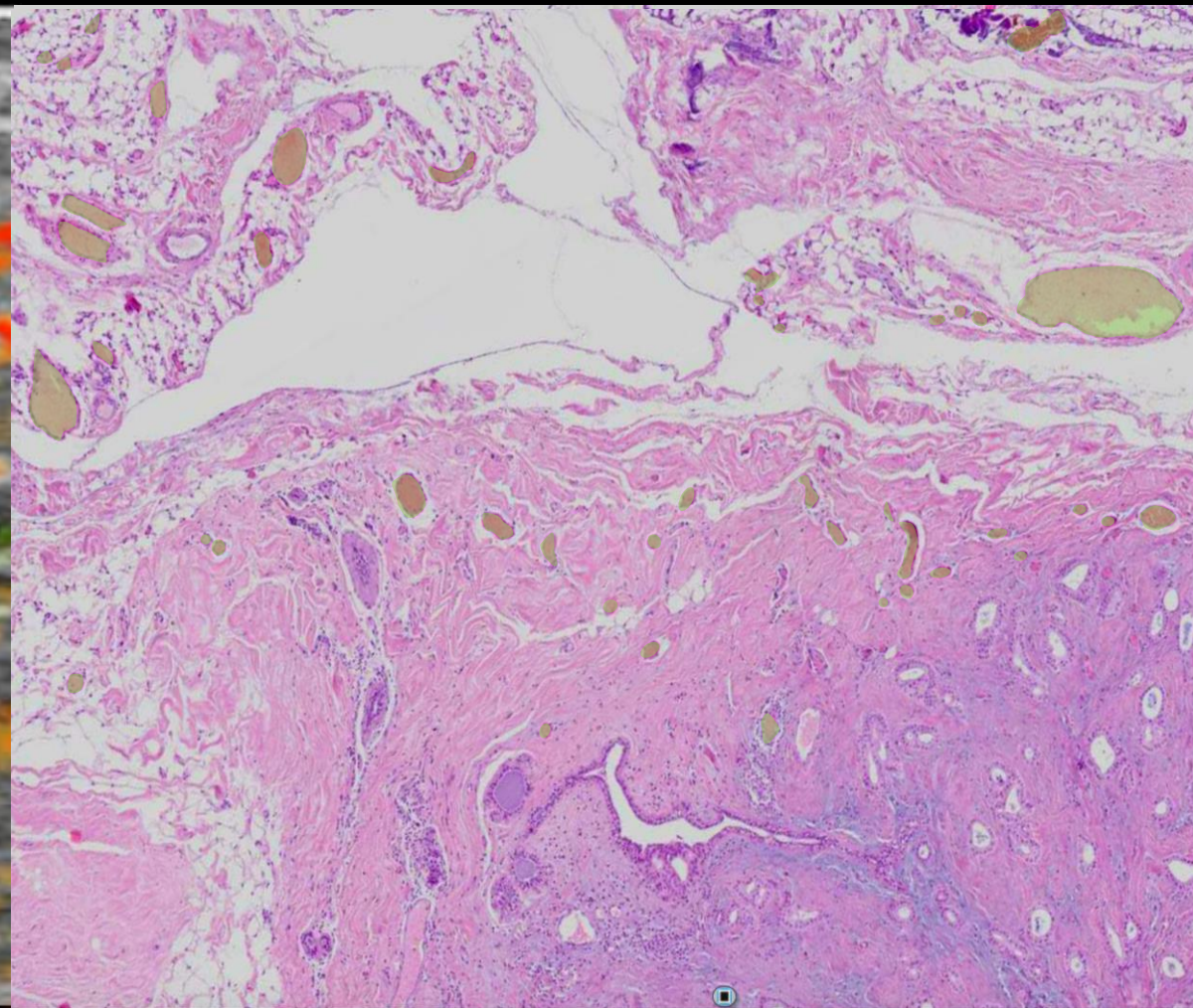
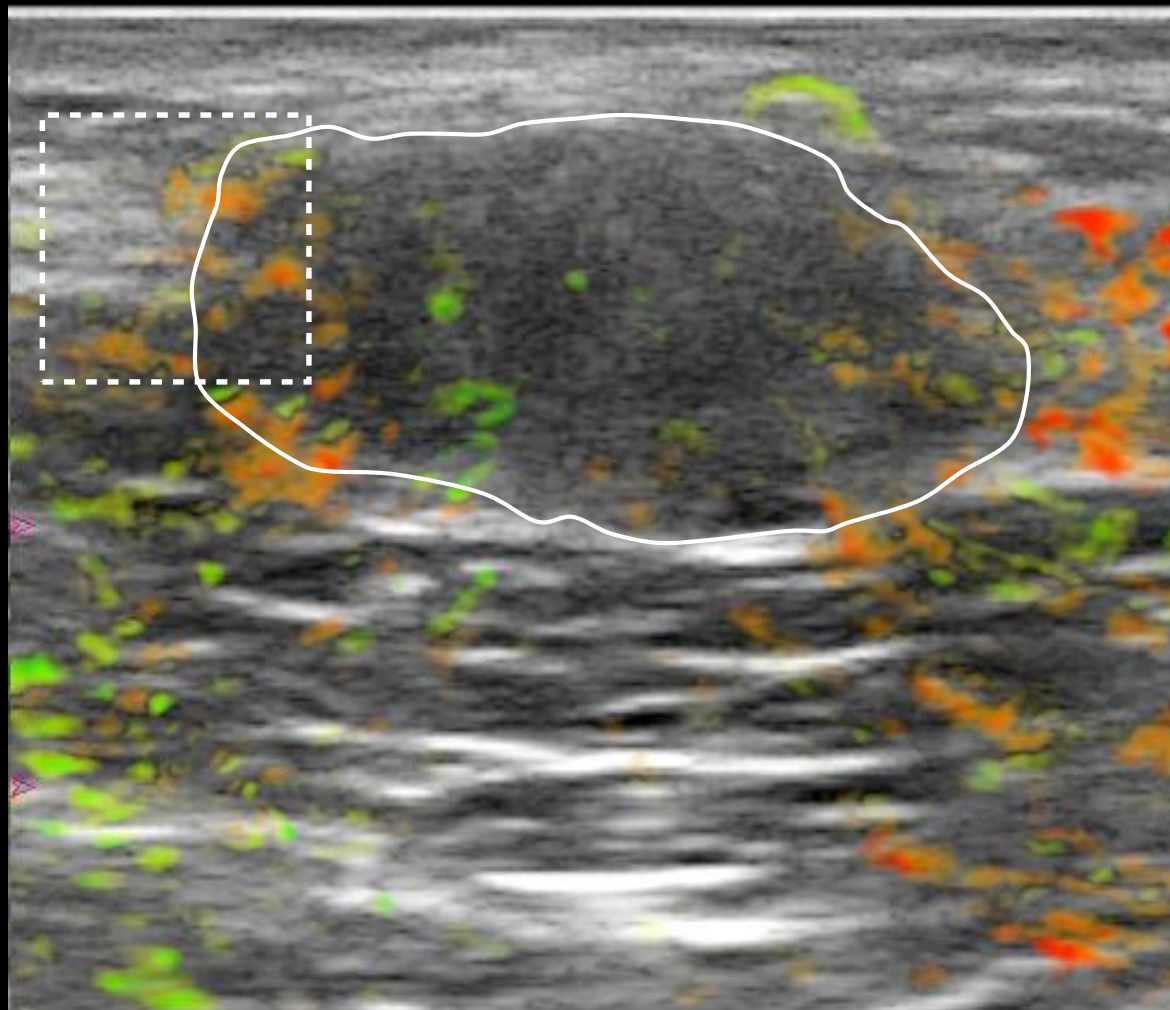
Results OA/US - Grades

| | Internal OA/US Features | External OA/US Features | Ratio Total Internal/Total External Features |
|----------------|--|--|--|
| GRADE 1 | <p>8.37 SD 2.78 95% CI 7.94 – 8.81</p>  | <p>7.57 SD 2.16 95% CI 7.23 – 7.90</p>  | <p>1.13 SD 0.42 95% CI 1.07 – 1.20</p> |
| GRADE 2 | <p>8.81 SD 2.67 95% CI 8.50 – 9.12</p> | <p>7.63 SD 2.10 95% CI 7.38 – 7.87</p> | <p>1.20 SD 0.41 95% CI 1.16 – 1.25</p> |
| GRADE 3 | <p>9.11 SD 2.78 95% CI 8.72 – 9.51</p>  | <p>7.11 SD 2.14 95% CI 6.81 – 7.41</p>  | <p>1.31 SD 0.35 95% CI 1.26 – 1.36</p> |

