

Osteoarthritis and Cartilage



Subchondral bone in osteoarthritis: association between MRI texture analysis and histomorphometry



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SUMMARY

Objective: Magnetic resonance imaging (MRI) texture analysis is a method of analyzing subchondral bone alterations in osteoarthritis (OA). The objective of this study was to evaluate the association between MR texture analysis and ground-truth subchondral bone histomorphometry at the tibial plateau. **Design:** The local research ethics committee approved the study. All subjects provided written, informed consent. This was a cross-sectional study carried out at our institution between February and August 2014.

Ten participants aged 57–84 with knee OA scheduled for total knee arthroplasty (TKA) underwent pre-operative MRI of the symptomatic knee at 3T using a high spatial-resolution coronal T1 weighted sequence. Tibial plateau explants obtained at the time of TKA underwent histological preparation to allow calculation of bone volume fraction (BV.TV), trabecular thickness (Tb.Th), trabecular separation (Tb.Sp) and trabecular number (Tb.N). Texture analysis was performed on the tibial subchondral bone of MRI images matched to the histological sections. Regression models were created to assess the association of texture analysis features with BV.TV, Tb.Th, Tb.Sp and Tb.N.

Results: MRI texture features were significantly associated with BV.TV ($R^2 = 0.76$), Tb.Th ($R^2 = 0.47$), Tb.Sp ($R^2 = 0.75$) and Tb.N ($R^2 = 0.60$, all $P < 0.001$). Simple gray-value histogram based texture features demonstrated the highest standardized regression coefficients for each model.

Conclusion: MRI texture analysis features were significantly associated with ground-truth subchondral bone histomorphometry at the tibial plateau.

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Introduction

At present, efficacious disease modifying treatments for osteoarthritis (OA) are lacking¹. Imaging has the potential to play an important role in the development of disease modifying treatments by assessing response to novel therapeutic approaches and improving understanding of OA natural history². For this potential to be realized, sensitive and reliable imaging biomarkers are required. OA is considered as a disease of the entire joint, involving

cartilage, bone, synovium, ligaments, menisci (for knee OA), capsule and juxta-articular muscle³. Much research interest has focused on assessment of cartilage, however it is also desirable to have reliable imaging biomarkers of other involved tissues such as the subchondral bone.

Texture analysis has been described as a method of analyzing subchondral bone on plain radiographs, computed tomography (CT) and magnetic resonance imaging (MRI)^{4–6}. Texture analysis is a statistical method of analyzing an image or region of interest (ROI) based on the distribution and spatial organization of gray (pixel) values within it⁷. Its utility in the setting of subchondral bone analysis in OA lies in detecting and quantifying alterations in structure that are not detectable or difficult to quantify reliably using qualitative or alternative quantitative methods.

The current study focuses on MRI texture analysis at the knee. The advantages of using MRI for texture analysis over plain radiographs or CT are the cross-sectional nature of the images

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(compared to plain radiographs), the lack of radiation exposure and the ability to assess other tissues involved in OA (particularly cartilage, synovium and meniscus) in a single examination.

MRI texture analysis has previously demonstrated significant differences in subchondral bone texture between controls and individuals with OA⁸. Alternative methods of assessing subchondral bone using MRI are available including direct estimation of microstructural parameters^{9,10}. However, texture analysis has the advantages of the ability to use standard clinical sequences, the lack of need to binarize images using an arbitrary threshold, and superior discrimination ability between subjects with OA and controls¹¹.

One of the principal disadvantages of MRI texture analysis is the current lack of histological validation. It is important to assess the relationship between MRI texture analysis and ground-truth subchondral bone structure to establish the construct validity of this technique before it can be considered for use in further longitudinal or interventional studies. The histological gold standard for assessment of bone structure is the technique of histomorphometry which is the quantitative analysis of microscopic bone structure¹².

Thus, the purpose of this study was to evaluate the association between MRI texture analysis and ground-truth subchondral bone histomorphometry at the tibial plateau.

Materials & methods

The local research ethics committee approved the study. All subjects provided written, informed consent. This was a cross-sectional study carried out at our institution between February and August 2014.

Participants

Ten participants (median age 70, range 57–84, seven females) who were scheduled to undergo total knee arthroplasty (TKA) at our institution for primary OA of the knee were recruited at the time of their clinic visit immediately prior to TKA.

Participants were excluded if there was a history of significant ipsilateral lower limb injury, previous ipsilateral lower limb surgery, inflammatory arthritis, hematological malignancy, bone metastases, metabolic bone disease, or if there was a contraindication to MRI.

