

## Operator Performance of Voxel Placement for Single-Voxel MRS of Breast Lesions

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**Introduction:** Single-voxel <sup>1</sup>H MR spectroscopy of human breast cancer has become increasingly common, with clinical applications in diagnosis and treatment monitoring, and multi-site clinical trials currently in progress. In order for these measurements to be useful in characterizing lesions, the MRS voxel placement must be accurate and consistent. Poor voxel placement creates partial volume errors and can introduce artifacts, reduce signal-to-noise, and lower measurement reproducibility.

To date, the potential problem of voxel placement inconsistency has not been directly addressed. This is difficult to test in the true setting as voxel placement is performed mid-study with the subject in the scanner. For this work, we performed a retrospective observer-performance study of voxel placement to measure the consistency of voxel placement by expert operators. Note that this study design only tests the agreement of voxel placement and does not determine which placements are more correct or lead to better-quality spectra. We also compared performance between different lesion types, with the expectation that the concordance between operators would be higher for masses than non-mass-like enhancement

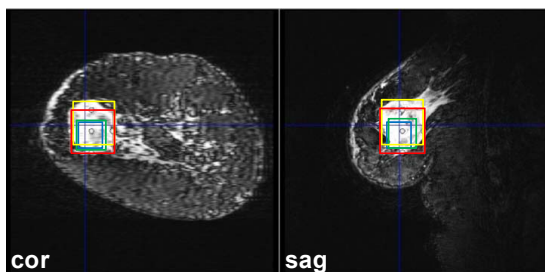
**Methods:** Fifty-seven cases of biopsy-proven locally advanced breast cancer were pre-divided into masses or non-mass-like enhancement. Ten cases were randomly selected from each category for a total of 20 cases. Four participants were selected as operators to perform voxel placements: two radiologists with expertise in breast MR and two MR physicists with expertise in MRS. After a brief training session, the operators were shown unilateral breast MR images (high-resolution, fat-suppressed 3D GRE images pre- and post-gadolinium at 4T with subtraction images and multiplanar reconstructions) from a baseline MRI dataset with a written BI-RADS MRI description of the target lesion for each case. Readers were given guidelines for voxel placement, including a size restriction of 10-50 mm per voxel side, avoidance of necrosis, hemorrhage and clips, and inclusion of less than 33% adipose tissue in the voxel. Using a custom software package that emulates an MR scanner's planning interface, readers were then asked to identify and place a voxel on the target lesion. Voxel rotation was prohibited. Readers were also asked to qualitatively rate their voxel placement (from 1=poor to 5=excellent) to reflect their confidence in sampling the target lesion successfully and complying with the guidelines.

To measure consistency of voxel placement between operators, the concordance between any two voxel placements was evaluated using the relative intersection (RI), defined as the intersection between the two voxel volumes expressed as a percentage of their average volume. The overall concordance for each case was measured using the median of the relative intersections between each inter-operator pair.

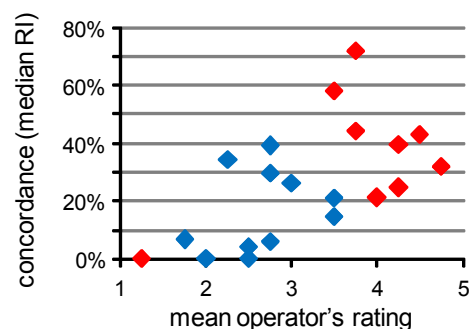
**Results:** A representative case with the four operators' voxel placements is shown in Fig 1. The concordance across all 20 cases ranged from 0-82.5%, with a mean of 31.2%. Values over 40% were qualitatively considered good, while values under 15% were clearly discordant. The overall concordance for masses (37.1%) was greater than that for non-mass-like enhancement (16.5%,  $p=0.01$ ), indicating that readers placed voxels more consistently in masses. The mean operator's rating was higher for masses (3.8) compared to non-mass-like enhancement (2.7,  $p=0.006$ ), indicating that readers were more confident in placing voxels in masses (see Fig 2). Performance in non-mass-like enhancement was better when there was a region of the lesion demonstrating homogeneous enhancement. Factors leading to discordance included non-mass-like enhancement, heterogeneous enhancement, necrosis and multifocality.

**Discussion and Conclusion:** In this study we developed a metric for quantitatively comparing voxel placement concordance between two operators that is based on voxel geometric overlap and reflects the operators' assessment of their performance. Overall, the concordance between operators was lower than anticipated. We found, as expected, that the consistency of breast MRS voxel placements is better for masses than non-mass-like enhancement. Consistent voxel placement is feasible in non-mass-like enhancement but depends on internal enhancement characteristics. These results suggest that more specific guidelines or automated tools should be developed to improve consistency of voxel placements, particularly for non-mass-like enhancement.

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**Fig 1.** A representative example showing the voxel outlines from each of the 4 operators in 2 planes. This example was a mass with a mean rating of 4.5 and median relative intersection of 42.8%.



**Fig 2.** Comparison of the operators' assessments of performance with the measured concordance (median relative intersection) between all operators. The correlation is significant ( $R=0.58$ ,  $p=0.006$ ). Red markers are masses, blue are non-mass-like enhancements.