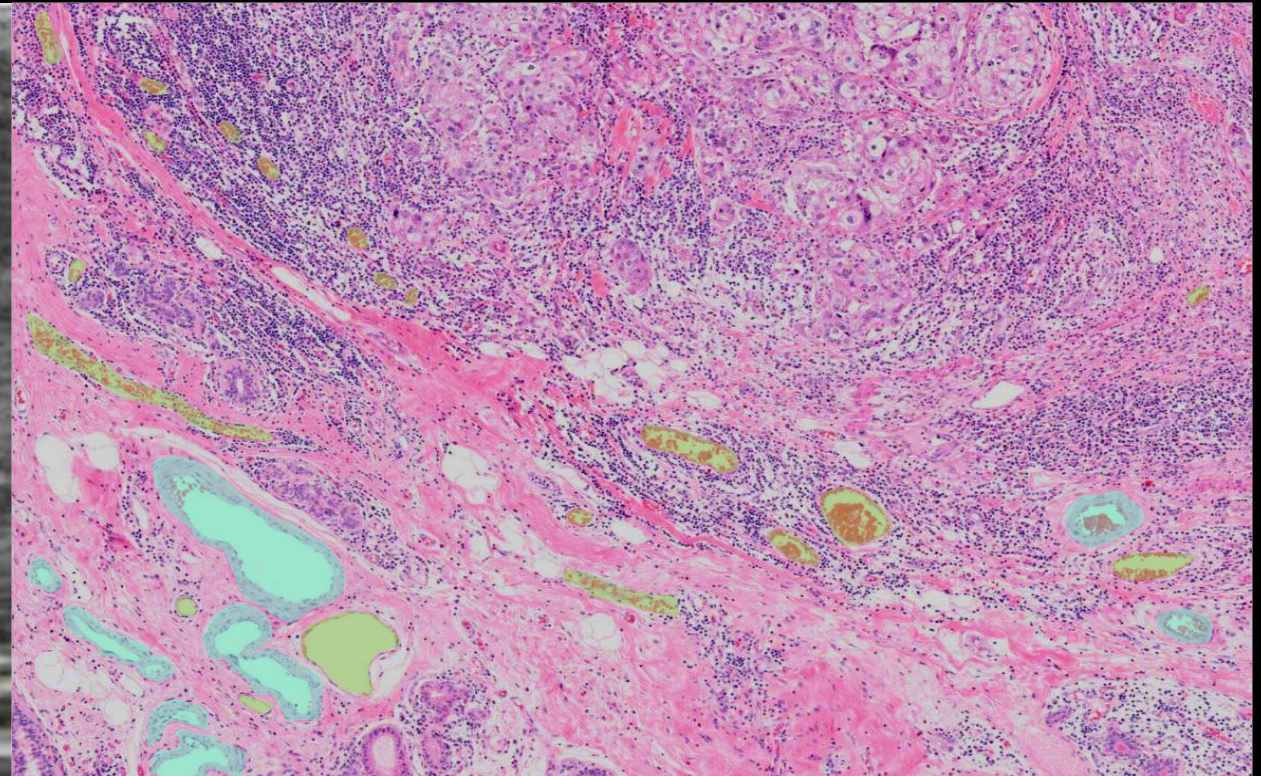
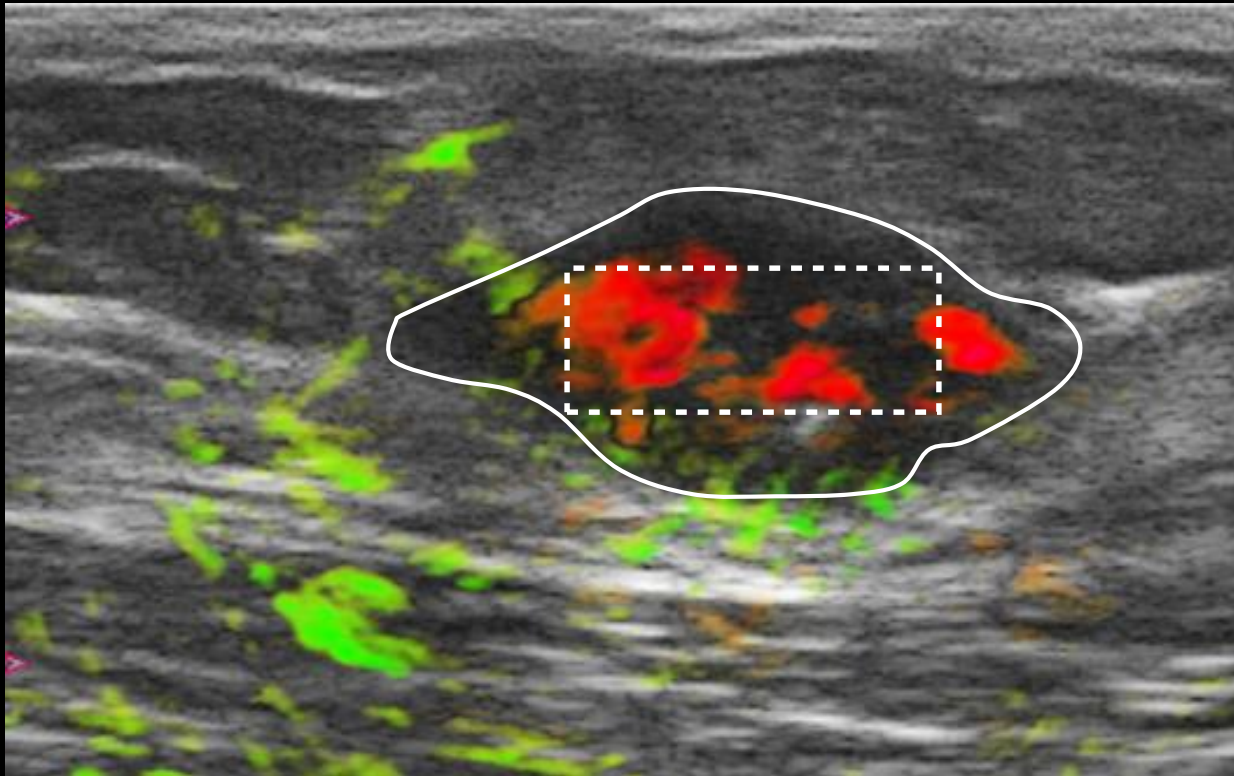
Grade 1 – Predominantly External Features



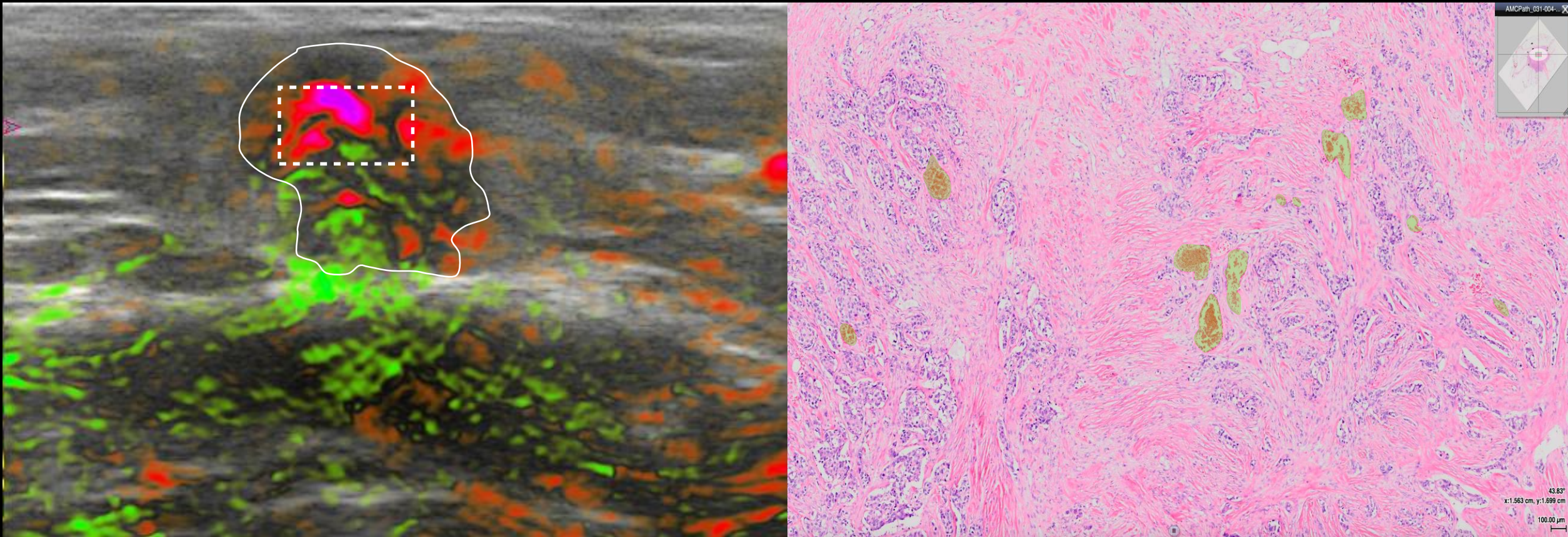
Grade 1 – Predominantly External Features



