T_2 anisotropy in articular cartilage - a model based approach

Peter Del-Manso[1]
delmanso@medphys.ucl.ac.uk
Bernard Siow[2]
b.siow@cs.ucl.ac.uk
Tryphon Lambrou[3]
tlambrou@medphys.ucl.ac.uk
Amaka Offiah[4]
amaka.offiah@nhs.net
Martin Fry[1]
mefry@medphys.ucl.ac.uk
Andrew Todd-Pokropek[1]
atoddpok@medphys.ucl.ac.uk

[1] Department of Medical Physics & Bioengineering, University College London
[2] Centre for Advanced Biomedical Imaging, University College London
[3] Institute of Nuclear Medicine, University College London
[4] Sheffield Children's NHS Foundation Trust

Abstract

We examine how the combination of image processing techniques and mathematical modelling can enhance understanding of the structure of articular cartilage and its relation to clinical MRI appearance, in order to aid the diagnosis, predication and evaluation of cartilage disease, the most prevalent of which being osteoarthritis. The orientation of these fibres, while not visible through clinical MRI or even μMRI, influences the T_2 relaxation time through dipolar interaction. We introduce a model to describe the variation in collagen fibre orientation through the depth of articular cartilage and the anisotropy of the T2 relaxation time. We demonstrate a novel application of the Laplace thickness method to solve the depth and orientation dependent problem and its application to high magnetic field images of bovine articular cartilage. The application of a quantitative model based approach may allow the development of a functional imaging technique to evaluate the early stages and progression of cartilage diseases and disorders such as osteoarthritis.

1 Introduction

Articular cartilage provides an extremely low friction wear-resistant surface for load support, transfer and motion between the bones of a diarthrodial joint. Articular cartilage is composed of a small population of specialist cells called chondrocytes, which are contained within a large extracellular matrix (ECM) [2]. The fluid phase is composed of water with ionic and non-ionic solutes, which constitutes 75-80% of the wet weight of cartilage. The solid phase is composed of approximately 10% chondrocytes, 10-30% collagen, 3-10% proteoglycans, and 10% lipids. The organization and composition of articular cartilage varies with depth,

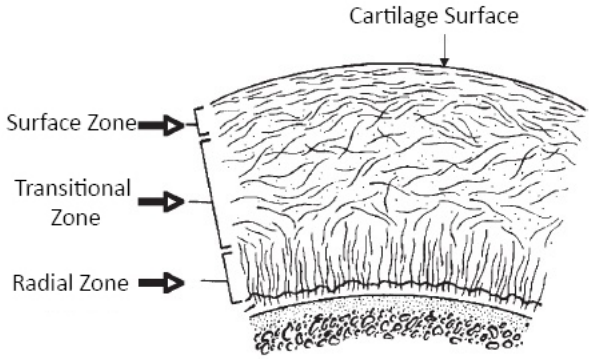

Figure 1: Collagen fibre orientations in the histological zones of articular cartilage, modified from [4]

resulting in the variation of the mechanical properties through its histological zones, defined by the changing orientation of the collagen fibres as shown in figure 1.

In cartilage, the fibrillar collagen within the cartilage matrix immobilizes the tissue water protons, which promotes dipole-dipole interactions between them. This dipolar interaction is an efficient mechanism for T_2 relaxation and is governed by the geometric factor $(3\cos^2\theta - 1)$. This reaches a minimum at approximately 54.7°, known as the "'magic angle"'.

Changes to cartilage ultra-structure are often among the first stages of degenerative disease, including osteoarthritis [8]. The ability to detect these changes is an important goal in the early detection and diagnosis of these conditions, and to establish biomarkers to allow monitoring of progression and potential treatment. This has resulted in a number of research studies using μMRI to access the structural properties of articular cartilage [1, 5, 9].

At any point through the depth of the cartilage the fibre direction distribution is a complex 3D distribution, with a directional bias towards the primary aggregating fibres but with smaller cross linking fibres orientated in all directions. The distribution can be simplified by considering the fibre distribution as a composite of radial, tangential and isotropic fibres [6, 12]. Functions can then be defined to describe the variation of these fractions with depth through the tissue. The observed depth and angular dependency of the T2 relaxation time can then be attributed to the dipolar interaction resulting from the weighted average of this composite.

2 Methods

We propose an alternative model for a 2D fibre distribution within the imaging plane which is based on exponential functions. The simple two parameter model is designed to approximate the standard arcade model of fibre orientation, which was first proposed by Benninghoff [3, 10]. In order to perform the analysis we will assume that the observed T_2 relaxation time occurs purely as a result of dipolar interaction due to the collagen fibre network. Three orientation populations are assumed, the main aggregate fibres which are orientated tangentially or radially and smaller fibrils which have an isotropic.

The surface zone is relatively thin (in human tissue around 7% of the total thickness) and the fraction of tangential fibres quickly reduces to the predominantly isotropic transitional zone. This is modelled by an exponential function where the boundary between the surface zone and the transitional zone (h_{sz}) is defined as the "half-life" of the exponential, the point at

which the fraction of isotropic fibres is greater than that of the tangential fibres. The fraction of tangential fibres with depth (d) through the tissue is given by

$$f_s = e^{-\beta_s d}, \text{ where } \beta_s = \frac{ln(2)}{h_{sz}} \tag{1}$$

The fibre orientation function for the radial zone is also defined using an exponential function. The boundary between the transitional zone and the radial zone (h_{tz}) is defined as the point at which the fraction of radial fibres is greater than that of the isotropic fibres.

$$f_r = e^{-\beta_r (d-h)}, \text{ where } h = h_{sz} + \frac{h_{tz}}{2}\ , \beta_r = \frac{ln(2)}{h_{tz}/2} \tag{2}$$

The remaining fraction of fibres is considered as isotropic.

