Machine Learning Segments and Classifies Rat Achilles Tendon and Peritendinous Tissues in Quantitative MRI

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INTRODUCTION: Quantitative magnetic resonance imaging (**qMRI**) enables a non-invasive window into the structure and composition of tendon and peritendinous tissue (e.g., paratenon and Kager's fat pad) [1]. Extracting qMRI metrics requires tissue segmentation in the images, which is labor-intensive and subjective. Further, drawing informed conclusions from numerous and potentially interrelated qMRI metrics is challenging. Machine learning (**ML**) approaches, specifically segmentation and classification, might unbiasedly reveal key qMRI metrics with clinical relevance. *This study developed ML segmentation and classification models to automatically identify qMRI patterns of the Achilles tendon and peritendinous tissues in a rat injury model.*

METHODS: *IACUC-approved Achilles Injury Model and qMRI:* Right ankles of male Sprague Dawley rats (n = 29; chosen based on prior work on male rats [2]) underwent Achilles tendon transection with primary repair, followed by 1 week of immobilization; the contralateral limb served as control. After 6 weeks, ankles were scanned with *in vivo* MRI (94 µm resolution) with proton density (**PD**) and T2 Dixon sequences to assess structure and composition (water and fat). This led to a total of four sequences: PD, T2 Dixon Water and Fat, T2 Dixon Water Only, and T2 Dixon Fat Only. *Manual Tissue Segmentation:* Achilles tendon, anterior and posterior paratenon, and Kager's fat pad were manually contoured in the PD sagittal plane in ITK-SNAP software [3] (Figure 1A). Paired MRI image and segmentation two-dimensional slices were imported into Python for qMRI analysis and ML model development, and slices from the same rat were kept together. *qMRI Metrics:* For each sequence, qMRI metrics (n = 224 total) of tissue area and signal characteristics of intensity and heterogeneity (i.e., correlation, contrast, energy, and entropy) were extracted in Python [4]. *ML Segmentation Models:* Multi-tissue ML segmentation models (i.e., one model segments all 8 tissues; n = 34 total) using both PD and T2 Dixon Combo sequences were developed with various model architectures (i.e., U-Net, Unet++, MAnet, Linknet, FPN, PSPNet, PAN, DeepLabV3, DeepLabV3+) and encoders (i.e., densenet2001, efficient-b5, resnet18, resnet34) in Python [5]. All models used the same model weights (ImageNet) and data scaling (min-max), splitting (50/50 ratio of train/test), and augmentation (blurring and rotation), as well as epochs (50), learning rate (0.00001), batch size (5), optimizer (Adam), and loss function (Cross-Entropy). Dice Coefficient evaluated model accuracy (ranging from 0 to 1, indicative of poor to perfect segmentation). *ML Classification Models:* Slice-wise qMRI metrics were imported into Python to develop ML classification models (n = 14 total) to classify the Achilles tendon, paratenon, and fat pad across health status with differing math assumptions: 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, Naïve Bayes, multi-layer perceptron). Data were scaled (zero-unit variance) and split for a 70/30 ratio of train/test. Model accuracies were assessed by the area under the receiver operating characteristic curve (**AUC**; ranging from 0 to 1, with 1 being perfect classification). SHapley Additive exPlanations (**SHAP**) analysis was used to interpret the key qMRI inputs driving model accuracy [6].

RESULTS: *ML Segmentation:* ML models segmented tissues with moderate-to-high accuracy for both healthy and injured Achilles tendons and fat pad (Dice Coefficient ~0.70-0.80), whereas paratenon showed more variability (Dice Coefficient ~0.40-0.80; Figure 1B); injured tissues followed similar patterns as healthy tissue (data not shown). *ML Classification:* ML models accurately classify the Achilles tendon, paratenon, and fat pad, with the best and worst models being linear discriminant analysis (AUC of 0.98) and adaptive boosting (AUC of 0.83), respectively. SHAP identified tissue PD signals of intensity deviations, variance, and magnitude, followed by tissue area as key qMRI parameters separating each tissue (Figure 1C).

DISCUSSION: ML models accurately segment and classify the Achilles tendon, paratenon, and fat pad of the rat ankles using qMRI. The choice of model architecture or model weights slightly improved the segmentation accuracy depending on the tissue, suggesting that a combination of models with ensemble decision making might be the best method moving forward. Tissue classification coupled with SHAP identified PD-based intensities as the key sequence qMRI features able to classify the tissues; however, all other qMRI metrics are likely impacting these results. Ongoing works aim to understand the limitations and improve segmentation models, and combine both workflows into an automated end-to-end manner, and test in other tendon pathologies and clinical contexts.

SIGNIFICANCE/CLINICAL RELEVANCE: ML can unbiasedly segment and classify between the Achilles tendon and peritendinous tissues in a rat injury model using qMRI. Identifying the key qMRI metrics between rat ankle soft tissues following injury may reveal key clinically relevant imaging markers.

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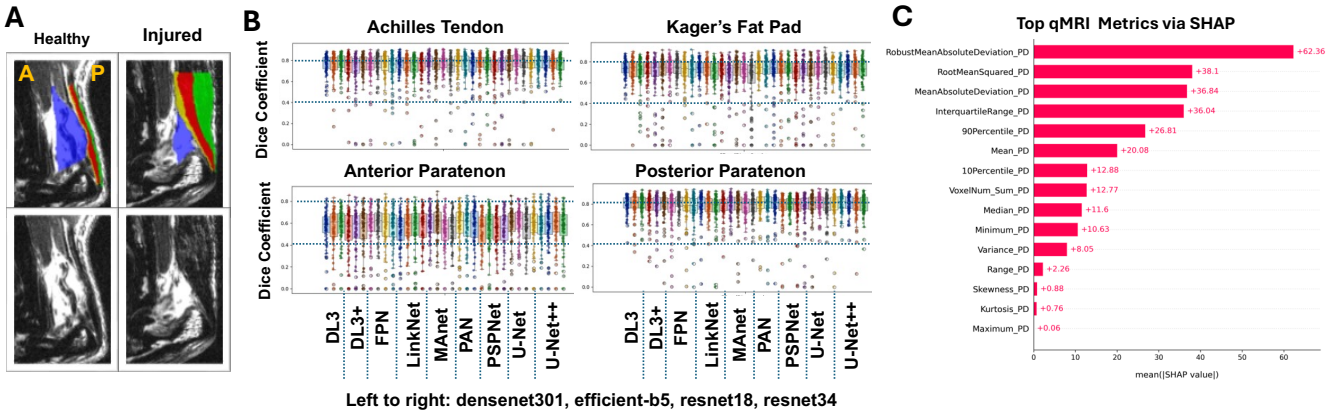

Figure 1. (A) Example of tissue segmentation in healthy and injured tissue in proton density (PD) sequence and ML model development. Note: A = anterior; P = posterior; blue = Kager's fat pad; yellow = anterior paratenon; red = Achilles tendon; and green = posterior paratenon. (B) Dice Score for healthy Achilles tendon and peritendinous tissues in numerous models. (C) SHAP identifies the top influential qMRI metrics distinguishing each tissue in the ML model with linear discriminant analysis framework.