Machine Learning Segments and Classifies Anterior Capsule Subtypes of the Rat Elbow in MRI

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INTRODUCTION: Post-traumatic elbow contracture is primarily driven by periarticular capsule fibrosis and adhesion, leading to loss of elbow range of motion and the patient's use of the upper extremity [1]. Magnetic resonance imaging (**MRI**) coupled with radiomic analyses provides non-invasive insight into elbow capsular morphology; however, the range of capsule subtypes makes it challenging to segment in MRI. Machine learning (**ML**) can help automate the segmentation and identification of biomarkers derived from capsule quantitative MRI (**qMRI**) patterns. *This study used three separate ML approaches to segment the anterior capsule and its subtypes to identify the key qMRI measures classifying capsule subtypes in the rat elbow (Figure 1A).*

METHODS: *Elbows and MRI:* Post-mortem male Long-Evans rat elbows from previously published studies [1] were formalin-fixed, contrast-soaked, and imaged under an MRI T1-weighted sequence (n = 24; Figure 1A). *Manual Capsule Segmentation and Pre-Processing:* The anterior capsule was segmented in the sagittal plane in ITK-SNAP software [2]. Paired MRI images and segmentations were imported into Python for downstream analysis. Slices from the same rat were kept together during analyses (n = ~150 slices/elbow). MRI scans were normalized using the histogram method [3]. *ML Segmentation Model:* An ML segmentation model was developed using a U-Net architecture with a ResNet34 encoder initialized from ImageNet initial weights accessible in Python [4]. The model was developed using data splitting (50/50 ratio of train/test) and augmentation (blurring and rotation) and trained using standard epochs (100), learning rate (0.001), batch size (5), optimizer (Adam), and loss function (Cross-Entropy). Dice Coefficient assessed model accuracies range from 0 to 1, indicative of poor to perfect segmentation. *ML Capsule Subtype Segmentation:* An ML model based on a Self-supervised Transformer with Energy-based Graph Optimization (**STEGO**) [5] was developed with all elbows setting 4 capsule subtypes (i.e., resembling fatty, fibrous, fibrotic, and amorphous), following standard model development and evaluation. *qMRI Analysis:* qMRI parameters (n = 72 total) involving tissue composition indicators of signal intensity and heterogeneity (i.e., correlation, contrast, energy, and entropy) [6] were quantified per slice per STEGO subtype. *ML Classification Model:* qMRI metrics were imported into Python to develop ML classification models (n = 14 total) to classify the STEGO subtypes with differing model frameworks: linear (e.g., logistic regression, support vector machine, linear discriminant analysis), boosting (e.g., gradient boosting, adaptive boosting, XGBoost), tree (e.g., balanced random forest, random forest), and other/neural network (k-nearest neighbors, multi-layer perceptron). Data was normalized (z-score) and split for a 70/30 ratio of train/test. Model accuracies were assessed by the area under the receiver operating characteristic curve (**AUC**) scores ranging from 0 to 1, indicative of poor to perfect classification. **SH**apley **A**dditive ex**P**lanations (**SHAP**) analysis was used to interpret the key qMRI inputs separating each STEGO subtype [7].

RESULTS: *ML Capsule Segmentation:* ML models segmented the anterior capsule with moderate accuracy (Dice Coefficient ~0.40-0.70), with performance varying by injury status and spatial location (Figure 1B). Accuracy was highest in the central sagittal regions, the primary area of clinical interests. However, the most sagittal locations (i.e., the central area of interest) displayed higher accuracy (data not shown). *ML Capsule Subtype Segmentation and qMRI patterns:* STEGO delineated 4 separate subtypes, which were essentially spatial and injury dependent. Three major tissue types qualitatively dominated (Figure 1B) and appeared hyperintense or a mixture of hyper and hypointense (likely fat/connective tissue). All ML models accurately classify the STEGO subtypes using qMRI with high accuracy (AUC = ~0.80-0.90); the best and worst models were logistic regression (AUC = 0.90) and decision tree (AUC = 0.72), respectively. SHAP with logistic regression model identified tissue signal intensity deviations, variance, and magnitude, followed by tissue entropy, as key qMRI parameters separating each STEGO capsule subtype (Figure 1C).

DISCUSSION: ML models segmented and classified, with moderate and high accuracy, respectively, the anterior capsule in rat elbow MRI. The injury and spatial dependence of the segmentation accuracy were anticipated, and improved segmentation in mid-sagittal anatomical locations was encouraging, given the clinical importance of capsular changes in this location following injury. The decreased accuracy with healthy tissue indicates a likely similar homogenous tissue that is also thinner and continuous with surrounding muscles, challenging the segmentation. The breadth of capsule shapes and sizes also makes this a challenging segmentation task. Two ML approaches, STEGO and classification, delineated 4 tissue types that were classified broadly by qMRI parameters of signal intensity and heterogeneity, indicative of fibrous and non-homogeneous tissue. Ongoing works aim to improve segmentation models, test alternative tissue subtype approaches, and combine both workflows into an end-to-end manner to automate tissue segmentation and classification.

SIGNIFICANCE/CLINICAL RELEVANCE: ML can unbiasedly segment and identify the anterior capsule and its subtypes in the rat elbow using qMRI. Automatic identification of elbow capsule tissue in healthy and diseased states may reveal key clinically relevant imaging markers.

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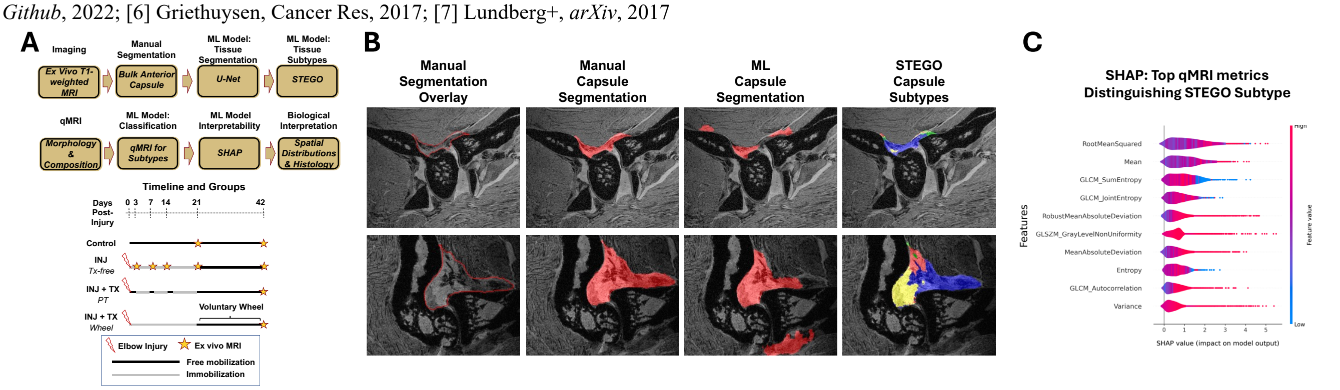

Figure 1. (**A**) Schematic of qMRI with ML pipeline and rat groups used. (**B**) Example of healthy and injured elbow with resulting ML segmentation and STEGO delineated capsule subtypes (i.e., the different colors in the STEGO overlay). (**C**). SHAP identifies logistic regression models' top influential qMRI, distinguishing each STEGO subtype using 72 total qMRI features. Note: GLCM = gray level co-occurrence matrix; GLSZM = gray level size zone matrix.