The 'scaling factor' (T_{2n}) applied to the T_2 relaxation time as a function of depth through the tissue and the angle between the normal to the surface and the B_0 field can then be described as

$$T_{2n}(d,\theta) = 1 - f_s(\frac{1-3\cos^2(90-\theta)}{2}) - f_r(\frac{1-3\cos^2\theta}{2}) \tag{3}$$

Cartilage regions are typically curved, with thickness that varies over the surface of the bone. To analyse the depth dependent properties of the tissue, a consistent definition of the tissue thickness is required which is provided by the Laplace thickness method of Jones *et al*. [7]. The Laplace equation is a second-order partial differential equation for a scalar field ψ, enclosed between boundaries S_1 and S_2. It takes the form

$$\frac{\partial^2\psi}{\partial x^2} + \frac{\partial^2\psi}{\partial y^2} + \frac{\partial^2\psi}{\partial z^2} = 0 \tag{4}$$

where $\psi = \psi_1$ on S_1 and $\psi = \psi_2$ on S_2. The Laplace equation describes a layered set of surfaces which constitute a smooth transition between surfaces S_1 and S_2. These values can be considered as electric potentials, which makes the solution analogous to an electrostatic field. Laplace's equation can be solved iteratively using the Jacobi method.

The orientation of each voxel relative to the B_0 field is calculated by defining the orientation in the element as being equal to the orientation of the vector between the point P_1 on S_1 determined by integrating from the centre of the element to S_1, and P_2 on S_2 determined by integrating from the centre of the element to S_2 (forming the field line passing through the centre of the element).

Bovine patellae were obtained from a local abattoir within 4 hours of slaughter, excised from surrounding tissue and prepared into six 8mm diameter discs. Once prepared the samples were stored in phosphate buffered saline solution (PBS).

Imaging was performed on a 9.4T Varian scanner. Anisotropic voxels of dimensions 0.234 x 0.0313 x 2 mm were chosen to provide increased depthwise resolution while preserving signal-to-noise ratio (SNR). The acquisition parameters for the Carr-Purcell-Meiboom-Gill (CPMG) imaging sequence were: Matrix 128x256; TE = 3.2 - 32 ms, 10 echoes 3.2ms intervals; TR=2500ms. A single slice was acquired through the central 2 mm of each disc.

Cartilage regions were manually segmented from the acquired images and a threshold was applied to the segmented region to remove points along the edge which have partial volume with the surrounding PBS. SNR values were calculated for each echo at each orientation in the deepest 20% of the cartilage region. T_2 values were then calculated. The d and

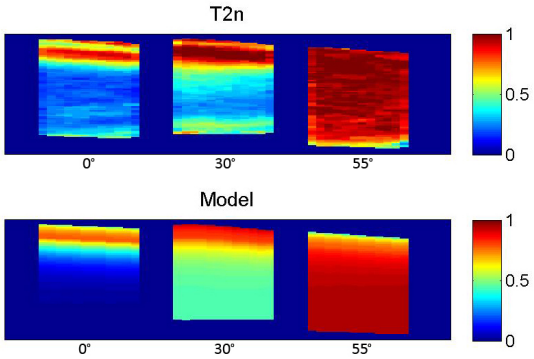

Figure 2: Normalized T_2 (T_{2n}) map and model generated T_{2n} map for a bovine patella cartilage sample

θ values for each pixel were calculated using the modified Laplace thickness method. The heights of the surface and transitional zones were optimized by minimizing the residual sum of squares between the normalized acquired T_2 map and the model generated map, using a constrained non-linear optimization implemented in Matlab.

3 Results

Figure 2 illustrates a normalized T_2 map, termed T_{2n} along with the model generated T_{2n} map and error map calculated for one of the samples. Goodness of fit was evaluated using RMSE and R^2. For the six control samples imaged the mean RMSE was 0.15 and the mean R^2 was 0.73 between the acquired and model generated T_{2n} maps.

4 Discussion

We have derived a simple model for describing the fibre orientations in articular cartilage and examined the feasibility of fitting this model to high field data, using a novel method for resolving a depth and angle dependent problem. The calculated goodness of fit measures illustrate that this simple two parameter model is able to describe the T_2 anisotropy observed in the cartilage sample.

We have assumed that the concentrations of the other matrix constituents remain approximately constant throughout the depth of the tissue, and that therefore they do not contribute to the observed T_2 value. In real cartilage this assumption is incorrect, and will introduce an error into the analysis. The acquisition technique we have chosen seeks to maximize the depth wise resolution while providing sufficient SNR. Similar protocols have been suggested for clinical imaging of articular cartilage [11]. Further experiments are required to establish the ability of the technique to provide quantitative information on the fibre orientations through comparison with histology.

There are currently no clinically applicable techniques to resolve the integrity of the collagen fibre network. Clinical images have decreased resolution and SNR, which complicates the interpretation of the observed T_2 anisotropy. We believe that the consistent definitions of depth and orientation provided by adapted Laplace thickness method will aid investigation of the influence of dipolar interaction in clinical cartilage imaging. The method, combined

with the application of our model based approach would allow the investigation of the spatial anisotropy of T_2 in clinical images, and particularly over the curvature of the femur which provides multiple angles for analysis.

It is hoped that the application of a quantitative model based approach may allow the development of a functional imaging technique and the evaluation of the early stages and progression of cartilage disease such as osteoarthritis.

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