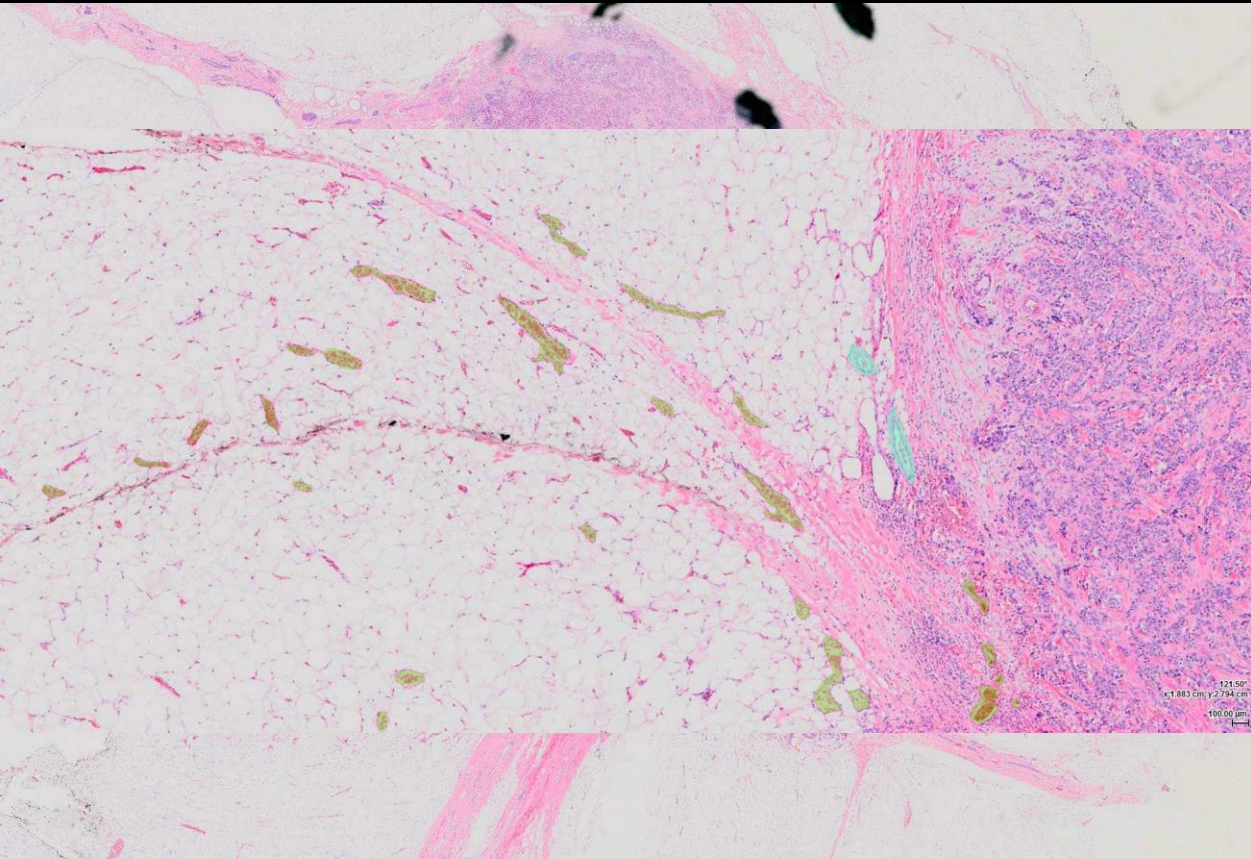
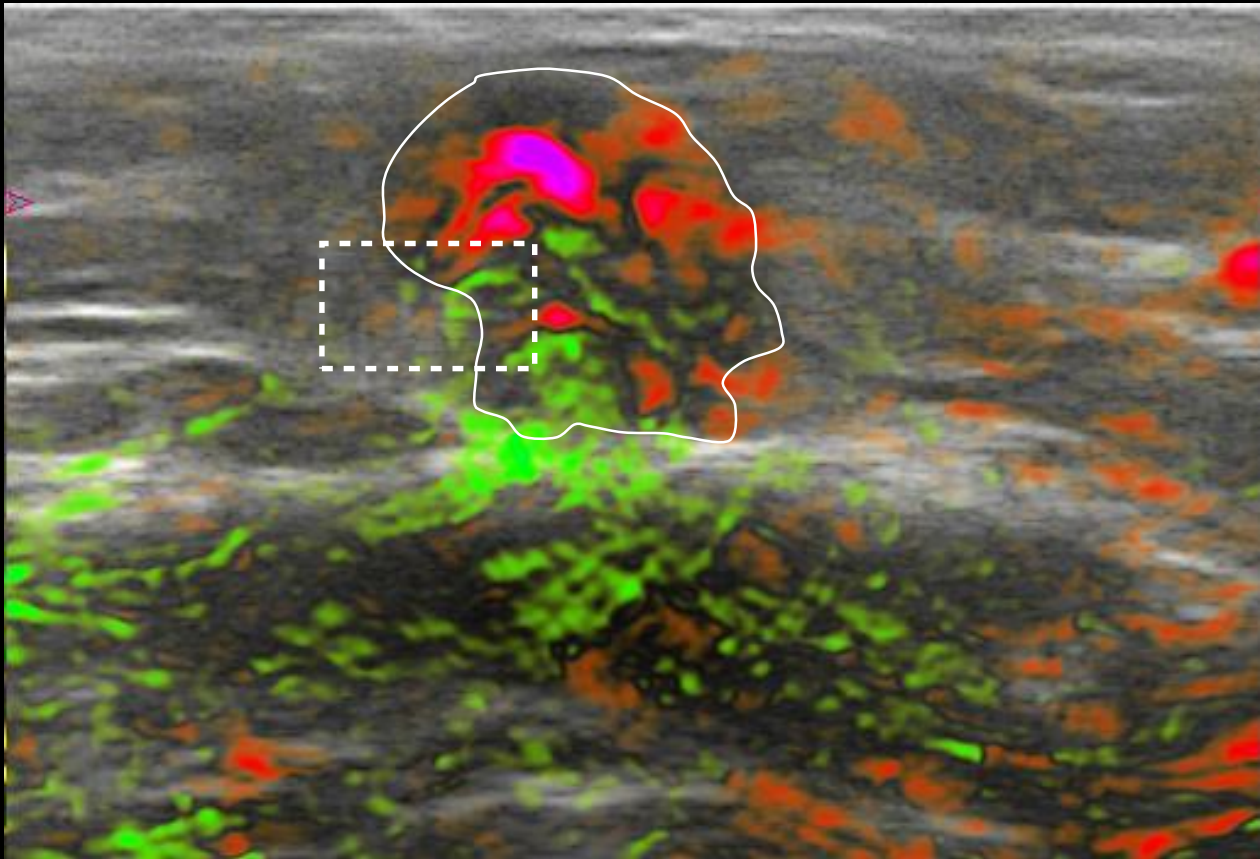
Grade 3 – Predominantly Internal Features



Grade 3 – Predominantly Internal Features



Grade 3 – Predominantly Internal Features



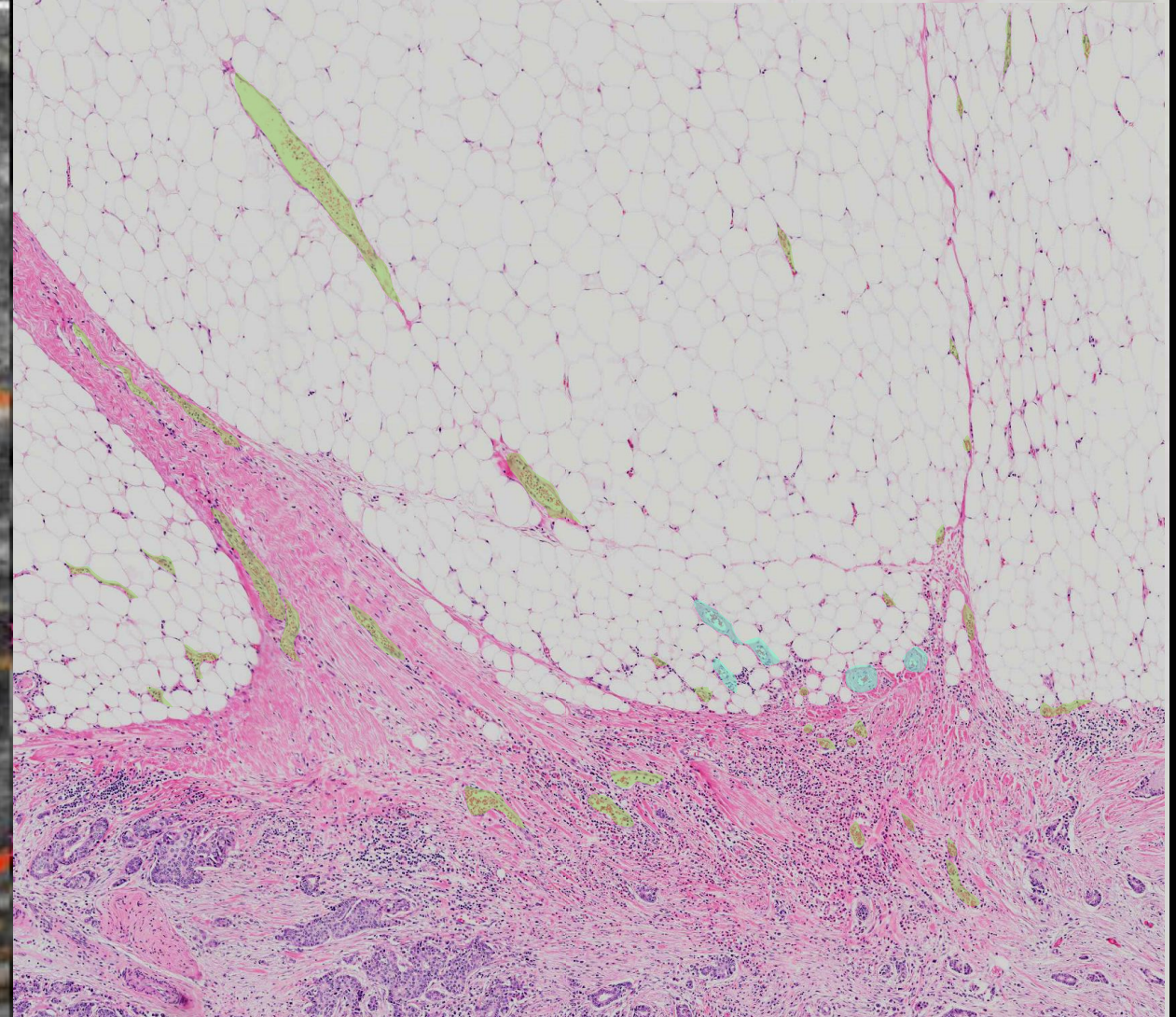
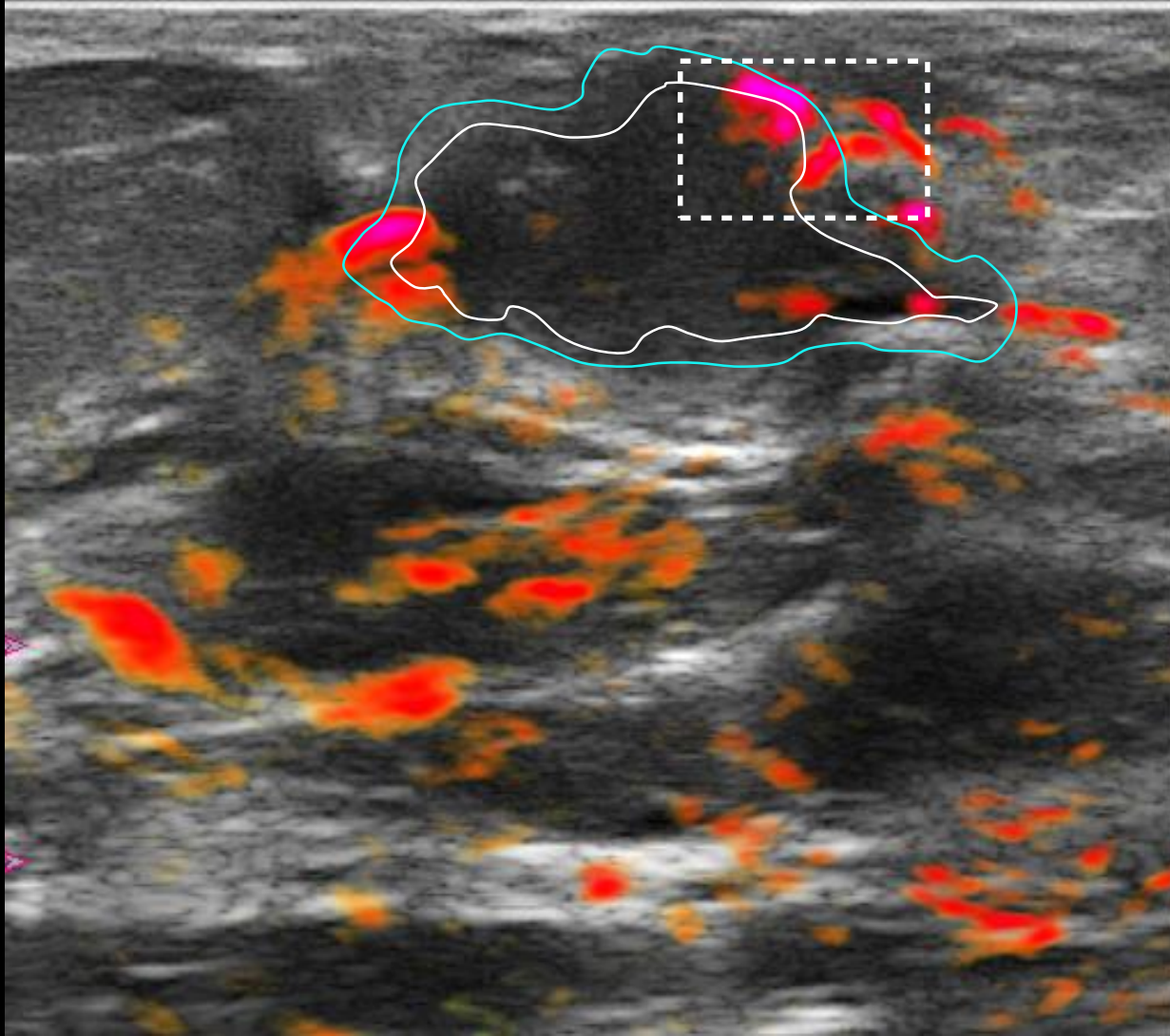
Results OA/US - Grades

