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T_2 Mapping Refined Finite Element Modeling to Predict Knee Osteoarthritis Progression

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***Abstract*— This paper presents a novel method for informing cartilage material properties in finite element models from T_2 relaxometry. In the developed pipeline, T_2 relaxation values are mapped to elements in subject-specific finite element models of the cartilage and menisci. The Young's modulus for each element within the cartilage is directly calculated from its corresponding T_2 relaxation voxel value. Our model was tested on a single subject (Subject ID 9932809, Kellgren-Lawrence grade 2) from the Osteoarthritis Initiative dataset at baseline imaging. For comparison, an identical finite element model was built with homogeneous material properties. Kinematics of the stance phase of a standard gait cycle were used as model constraints. Simulation results were compared qualitatively to the MRI Osteoarthritis Knee Score (MOAKS) from the same baseline timepoint. Our T_2-refined material model showed higher maximum shear strain in regions with moderate cartilage loss as compared to the homogeneous material model, and the homogeneous model showed higher maximum principal stress and maximum shear strain in regions with no cartilage loss. These results show that a homogeneous material model likely underestimates tissue strains in regions with cartilage damage while overestimating strains in regions with healthy cartilage. This preliminary study demonstrates that T_2-refined material properties are more appropriate than assumptions of homogeneity in predictive models of cartilage damage.**

***Clinical relevance*— The proposed pipeline demonstrates a computationally efficient way to improve the subject-specificity of finite element models used for evaluation of osteoarthritis.**

I. Introduction

Osteoarthritis (OA) is characterized by cartilage degeneration, specifically loss of proteoglycans and collagen content within the extracellular matrix, thus altering the mechanical properties of the tissue [1]. OA is typically evident in X-ray imaging via joint space narrowing and osteophytes, however, early stages of cartilage degeneration occur before any clinical signs are visible in a typical plain X-ray examination. Using a predictive model to detect evidence of early cartilage degeneration would give clinicians additional time to try the increasing number of nonoperative treatment options available. However, since OA is a heterogeneous disease, clinicians also need reliable predictive models that can be customized for a subject's unique joint geometry and cartilage material properties. For this reason, finite element (FE) modeling is an optimal tool for creating subject-specific predictive models of cartilage degeneration and osteoarthritis progression.

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FE models are commonly used to analyze tissue loading, estimate stress concentrations, and predict areas at increased risk of mechanical failure due to OA progression in a subject-specific way [2]. Current subject-specific FE models may use joint geometry, joint mechanics, or loading conditions to create more accurate predictive models. Joint geometry can be obtained through imaging and subsequent segmentation of tissues while joint motion from a gait cycle can be implemented to approximate *in vivo* motion [3]. While geometry and kinematics play a critical role in making FE models specific to a given subject, researchers are still developing ways to elucidate cartilage microstructure health and material properties for a given subject.

Magnetic resonance imaging (MRI) can be used to estimate the matrix constituents and material properties of articular cartilage. Since T_2 MRI captures several factors essential to the macromolecular framework of cartilage, it is also correlated with the mechanical properties of the tissue [4]. Previous work has shown that FE models with collagen fibril orientation refined by T_2 relaxation or diffusion tensor MRI produce significantly different predictions of maximum principal stresses than models with collagen fibril orientation obtained from literature [5], [6]. We therefore hypothesize that a subject-specific FE model with element-wise elastic modulus informed by T_2 relaxation time will improve predictions of regions of high stress and strain and thus identify regions with an increased risk of tissue degeneration. The desired outcomes of this study are twofold:

1) Develop an FE model which utilizes T_2-refined material properties to improve subject specificity;
2) Assess whether a subject-specific FE model with T_2-refined material properties predicts different maximum principal stresses and shear strains compared to a model with homogeneous material properties.

