Platelet Rich Plasma Effects on Knee Cartilage and Osteoarthritis Symptoms: MRI T2, UTE-T2* and Patient Reported Improvements Over 6-months Follow-Up

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INTRODUCTION: Autologous platelet rich plasma (PRP) injections are increasingly used to treat painful knee osteoarthritis (OA)[1]. PRP therapy is postulated to have anti-inflammatory and regenerative effects, however, individual responses to PRP treatment vary widely[2] and clinical evidence of potential benefits to cartilage structure remain lacking[3]. Our aim was to study osteoarthritis symptoms and articular cartilage structure assessed before and 6 months after completion of PRP treatment for painful knee OA using patient reported outcomes and T2 and UTE-T2* relaxation times, quantitative magnetic resonance imaging (qMRI) parameters known to be sensitive to cartilage matrix composition and organization[4-6].

METHODS: Fifty participants seeking treatment for painful knee OA (22 females; mean age 55±10 years; mean BMI 28±3 kg/m^2; mean Kellgren-Lawrence grade 2.1±0.8) consented to participate in this IRB-approved study. PRP treatment consisted of a three-injection series (3.5-4ml) of autologous leukocyte-poor PRP administered within 1 month. Prior to PRP treatment and again 6 months after the last treatment, all participants completed patient reported outcome (PRO) surveys, including Knee injury and Osteoarthritis Outcome Score (KOOS)[7] and Western Ontario and McMasters Arthritis Index (WOMAC)[8] questionnaires, and underwent 3T knee MRI (GE Healthcare). T2 maps were acquired using a 2-D fast spin echo sequence with 8 echo images[9] (TEs: 5-70ms, TR=1500ms, FOV=12cm, matrix=384x256 zero-filled to 512x512, 3mm slice-thickness, no gap). In a subset of 27 participants, UTE-T2* maps were acquired using a radial-out 3-D Cones sequence with 8 echo images[10,11] (TEs: 32µs-16ms, TR=23ms, FOV=12cm, matrix=384x384 interpolated to 512x512, 3mm slice thickness). T2 and UTE-T2* maps were generated pixel-wise from mono-exponential fitting using Matlab (TheMathWorks) and Olea Sphere (Olea Medical), respectively. All maps were manually segmented to include 9 mm-wide strips of cartilage (largely consistent with known areas of contact during common daily activities[12]), from 3 contiguous slices on each of 6 surfaces of the knee: medial and lateral femurs (MFC, LFC), medial and lateral tibias (MTP, LTP), patella (PAT) and trochlea (TRO). T2 regions included full-thickness cartilage; UTE-T2* regions included only deep cartilage. Shapiro Wilks tests assessed normality of data sets. Paired t-tests (Wilcoxon Signed Ranks tests for non-normal data distributions) assessed longitudinal changes in PROs, T2 and UTE-T2*. Univariate Pearson correlations (Spearman's *rho* for non-normal data) assessed relationships between longitudinal (6 month – baseline) KOOS and T2 or UTE-T2* changes. Effects of age, BMI, sex and KL grade were assessed with linear regression. Significance was accepted for $p<0.05$. Statistical analyses were performed with SPSS (IBM).

RESULTS: ***PRO Changes:*** Successful pain reduction (*i.e.* exceeding minimal important change (MIC) after non-surgical intervention for KOOS Pain change > 12.4pts[13]) was achieved in 21/50 (42%) of PRP recipients 6 months following completion of the injection series. Successful functional improvement (exceeding MIC for WOMAC function change < -17pts[13]) was achieved in 9/50 (18%) of PRP recipients. Averaged across all participants, 4 of 5 KOOS subscores and 3 of 3 WOMAC subscores demonstrated improvements, Figure 1. ***Cartilage MRI T2 Changes:*** Averaged across all participants, a small but significant T2 decrease was detected in LFC cartilage while a small increase was detected in PAT cartilage 6 months following completion of the PRP intervention, Figure 2a. In the subset of participants who underwent UTE-T2* mapping, substantial and significant decreases to deep cartilage UTE-T2* were detected in MFC, MTP and TRO regions, Figure 2b. ***PRO Changes v T2 Changes:*** At the individual level, increases (improvements) in KOOS Sports & Recreation scores correlated to decreases (improvements) in both T2 and UTE-T2* (R=-0.37, -0.50; p=0.009, 0.009) in MFC cartilage, Figure 3a,b. Similarly, decreases (improvements) in WOMAC Stiffness correlated to decreases (improvements) in UTE-T2* (*rho*=0.53, p=0.005) in LTP cartilage, Figure 3c. Linear regression found no effects of age, BMI, sex or KL grade on these results.