| | Internal OA/US Features | External OA/US Features | Ratio Total Internal/Total External Features |
|---------|--|--|--|
| GRADE 1 | 8.37 SD 2.78 95% CI 7.94 – 8.81 | 7.57 SD 2.16 95% CI 7.23 – 7.90 | 1.13 SD 0.42 95% CI 1.07 – 1.20 |
| GRADE 2 | 8.81 SD 2.67 95% CI 8.50 – 9.12 | 7.63 SD 2.10 95% CI 7.38 – 7.87 | 1.20 SD 0.41 95% CI 1.16 – 1.25 |
| GRADE 3 | 9.11 SD 2.78 95% CI 8.72 – 9.51 | 7.11 SD 2.14 95% CI 6.81 – 7.41 | 1.31 SD 0.35 95% CI 1.26 – 1.36 |

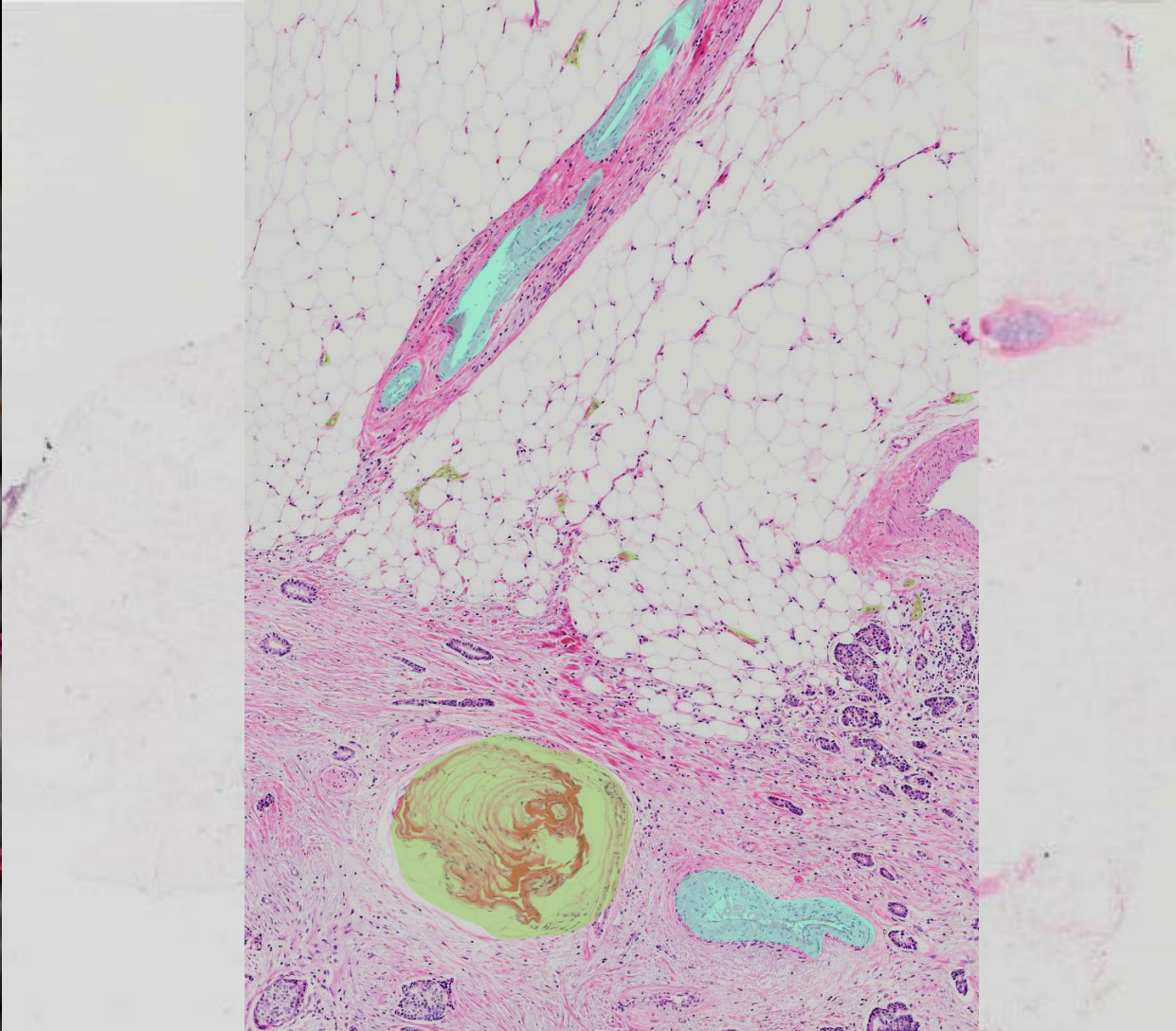
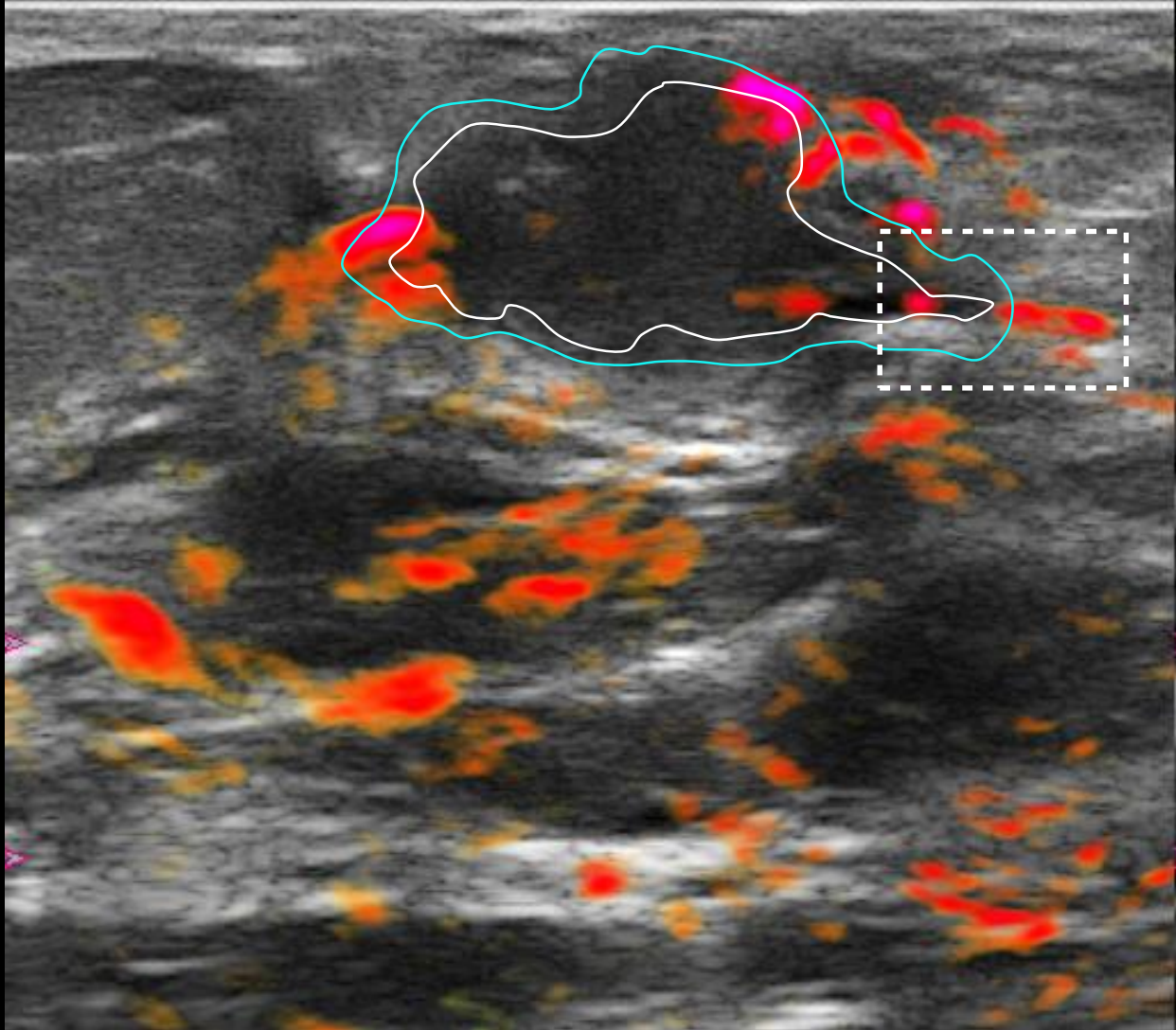
Results OA/US - Grades

| | Internal OA/US Features | External OA/US Features | Ratio Total Internal/Total External Features |
|---------|--|--|--|
| GRADE 1 | <p>8.37 SD 2.78 95% CI 7.94 – 8.81</p> | <p>7.57 SD 2.16 95% CI 7.23 – 7.90</p> | <p>1.13 SD 0.42 95% CI 1.07 – 1.20</p> |
| GRADE 2 | <p>8.81 SD 2.67 95% CI 8.50 – 9.12</p> | <p>7.63 SD 2.10 95% CI 7.38 – 7.87</p> | <p>1.20 SD 0.41 95% CI 1.16 – 1.25</p> |
| GRADE 3 | <p>9.11 SD 2.78 95% CI 8.72 – 9.51</p> | <p>7.11 SD 2.14 95% CI 6.81 – 7.41</p> | <p>1.31 SD 0.35 95% CI 1.26 – 1.36</p> |