II. Materials and Methods

A. Data

This study used imaging data from the Osteoarthritis Initiative (OAI), a publicly available dataset for OA research. OAI (https://nda.nih.gov/oai/) is a multi-center, ten-year observational study investigating knee OA in 4,796 subjects in the United States. The OAI includes three cohorts: a progression cohort displaying symptomatic knee OA, an incidence cohort not displaying OA but at an increased risk of developing OA, and a control cohort with no display or risk of developing OA. For this study, we used imaging data from one subject in the progression cohort. Right knee images

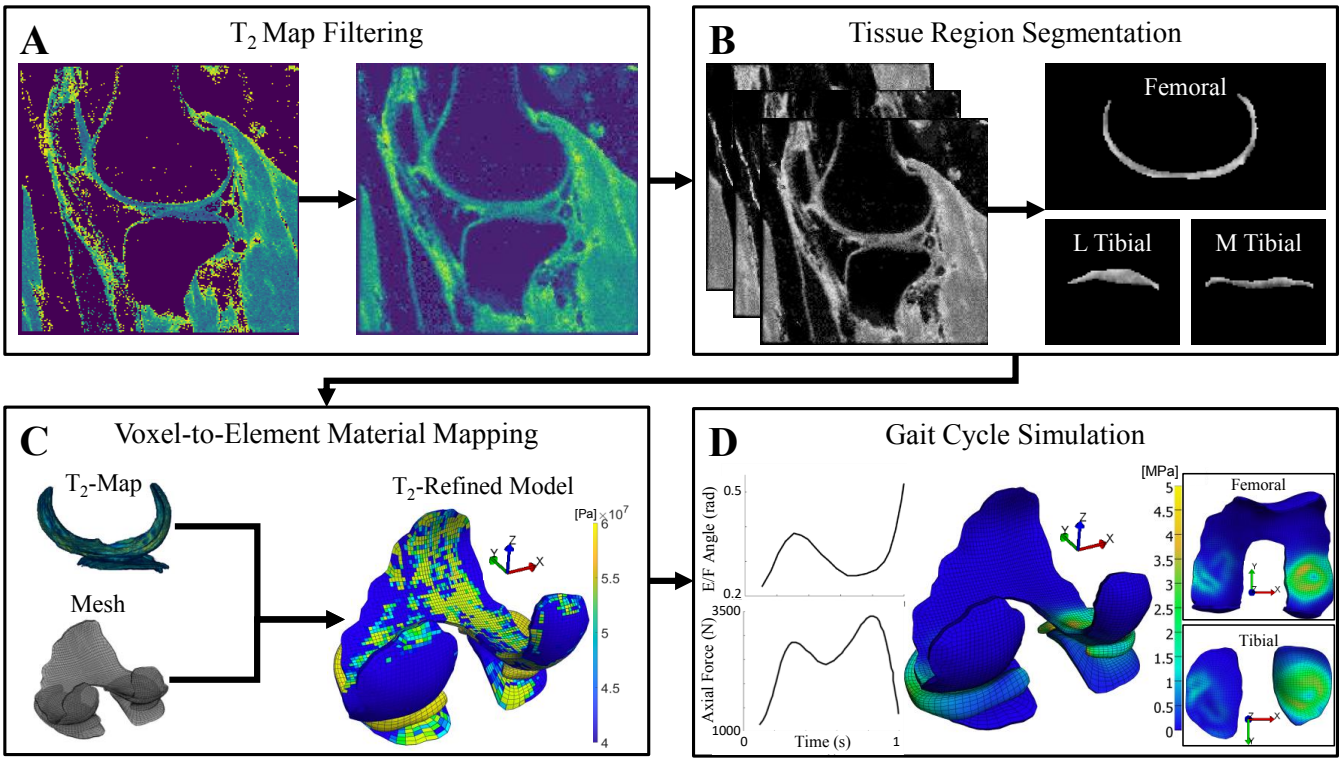

Fig. 1: Overview of the developed T_2-refined material model analysis

from Subject ID 9932809 at the baseline time point were used, and at the time of imaging, the subject was classified as Kellgren-Lawrence (KL) grade 2, which is considered to be minimal OA. A subject with KL grade 2 OA was chosen because changes to the extra-cellular matrix would have occurred by this stage without major loss of cartilage tissue volume [7]. The MRI Osteoarthritis Knee Score (MOAKS) [8], a semi-quantitative osteoarthritis scoring assessment, was also performed at baseline imaging for the subject of interest (Tab. I). MOAKS cartilage morphology scores are assigned based on the percent of cartilage loss observed in a given region, where grade 0 indicates no loss, grade 1 indicates $< 10\%$ loss, grade 2 indicates $10 - 75\%$ loss, and grade 3 indicates $> 75\%$ loss.

