ACL Specific Signal Intensity Normalization across MRI Sequences

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INTRODUCTION: Quantitative magnetic resonance imaging (qMRI) is a noninvasive way to track tissue integrity. A pre-clinical model has shown how the combination of ACL size and signal intensity (SI), a measure of tissue quality, are predictive of structural properties of the healing ACL.[1] Using the ACL voxel signal intensities extracted from the CISS sequence, qMRI-measured predicted failure load at an early timepoint has shown promise as a predictive biomarker of re-injury risk 2 years after of ACL surgery.[1] Images from different sequences may have large SI differences that affect the results of quantitative image analysis and qMRI biomarkers.[2] Identifying a means to accommodate these differences is necessary to validate the harmonization of large heterogeneous datasets obtained across scanners and sequences at various institutions.[2] It was hypothesized that there will be no significant differences in SI values between sequences (CISS and DESS) after harmonizing and adjusting the SI distributions of the DESS to match that of the CISS sequence.

METHODS: All MRI scans of patients undergoing ACL surgery were conducted on a 3T TRIO (Siemens, Germany) using a 15-channel transmit/receive knee coil. Data were collected from CISS scans (FA=35°; TR=12.78ms; TE=6.39ms; FOV=140mm; 384x384) and DESS scans (FA=25°; TR=16.48ms; TE=4.83ms). Data were acquired from patients enrolled in the BEAR I (NCT02292004; IRB-P00012985), BEAR II (NCT02 664545; IRB-P00021470),[3, 4] and from the ACL reconstruction subjects of the Tension Trial (NCT00434837). CISS scans were collected from 16 BEAR I patients and DESS scans were collected from 11 BEAR I patients; 5 patients did not have an MRI or were lost due to follow-up.[4] CISS scans were collected from 49 BEAR II patients and DESS scans were collected from 35 BEAR II patients where 14 patients did not have an MRI or were lost due to follow-up.[3] DESS scans were collected from 35 patients from the Tension Trial. Contralateral limbs of intact ACLs were evaluated, though contralateral limbs that had undergone surgery at any time were excluded. The ACL was segmented from the MR image stacks using commercial software. ACL SI was normalized to the posterior cortex of the femur. DESS scans were scaled to the CISS scans which are used in the qMRI-measured predicted failure load using Ratio of Mean Intensities (RMI).[5] RMI was calculated for each dataset by collecting the mean signal intensities of the subject's ACL and bone signal intensities. The calculated RMI for each subject was used to adjust the signal intensities of the ACL and bone by dividing the signal intensity of the ACL and bone by the respective RMI value. The adjusted ACL and bone signal intensities were used in a log normalization equation.[2] The normalized and adjusted SI values were recorded and used to calculate qMRI predicted failure load and qMRI predicted stiffness. The normalized and adjusted SI values were recorded and used to calculate qMRI predicted failure load and qMRI predicted stiffness. The mean absolute error (MAE) was calculated between the DESS scans and the DESS scans adjusted with the RMI across each dataset to ensure accuracy was maintained through the normalization process. A percentage of error was calculated by dividing the MAE by the respective average CISS SI. BEAR I and II had paired data, therefore, a Wilcoxon signed-rank test was performed to compare determine the difference between the CISS and DESS adjusted signal intensities with p-value less than or equal to 0.05 indicating a significant difference. However, this test was not performed on the Tension trial patients as there were no CISS scans.

RESULTS: The figure shows how the DESS signal intensities from each study were adjusted to CISS intensity range (Fig. 1). The MAE was 0.82, 0.83, and 1.12 for BEAR I, BEAR II, and Tension Trial patients, respectively. The percent error between the adjusted DESS SI and CISS SI was found to be 74.5%, 87.3%, and 93.3% for BEAR I, BEAR II, and Tension Study respectively. The p-value was found to be 0.10 and 0.02 for BEAR I and BEAR II respectively. The p-value indicates that the difference between CISS and DESS adjusted values were not significantly different for BEAR I, however, for BEAR II the values were found to be significantly different.

DISCUSSION: The CISS and DESS-adjusted SI values for BEAR II were found to be significantly different when using the RMI to scale the SI values. The Tension Trial also had the highest MAE. This result indicates that applying the RMI calculated from the BEAR Trials to the Tension Trial DESS SI values may not accurately normalize DESS SI values to the expected CISS SI values for this dataset. While RMI may be the simplest method to get an approximate measure of the intensity ratio between two sequences,[5] our findings suggest that scaling intensities with a simple linear transformation on a bulk parameter (i.e., mean SI) may not be sufficient. Given that the influence of MRI acquisition parameters on the image intensities is nonlinear, histogram matching that does a pixel-wise correction estimation may lead to better results. Future work will explore the use of histogram matching to establish an ACL specific SI normalization across MRI sequences.

SIGNIFICANCE/CLINICAL RELEVANCE: Developing a standardized procedure to normalize signal intensities across sequences will allow qMRI-predicted failure load, shown to be a predictor of healing ACL strength,[6] to be used in various clinical settings. The RMI transformation was not adequate.

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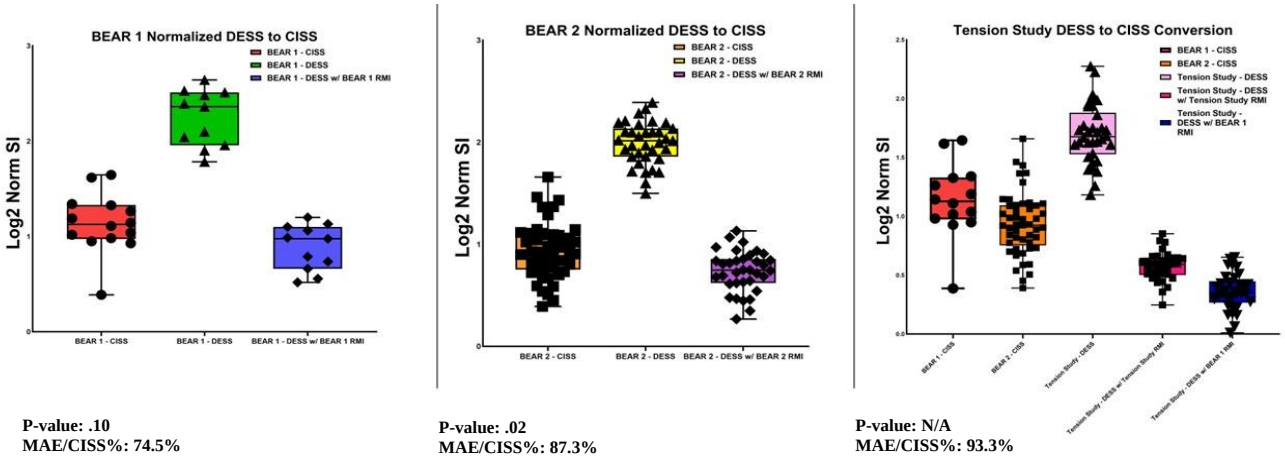

P-value: .10
MAE/CISS%: 74.5%

P-value: .02
MAE/CISS%: 87.3%

P-value: N/A
MAE/CISS%: 93.3%

Figure 1 A) BEAR 1 (Red) CISS SI, (Green) DESS SI, (Blue) DESS SI Adjusted; B) BEAR 2 (Orange) CISS SI, (Yellow) DESS SI, (Purple) DESS SI Adjusted; C) Tension Study (Pink) DESS SI, (Magenta) DESS SI Adjusted