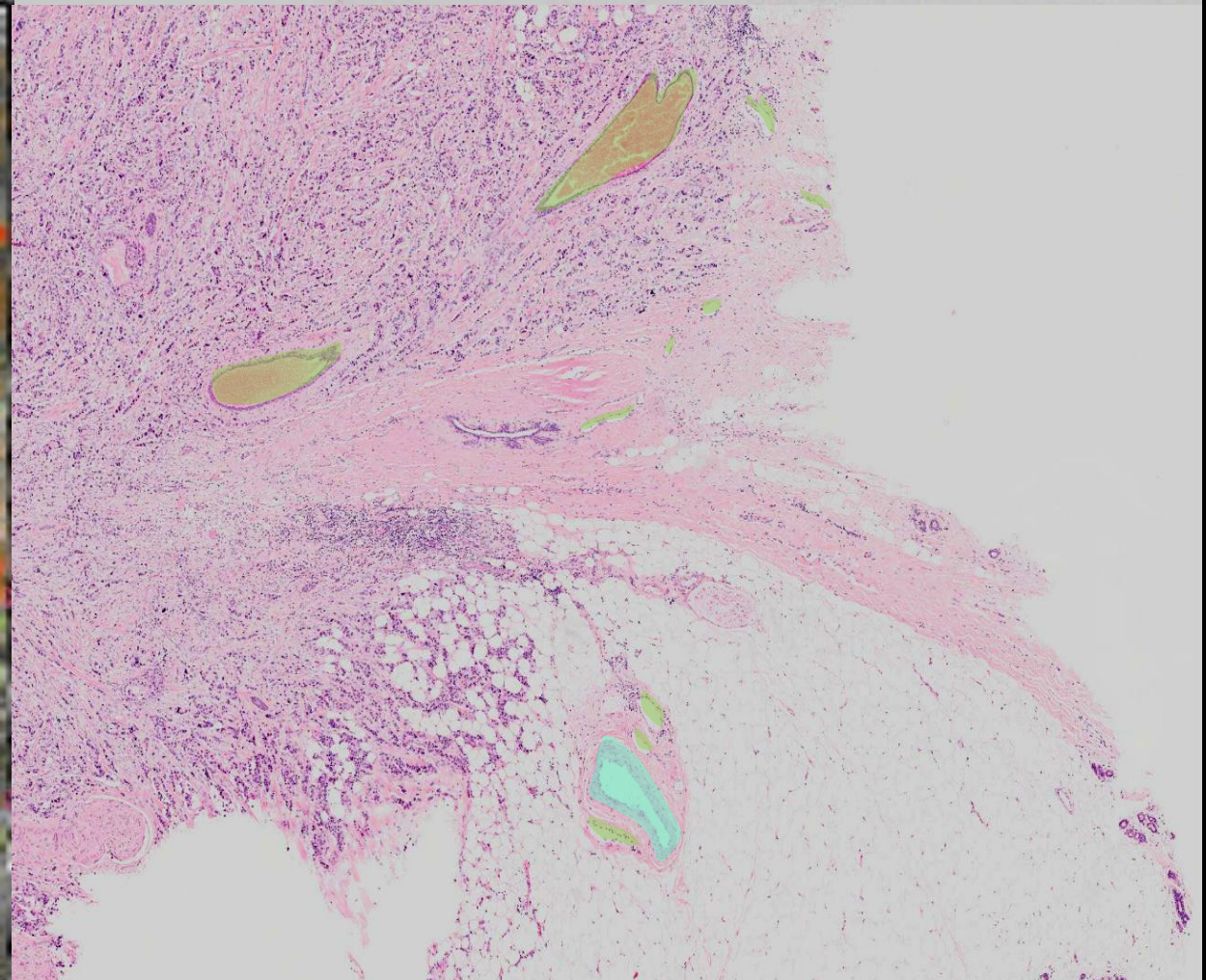
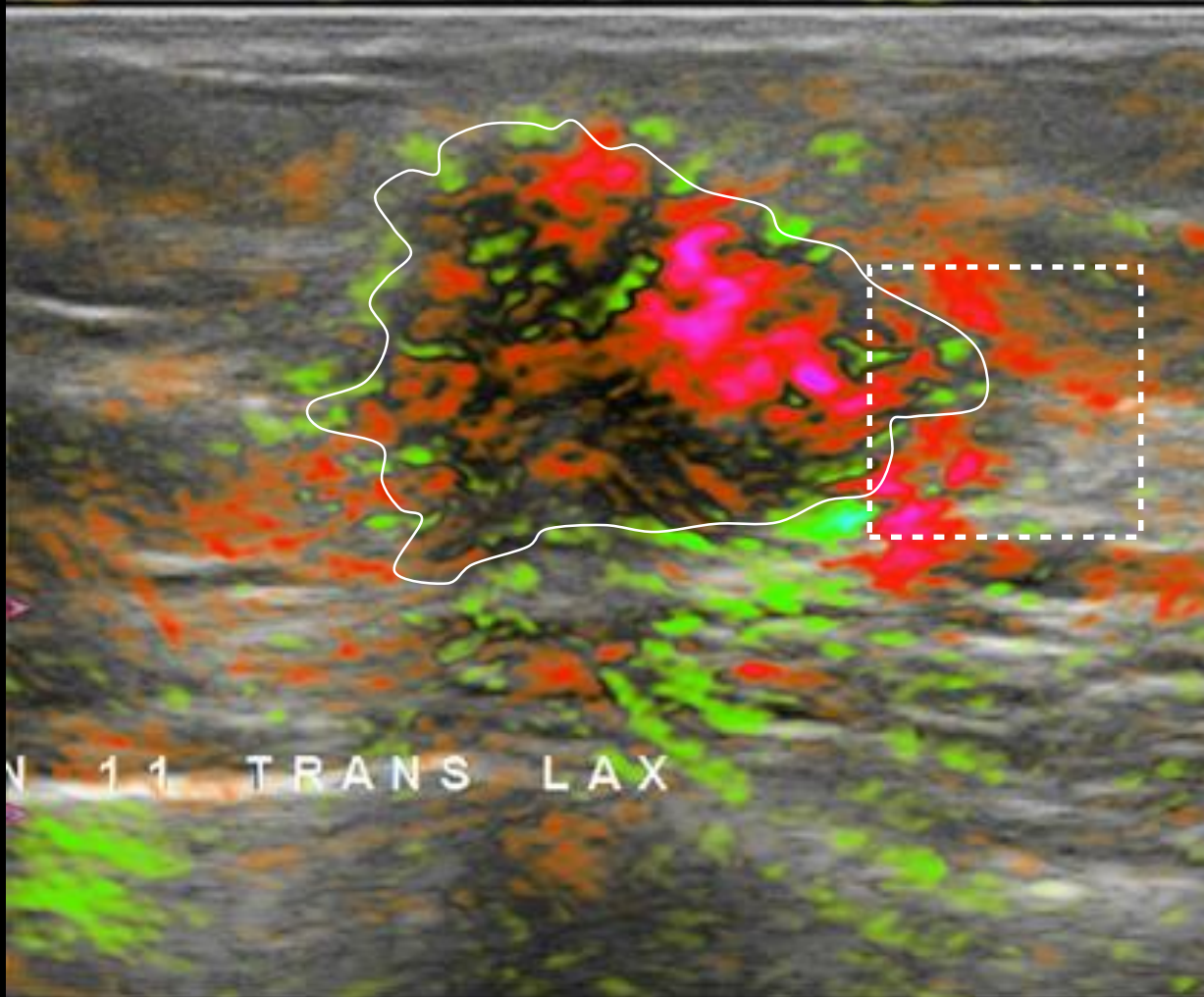
Grade 2 – In between Grades 1 and 3