MRI scans of the knees were obtained using a Siemens Trio 3.0 T scanner with quadrature transmit-receive coils (USA Instruments, Aurora, OH, USA). The scan protocol included the following sequences: (1) sagittal 3-D dual echo in the steady state (DESS) with selective water excitation, TE = 4.7 ms, TR = 16.3 ms, flip angle = 25° and (2) sagittal T_2-Map, TE = 10, 20, 30, 40, 50, 60, 70 ms, TR = 2700 [9]. Segmentation masks and FE meshes of cartilage and menisci for the selected subject based on 3D DESS MRI were obtained courtesy of David Pierce [10]. FE meshes of the articular cartilage and menisci were constructed using solid, 8-node trilinear hexahedral elements [10]. The mensici were constrained using a fixed displacement boundary condition applied to the meniscal horns where the meniscal roots would typically attach.

B. Methods

Our modeling workflow is shown in Fig. 1. First, T_2 maps are filtered for the subject of interest (Fig. 1A). Next, all regions of articular cartilage are selected from the T_2 maps (Fig. 1B). Material properties within a subject-specific finite element mesh are then calculated from the segmented T_2 maps (Fig. 1C). Finally, a simple gait cycle is simulated and key measures of stress and strain are computed for model evaluation (Fig. 1D). In the following sections, we describe each of these steps in depth.

1) Preprocessing T_2 Maps: We used T_2 maps as an input to the model. T_2 maps were filtered using a gradient anisotropic diffusion filter from SimpleITK[1] with 5 iterations, timestep $= 0.125$, and conductance $= 3$. Filtering was performed on the T_2 maps to smooth changes occurring between adjacent pixels (Fig. 1A). Filtering reduces the likelihood of large differences in material properties between adjacent elements in later modeling steps. Voxels were then binned based on their relaxation values using a bin width of 0.5 ms to decrease the number of unique T_2 values.

2) Mapping T_2 Relaxation Times to Material Properties: A Neo-Hookean material model was created for all articular cartilage and meniscus regions using a custom built voxel-to-element mapping method created in MATLAB. The T_2 map was first registered with the corresponding fixed 3D DESS MRI image. Segmentation masks from the 3D DESS image [10] were then overlaid to select cartilage regions within the T_2 map (Fig. 1B). The cartilage and meniscus regions were

[1]https://simpleitk.org/index.html

converted to the same global coordinate system used by the FE mesh. Next, k nearest neighbor (k-NN) interpolation was used to map T_2 values to their respective elements in the FE model (Fig. 1C). In this process, the k-NN algorithm used the centroid coordinates of each element in the FE model to search for the k nearest voxels in the segmented T_2 map. Voxel relaxation values were then used to determine the Young's modulus of the respective elements [4].

$$E = \left(\frac{-1}{3} \times 10^6\right) T + 65 \times 10^6 \quad (1)$$

Equation (1) was used to calculate Young's modulus (E) in (Pa) from T_2 time (T) in (ms). All voxels within a defined bin were converted to the same E value to decrease the number of distinct materials, reducing model complexity.