Participants had their height and weight recorded at the time of examination. All participants had recent AP weight bearing knee radiographs available (median 30 days previously, range 0–160 days). These were used to record the severity of medial and lateral tibiofemoral compartment OA using the Kellgren–Lawrence grading system¹³. Kellgren–Lawrence grading was performed by two radiology residents (JM & PM) with 3 years' experience. Participants completed an Oxford Knee Score questionnaire in order to assess severity of symptoms¹⁴.

MRI acquisition

The knee scheduled for TKA of each participant was imaged using a dedicated 8-channel transmit/receive knee coil (InVivo, Gainseville, FL, USA) on a wide-bore 3.0 T platform (GE 750w, GE Healthcare, Amersham, UK). Sequences obtained included a 2 dimensional (2D) coronal T1 weighted sequence (FOV 12 × 12.3 cm, matrix 512 × 512, TR 593 ms, TE 17.65 ms, NEX 1, slice thickness 2.8 mm, slice gap 2.5 mm, sequence duration approximately 3 min) designed to maximize in-plane spatial resolution (0.23 × 0.24 mm) and signal-to-noise ratio for optimal assessment of subchondral bone (Fig. 1). The MRI examination was performed at the time of

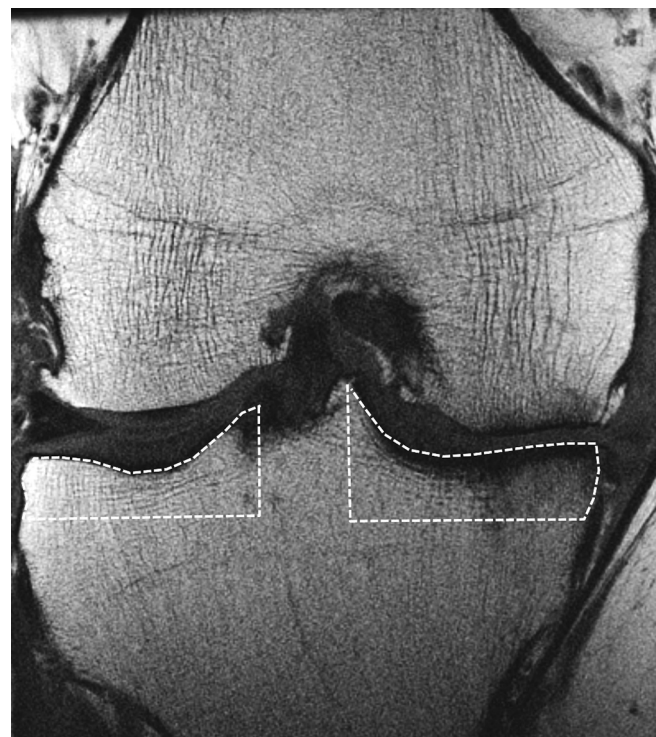


Fig. 1. Sample coronal T1w MR image. White dashed line outlines typical ROI placement. Note lower signal in medial tibial ROI.

the participant's pre-operative assessment to ensure a short interval between MRI and TKA (median 13 days, range 6–29 days).

Bone specimens

The tibial plateau of each participant was removed as part of the TKA procedure as a single block of tissue. This was placed in 10% buffered formal saline for fixation and stored at room temperature while awaiting processing. Surgical sutures were used to identify the medial/lateral and anterior/posterior margins of the tibial plateau at the time of resection.

Histological processing involved dividing the tibial plateau in half in the sagittal plane into medial and lateral portions using a bone saw (Exakt Diamant Band Saw, Exakt Advanced Technologies GmbH, Germany), to enable the samples to fit standard 30 × 25 mm histological cassettes. The central portion of the tibial plateau specimens was then sectioned in the coronal plane (to match the orientation of the MRI images) using the bone saw with the location of the blocks taken recorded on a schematic diagram of the plateau. The tissue block then underwent decalcification, embedding in paraffin, cutting then staining with hematoxylin and eosin. The blocks were typically 30 mm in width and included between 5 and 10 mm in depth of tibial subchondral bone. Preparation of the blocks was supervised by an experienced bone pathologist.

Histomorphometry

Prepared histological blocks were converted to digital format using a high-resolution histological scanner (Hamamatsu Photonics, Welwyn Garden City, UK). The digital blocks were exported in TIFF format and analyzed using ImageJ (NIH, Bethesda, MD, USA).

For each sample, following calibration for magnification, ROIs were created to enclose the subchondral bone. ROIs were defined superiorly by the bone/cartilage interface, laterally/medially by the

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