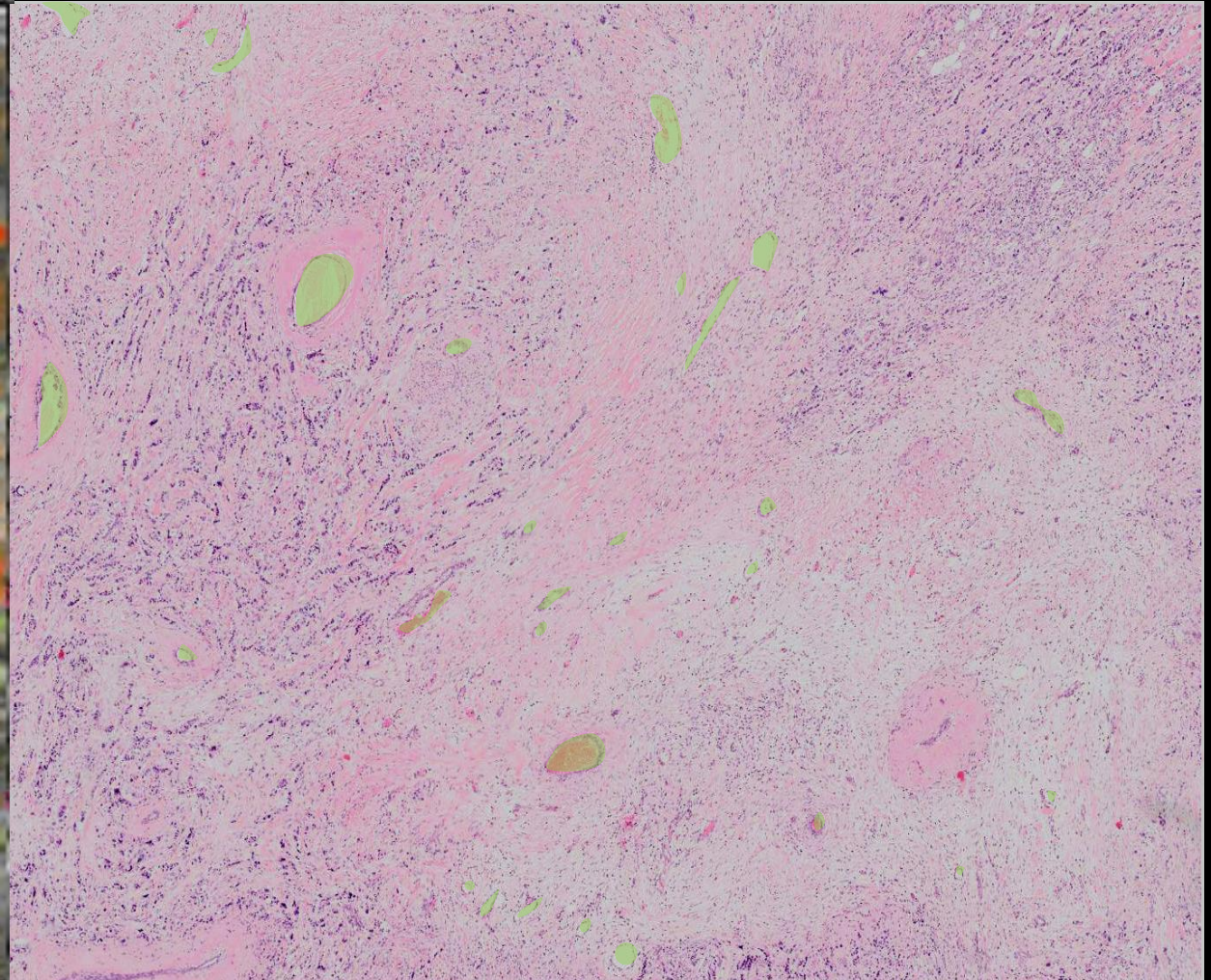
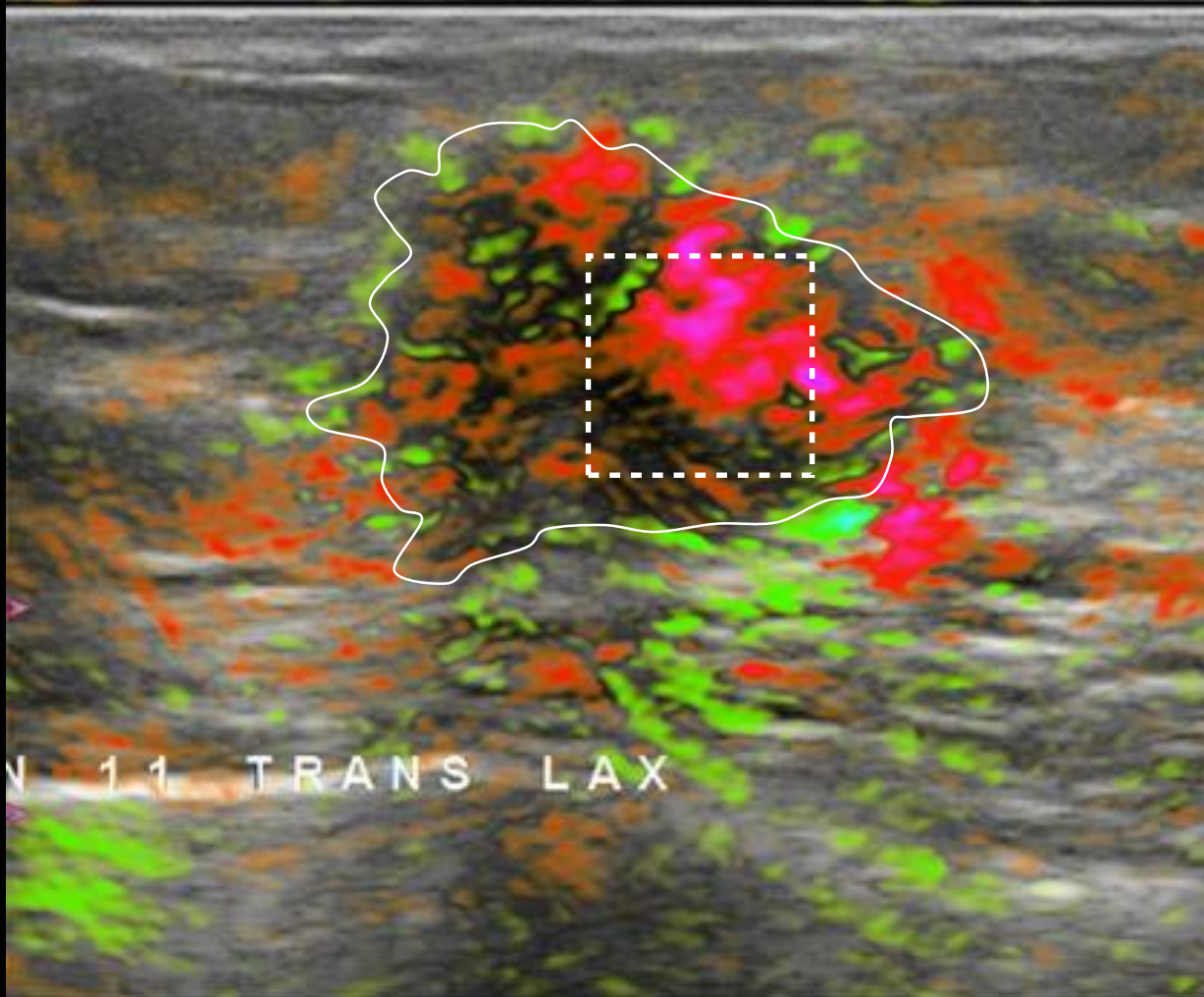
Grade 2 – In between Grades 1 and 3



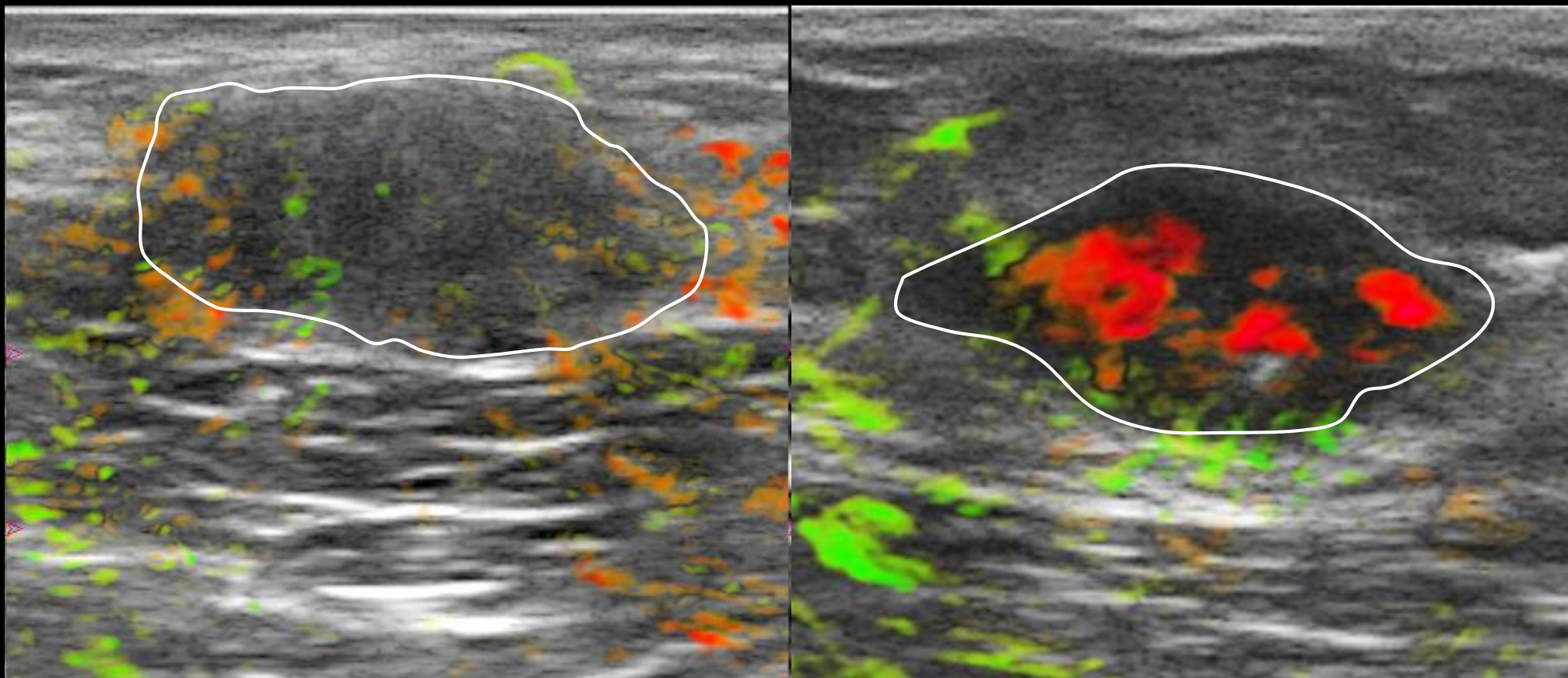
Grade 2 – In between Grades 1 and 3



Grade 2 – In between Grades 1 and 3



Grade 1 vs. Grade 3



Results OA/US – Lymph node (LN) status

| | Negative LN vs. ≥ 3 Positive LN p-values | Negative LN vs. 1 or 2 Positive LN p-values | 1 or 2 Positive LN vs. ≥ 3 Positive LN p-values | Negative LN vs. Others p-values | 1 or 2 Positive LN vs. Others p-values | ≥ 3 Positive LN vs. Others p-values |
|---|--|--|---|------------------------------------|---|---|
| OA/US Total Internal Scores | 0.018 | 0.009 | 0.351 | 0.001 | 0.020 | 0.040 |
| OA/US Total External Scores | 0.000441 | 0.001 | 0.070 | 0.000016 | 0.003 | 0.002 |
| OA/US Ratio Total Internal/Total External | 0.639 | 0.936 | 0.534 | 0.913 | 0.873 | 0.603 |