3) FE Mechanical Simulation: Finally, a simple mechanical simulation was performed to test the T_2-refined FE model. Moderate activity (e.g. walking) comprises around 30% of daily activity [11]. Therefore, we applied average motion and loading from the stance phase of a walking gait cycle [12]. Meshes with T_2-refined material properties were imported into FEBio [13]. A simplified gait cycle with transient loading ($\approx [1000, 3500]$(N)) and knee extension-flexion angle ($\approx [0.2, 0.5]$(rad)) was assigned to the models as time-dependent boundary conditions [12], seen in Fig. 1D. The gate loading acted along an axis defined through a reference point in the middle of the femoral epicondyles parallel to the tibial-diaphyseal axis in the negative z-direction. The proximal surface of the femoral cartilage was fixed to the reference point using a rigid interface contact and all nodes on the distil surface of the medial and lateral tibial cartilage were fixed [3]. Before the stance phase commenced, models underwent a 0.1 second ramping stage, which adjusted the model to match the initial placement and force at the beginning of the stance phase. The stance phase lasted 0.9 seconds. Two models were built for the subject: (i) a model with voxel-to-element T_2-refined E ranging from 40 - 60 MPa and (ii) a model with a homogeneous E of 50 MPa.

III. Experiments and Results

The simulation results from the T_2-refined and homogeneous models were compared by investigating principal and shear stresses and strains within the articular cartilage. The femoral and tibial cartilage were split into anterior, central, and posterior regions as defined by the MOAKS evaluation method [8] and all measures of stress and strain were tracked in these regions through the stance phase (Tab. I). Previous studies have assumed maximum principal stresses exceeding 7 MPa to trigger degeneration of collagen, while strains above 30% trigger proteoglycan degeneration [14], [15] within articular cartilage. For this reason, maximum principal stress and maximum shear strain are presented.

The mean principal stresses and strains, as well as the mean shear stresses and strains, were very similar in all regions between the homogeneous and T2-refined model simulation results (data not included). This is because changes to material properties at the element level are not likely to impact regional averages. However, the T_2-refined material model generally showed higher maximum shear strain in regions with moderate cartilage loss, as indicated by the MOAKS (Fig. 2). Comparatively, the homogeneous model frequently showed higher maximum principal stresses and higher maximum shear strains in regions with no cartilage loss, as indicated by the MOAKS (Fig. 2). The stress and strain thresholds for collagen and proteoglycan degeneration as defined by [14], [15] were not exceeded in any regions of the cartilage for either model, although maximum principal stresses above 5 MPa were observed in the meniscus.

TABLE I: Regional MOAKS, Stress, and Strain Measures

Femoral	MA	MC	MP	LA	LC	LP
MOAKS[a]	2	2.2	2	2	0	1
Max Principal Stress[b]	–	–	–	–	–	↓
Min Principal Stress	–	–	–	–	↓	–
Max Shear Stress	–	↑	–	–	↑	↑
Max Principal Strain	–	↑	↑	–	↑	–
Min Principal Strain	–	↓	↓	–	↓	–
Max Shear Strain	–	↑	↑	–	↑	–

Tibial	MA	MC	MP	LA	LC	LP
MOAKS	2	2.1	0	0	1	0
Max Principal Stress	↑	↑	↑	↑	↑	↑
Min Principal Stress	–	↓	–	↓	↓	–
Max Shear Stress	↑	↑	–	↑	↑	–
Max Principal Strain	↓	↑	↑	↓	↑	↑
Min Principal Strain	↑	↓	↓	↑	↓	↓
Max Shear Strain	↓	↑	↑	↓	↑	↑

[a] Cartilage regions were scored at baseline imaging according to the MOAKS criteria. Femoral and tibial cartilage are split into medial (M) and lateral (L) halves, then further into anterior (A), central (C), and posterior (P) regions.

[b] T_2-refined model values consistently higher than homogeneous model values (↑), T_2-refined model values consistently lower than homogeneous model values (↓), or no clear difference between models (–)

The observed difference in results suggests that a model with T_2-refined material properties may predict higher strains in a region with moderate cartilage loss, thus indicating increased risk for further cartilage degeneration and loss. Alternately, a model with homogeneous material properties may overestimate localized stress and strain in areas with relatively healthy cartilage which could be incorrectly interpreted as an increased likelihood of cartilage degeneration. Since our simulation only consisted of loads consistent with moderate walking, ultimately we were not surprised that the degeneration thresholds were not exceeded. We do not believe it subtracts from the simulation results as this is a proof-of-concept study.

