PhD Thesis Title: "Multinuclear Magnetic Resonance Imaging for in-vivo Physiological and Morphological Measurement of Articular Cartilage"

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ABSTRACT:

Osteoarthritis (OA) is a serious, painful and life altering joint disease that is most common in the knee joint. Knee OA can be characterized by the gradual loss of articular cartilage (AC). Early detection of knee OA is important, as it will allow physicians to start hyaluronic acid or nonsteroidal anti-inflammatory drugs (NSAIDs) treatment to stop further degeneration of AC. For the early knee OA detection, AC thickness and volume as morphology, and AC water and proteoglycan (PG) contents as physiology are suitable features. The above features have not been measured with certainty using a single non-invasive modality under *in vivo* conditions. So far, traditional Magnetic Resonance Imaging (MRI) has shown promising results in quantifying the above mentioned features but exhibit certain drawbacks. First, Magnetic Resonance (MR) technique such as delayed gadolinium enhanced MRI of cartilage (dGEMRIC) used to measure PG content of *in vivo* AC requires the use of a contrast agent; this makes the method invasive. Secondly, traditional MR images of knee exhibit the followings: (a) low visibility of AC region, (b) varied intensities on AC region, and (c) homogeneous intensities in AC and surrounding regions; all these conditions resulted in difficulties to segment AC automatically for accurate measurement of volume and thickness. In the current thesis, multinuclear MR imaging at 1.5 T MRI using a dual tuned ($^{23}Na/^{1}H$) knee coil, and an optimized pulse sequence is proposed to acquire knee MR data with significant signal-to-noise ratio (SNR) that would enable a combined non-invasive and *in vivo* measurement of AC thickness, volume, water, and proteoglycan content using signal and image processing techniques.

Sodium MR imaging is performed using a selective MR pulse sequence (3D Gradient Echo-GRE) that is optimised by taking SNR, resolution, image contrast, and field of view (FOV) into consideration followed by measurement of SNR for performance evaluation. In the experiment, significant SNR (>18 dB) is achieved in the AC region of sodium MR images that shows clinical significance. AC sodium concentration from sodium MR images is measured by developing a method using image-processing technique. Using this method, the absolute sodium concentration measured from four data sets is found to be 225 ± 18 mmol/L which corresponds to the values reported earlier for normal human AC sodium concentration measured with a >4 T MR scanner. Furthermore, T2 relaxation times associated with water content of AC are measured from multi-echo spin-echo (echo-time: 13.8, echo spacing: 13.8, no of echos: 5, total slices: 55) MR data. For each slice, signal intensity values obtained from the

region of interest was fitted to a *mono-exponential* function pixel by pixel as a function of echo-time and the T2 values are estimated. The mean T2 relaxation times values (31.87±1.53ms, coefficient of variation-4.81%) obtained for five subjects are in the agreement with earlier studies and shows significance (coefficient of variation (CV) <10%) for clinical settings. Morphological measurement of AC is performed using combined assessment of multinuclear (proton and sodium) MR data. First, fusion of original proton and extracted sodium slices were performed to enhance the visibility contrast of AC (obtained contrast improvement factor >3.0) that enables automatic segmentation of AC using a threshold algorithm (Otsu). Against the ground truth (observer segmentation), the proposed automatic method gave an average sensitivity >80.20% and specificity >99.64% with CV ~8% that shows significantly better performance compared to existing methods. The 3D AC models are further reconstructed by applying the marching cubes algorithm on segmented slices, and computation of volume (using divergence theorem) and thickness (computing normal vectors) is performed. The average value of AC volume obtained from four datasets is 23,197 ± 1384 mm^3 with a better CV of 5.9%, is in agreement to the average volume (23,245 ± 4416 mm^3, CV-19%) reported earlier. Similarly, mean thicknesses (2.51±0.13, CV-5.6%) calculated from 3D AC models of four subjects show an agreement to the values reported in the earlier.

In summary, this thesis presents the development of non-invasive quantitative methods to evaluate AC physiology (water and sodium concentration), and morphology (volume and thickness) using multilevel image and signal processing of multinuclear MR data with a 1.5 T MR scanner. The results obtained in this thesis demonstrated the applicability of developed methods to be utilized for automatic, *in vivo* and non-invasive diagnostic tool that can detect and monitor early knee OA.

References to author publications that relate specifically to the dissertation:

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