Results OA/US – Lymph node (LN) status

| | Negative LN vs. ≥ 3 Positive LN p-values | Negative LN vs. 1 or 2 Positive LN p-values | 1 or 2 Positive LN vs. ≥ 3 Positive LN p-values | Negative LN vs. Others p-values | 1 or 2 Positive LN vs. Others p-values | ≥ 3 Positive LN vs. Others p-values |
|---|--|--|---|------------------------------------|---|---|
| OA/US Total Internal Scores | 0.018 | 0.009 | 0.351 | 0.001 | 0.020 | 0.040 |
| OA/US Total External Scores | 0.000441 | 0.001 | 0.070 | 0.000016 | 0.003 | 0.002 |
| OA/US Ratio Total Internal/Total External | 0.639 | 0.936 | 0.534 | 0.913 | 0.873 | 0.603 |

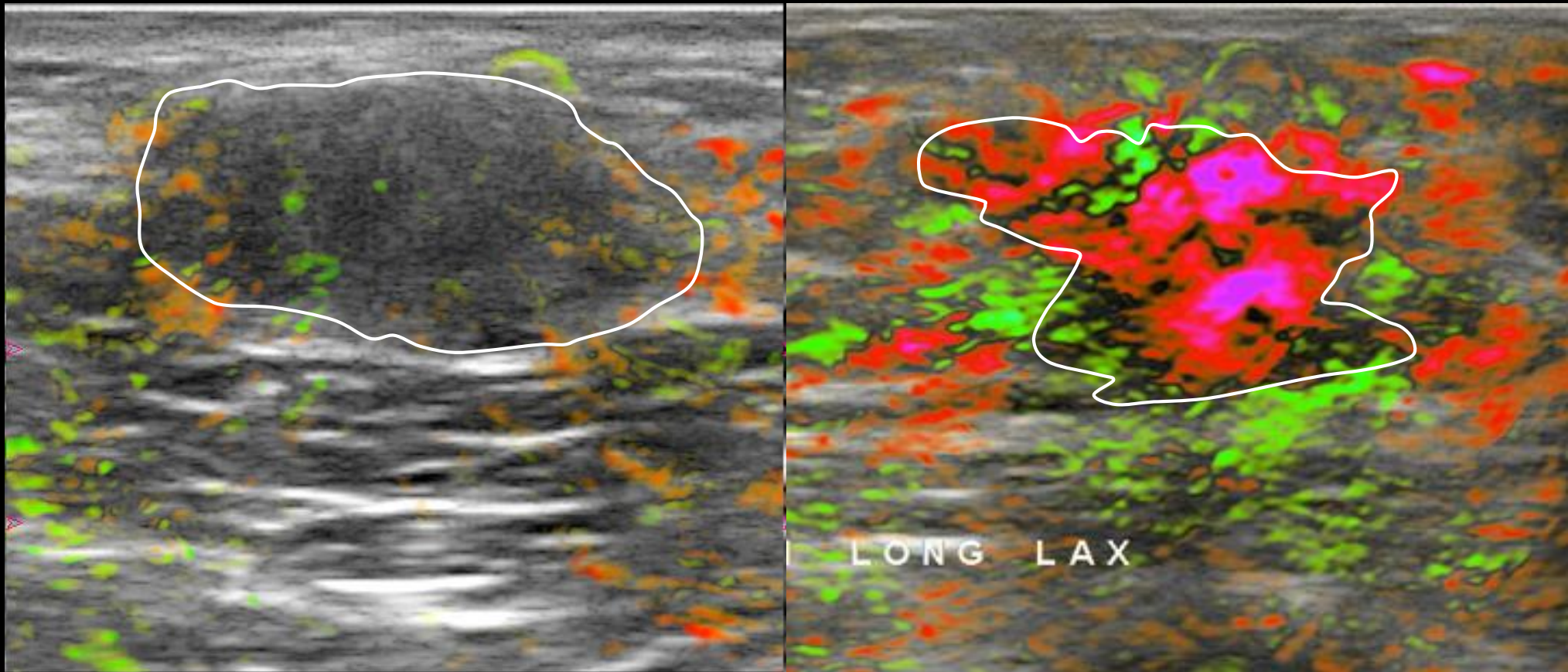
Results OA/US – Lymph node (LN) status

| | Negative LN vs. ≥ 3 Positive LN p-values | Negative LN vs. 1 or 2 Positive LN p-values | 1 or 2 Positive LN vs. ≥ 3 Positive LN p-values | Negative LN vs. Others p-values | 1 or 2 Positive LN vs. Others p-values | ≥ 3 Positive LN vs. Others p-values |
|--|--|---|---|---------------------------------------|---|---|
| OA/US Total Internal Scores | 0.018 | 0.009 | 0.351 | 0.001 | 0.020 | 0.040 |
| OA/US Total External Scores | 0.000441 | 0.001 | 0.070 | 0.000016 | 0.003 | 0.002 |
| OA/US Ratio Total Internal/Total External | 0.639 | 0.936 | 0.534 | 0.913 | 0.873 | 0.603 |

Results OA/US – Lymph node (LN) status

| | Internal OA/US Features | External OA/US Features | Ratio Total Internal/Total External Features |
|--------------------|--|---|--|
| ≥ 3 Positive LN |  <p>9.74 SD 2.28 95% CI 8.67 – 10.81</p> |  <p>8.77 SD 1.71 95% CI 7.97 – 9.57</p> | <p>1.09 SD 0.12 95% CI 1.04 – 1.16</p> |
| 1 or 2 Positive LN | <p>9.13 SD 2.66 95% CI 8.56 – 9.70</p> | <p>8.07 SD 1.96 95% CI 7.65 – 8.50</p> | <p>1.15 SD 0.30 95% CI 1.08 – 1.21</p> |
| Negative LN | <p>8.34 SD 2.71 95% CI 8.01 – 8.65</p> | <p>7.27 SD 2.18 95% CI 7.00 – 7.52</p> | <p>1.19 SD 0.41 95% CI 1.14 – 1.24</p> |

Negative LN vs. Positive LN



Results OA/US and Ki-67

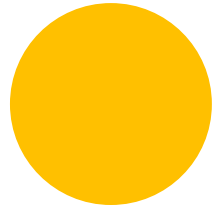
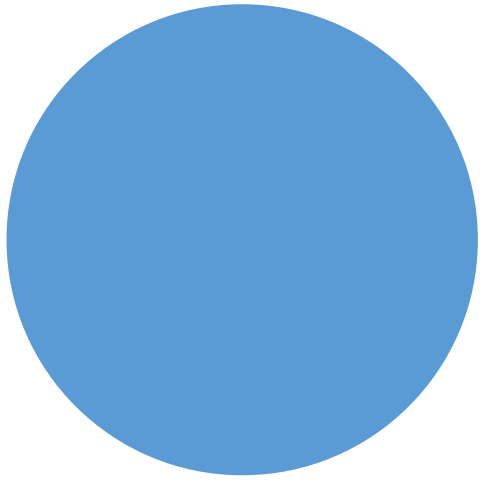
| OA Features | Ki-67 (N=519) Spearman's Correlation | Ki-67 (N=519) Correlation Coefficient |
|---------------------|--------------------------------------|---------------------------------------|
| Internal Vessels | p = 0.001 | 0.146 |
| Internal Blush | p = 0.011 | 0.111 |
| Internal Hemoglobin | p = 0.0003 | 0.157 |
| Boundary Zone | p = 0.0081 | -0.116 |
| Peripheral Zone | p = 0.0024 | -0.133 |
| Sum Total Internal | p = 0.001 | 0.144 |
| Sum Total External | p = 0.002 | -0.134 |
| Ratio Int/Ext | p = 1.23x10 ⁻¹⁰ | 0.278 |

Results OA/US and Ki-67

| OA Features | Ki-67 (N=519) Spearman's Correlation | Ki-67 (N=519) Correlation Coefficient |
|----------------------|--------------------------------------|---------------------------------------|
| Internal Vessels | p = 0.001 | 0.146 |
| Internal Blush | p = 0.011 | 0.111 |
| Internal Hemoglobin | p = 0.0003 | 0.157 |
| Boundary Zone | p = 0.0081 | -0.116 |
| Peripheral Zone | p = 0.0024 | -0.133 |
| Sum Total Internal | p = 0.001 | 0.144 |
| Sum Total External | p = 0.002 | -0.134 |
| Ratio Int/Ext | p = 1.23x10⁻¹⁰ | 0.278 |