IV. Conclusions

In this study, a subject-specific FE model was developed which implements T_2 MRI to inform the Young's modulus of the cartilage at an element level using a custom built voxel-to-element pipeline. In a subject with KL grade 2 osteoarthritis, our T_2-refined material model produced higher

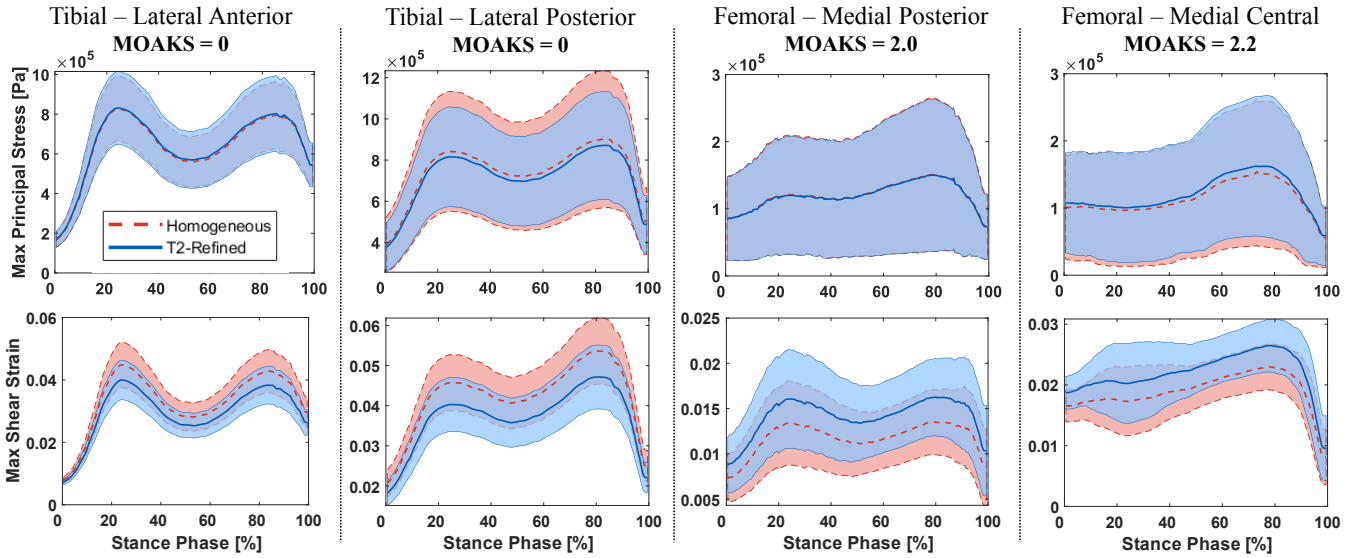

Fig. 2: In regions with no cartilage loss (MOAKS=0), higher maximum principal stresses and maximum shear strains were estimated by the homogeneous model (red dashed lines) as compared to the T_2-refined model (blue solid lines). The center lines indicate mean within the 95-100th percentile while shaded regions indicate standard deviation. Alternately, the T_2-refined model predicted higher maximum shear strains in regions with moderate cartilage loss (MOAKS$\geq$ 2).

maximum shear strain in regions with moderate cartilage loss than a homogeneous material model, which produced higher maximum principal stress and maximum shear strain in regions with no cartilage loss. Our results suggest that a T_2-refined material model could improve simulation sensitivity to regions at risk of increased stress and strain and therefore susceptible to tissue degeneration. In future studies, we will test the ability of T_2-refined FE models to predict regional cartilage loss by testing these methods on a larger sample size from the OAI and comparing FE model outputs to semi-quantitative scoring and T_2 relaxometry in follow-up evaluations. We will also integrate spatial statistical methods to identify differences between homogeneous and T_2-refined models, such as Statistical Parametric Mapping [16]. In conclusion, we have developed a novel method for defining cartilage material properties from T_2 maps and demonstrated its potential to improve subject-specificity of FE models.

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