DISCUSSION: Recipients of PRP injections in this study demonstrated wide variations in their responses to treatment but on average reported improvements to knee pain, symptoms and function 6 months following PRP intervention. Significant qMRI changes, including decreases to average deep cartilage UTE-T2* relaxation times, were also observed. On an individual level, changes in participants' self-reports of osteoarthritis symptoms associated with 2 different quantitative MRI markers of concurrent cartilage compositional change where improved knee function or stiffness correlated to improved T2 or UTE-T2* assessments of cartilage structure. These findings are particularly notable given that a discordance between OA symptoms and structural evidence of disease is common, especially in early stages of disease[14-17]. **SIGNIFICANCE:** qMRI evaluation of the clinical efficacy of PRP treatment of symptomatic knee OA shows that changes to patient reported knee function associate with concurrent changes to cartilage structure assessed with T2 and UTE-T2*.

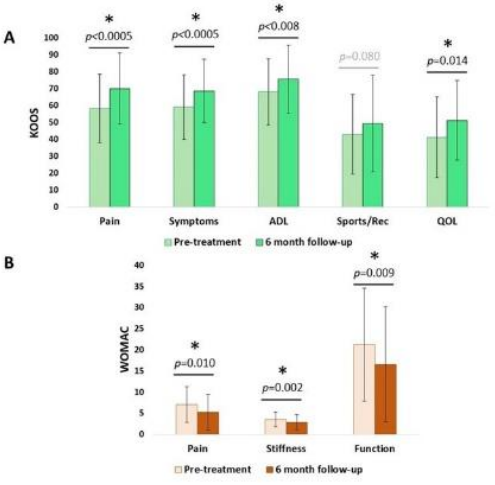
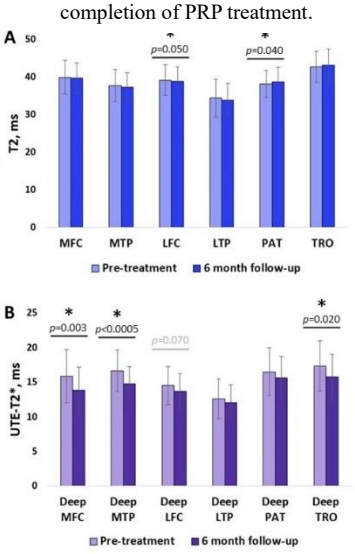


Figure 1. Average patient reported outcomes improved 6 months after completion of PRP treatment.

Figure 2. Average cartilage T2 and UTE-T2* before and 6 months after completion of PRP treatment.



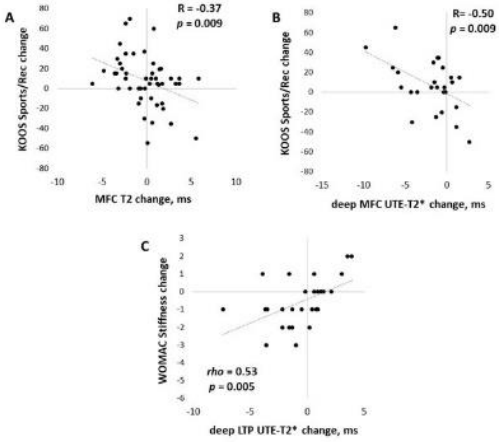


Figure 3. Recipients of PRP injections demonstrated wide variations in their responses to treatment, but on an individual level, changes to PROs associated with changes to cartilage T2 and UTE-T2* values.

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