Conclusions

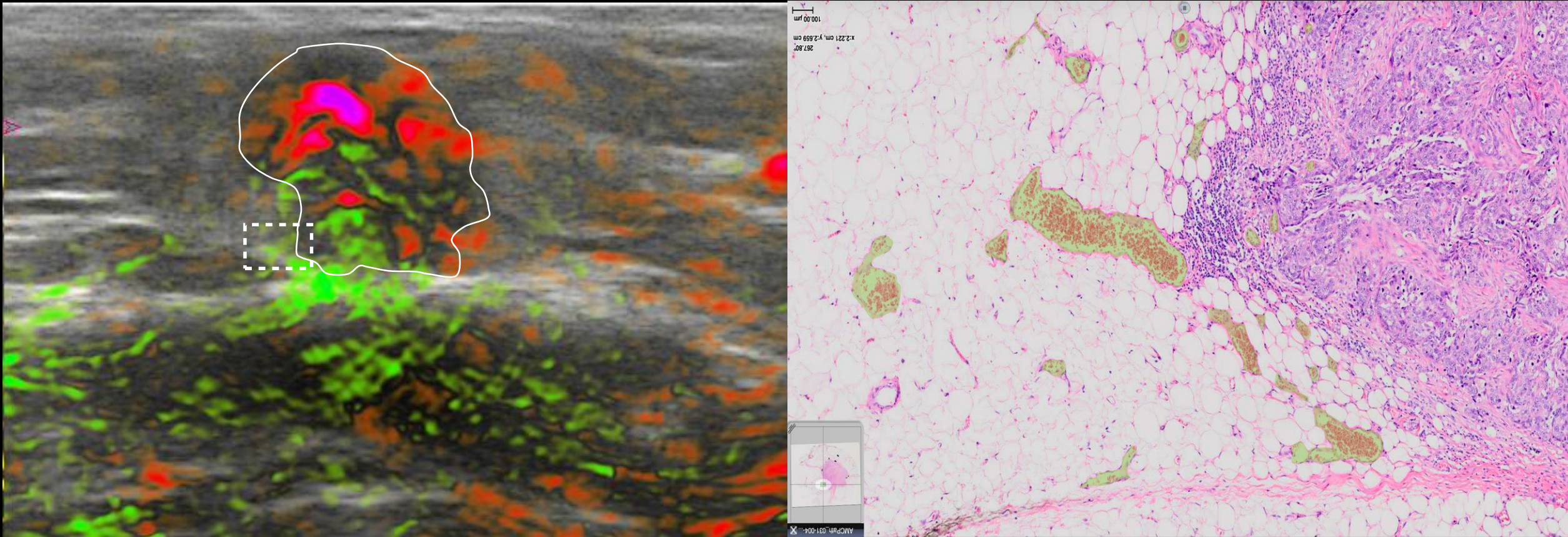
- Limitations: Missing data.
- OA/US features correlate with breast cancer clinicopathological prognostic factors of histologic grade, Ki-67, and axillary LN status.
- Imaging will not replace biomarkers analyses, but it can help the radiologist to take a clinical decision.
- Future studies are needed to confirm these preliminary results.



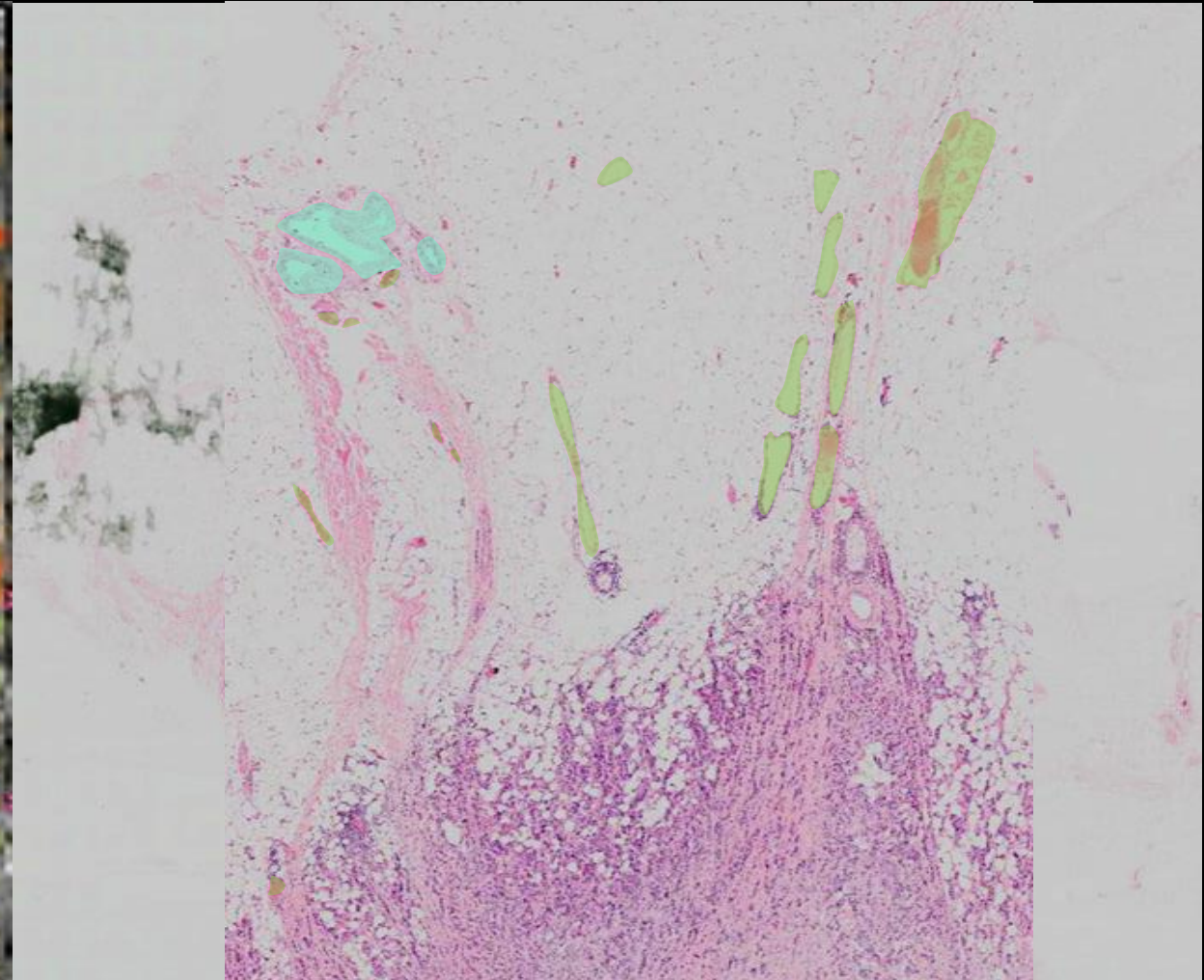
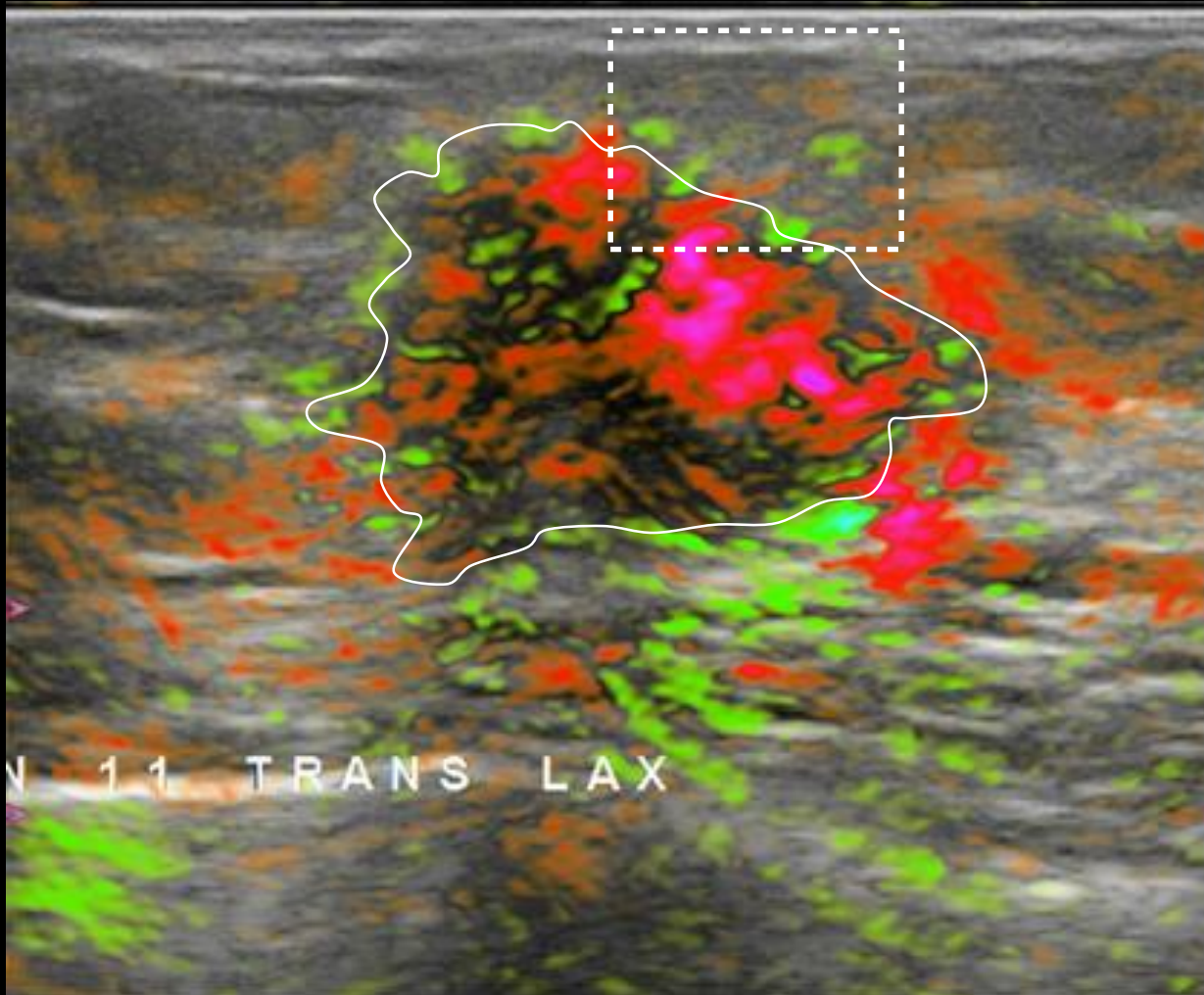
Thank you



Grade 3 – Both Internal and External Features



Grade 2 – In between Grades 1 and 3



Grade 2 – In between Grades 1 and 3

