Non-invasive MRI reveals depth-dependent biochemical signatures of osteoarthritic cartilage degeneration

Ikram Mohout[1], Seyed Ali Elahi[1], Yixuan Zhang[1], Dennis Minton[1], Shannon Helsper[1], Willy Gsell[2], Uwe Himmelreich[1], Ilse Jonkers[1]

[1] KU Leuven, Leuven, Belgium
[2] Bruker Preclinical Imaging, Kontich, Belgium

Ikram.mohout@kuleuven.be

Introduction

Articular cartilage degeneration is *the* hallmark of osteoarthritis (OA). Alterations in the extracellular matrix, particularly involving the collagen network and proteoglycan (PG) content, lead to changes in the tissue's mechanical behaviour [1]. Quantitative MRI (qMRI) has been associated with cartilage biochemical composition; however, the precise relationships between qMRI parameters and structural degeneration remain incompletely understood [2]. In this study, we propose a non-invasive MRI-based approach, with ultimate potential for *in vivo* translation, to extract quantitative signatures of disease progression by analyzing qMRI profiles in relation to histopathological grading.

Methods

Osteochondral cylindrical plugs (10 mm diameter) were harvested from 14 OA patients undergoing total hip arthroplasty (one plug per subject) and snap-frozen. After thawing, plugs were imaged in PBS using a 7T system (Bruker Biospec) with quantitative T1, T2, and T1ρ mapping sequences [3]. Following MRI, plugs were cut along the imaging plane, fixed in formaldehyde, decalcified in EDTA, embedded in paraffin, and sectioned at 3 μm. Sections were stained with Safranin O and imaged using bright-field microscopy (Zeiss Axio Scan Z1); three sections per sample were analyzed. Cartilage degeneration was graded using OARSI (Osteoarthritis Research Society International) grading by two independent, blinded evaluators [4]. Based on the OARSI scores, samples were grouped into four severity categories (OARSI 1–1.5, 2–2.5, 3–3.5, and 4–5), with each category containing two to four samples. Pixel-wise qMRI values were mapped to a normalized cartilage depth axis and averaged across severity groups to generate depth-dependent MRI profiles, from which additional quantitative features were extracted by linearly fitting gradients in the superficial cartilage zone.

Results and Discussion

Figure 1 shows depth-dependent T1ρ and T2 profiles and their superficial-zone slope features, which display tendencies toward higher values and steeper gradients in the most advanced OARSI group. These tendencies are indicative of more severe collagen damage and

loss of PG content that exacerbates throughout the tissue depth, hence affecting the ability of cartilage to maintain swelling pressure. These tendencies were less pronounced for T1, consistent with the known sensitivity of qMRI parameters, as T1ρ and T2 are more strongly associated with PG content and collagen organization, respectively [3]. Given the relatively small sample size, these findings should be interpreted as indicative trends rather than definitive group differences. Future work will integrate more biologically oriented grading systems, such as the Mankin score, and explore interactions between multiple qMRI parameters and quantitative histological parameters to elucidate coupled biochemical cartilage alterations. Together, these results demonstrate the added value of depth-resolved qMRI features to non-invasively characterizing biochemical signatures of OA cartilage degeneration.

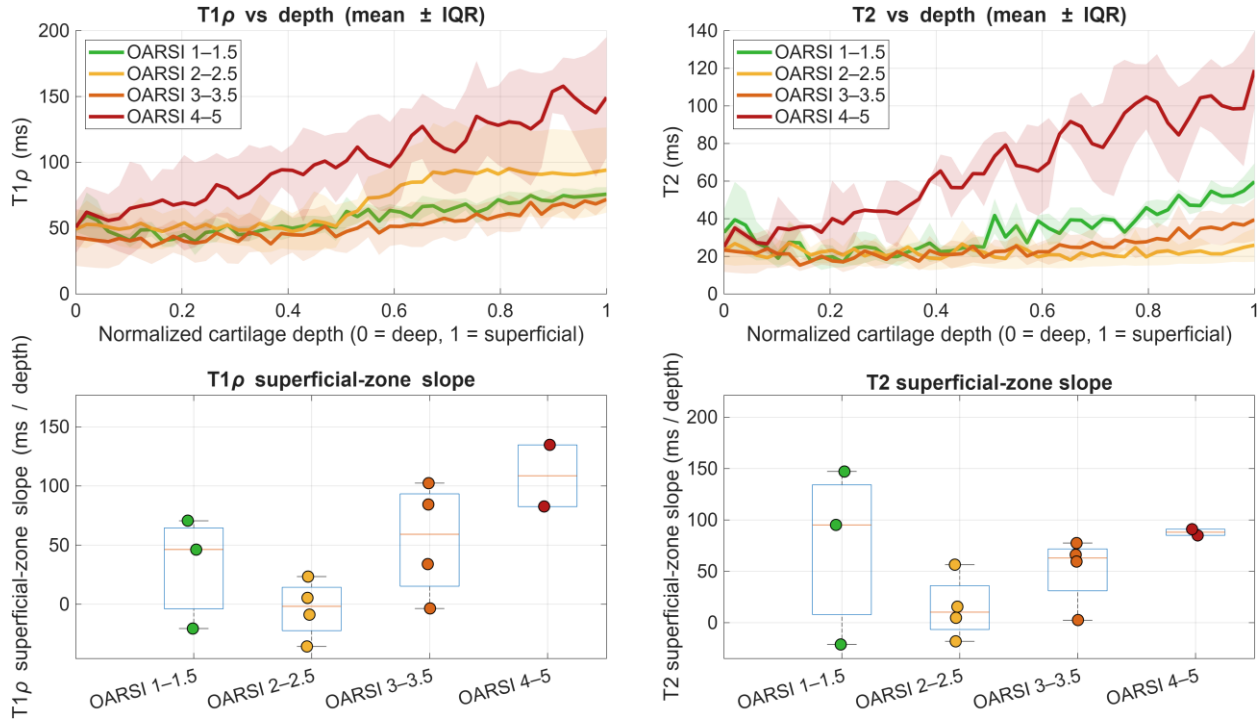

Figure 1 Depth-dependent qMRI profiles and superficial-zone slope features across OARSI groups. Top: Group-mean T1ρ (left) and T2 (right) profiles plotted as a function of normalized cartilage depth, mean ± interquartile range (IQR) for OARSI severity groups (OARSI 1–1.5, n = 3; OARSI 2–2.5, n = 4; OARSI 3–3.5, n = 4; OARSI 4–5, n = 2). Bottom: Boxplots of the superficial-zone slopes (range 0.80–1.00 of normalized depth).

Acknowledgement

This work was supported by the FWO fundamental fellowship (11M9422N). We gratefully acknowledge the Skeletal Biology and Engineering Research Center and VIB Bioimaging Core Leuven for assistance with histology.

References

[1] S. A. Elahi, et al., Osteoarthritis and Cartilage, 2023
[2] K. Linka et al., Osteoarthritis and cartilage, 2021
[3] L. Zevenbergen et al., Osteoarthritis and Cartilage, 2018
[4] K. P. H. Pritzker, et al., Osteoarthritis and cartilage, 2006