Pathophysiology of Bone Marrow Edema: Insights from Dynamic Contrast Enhanced MR Imaging

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Purpose

Excessive water in subchondral bone, i.e. bone marrow edema (BME), has been associated with osteoarthritis (OA), traumatic injury (i.e. bone contusion), osteonecrosis, altered biomechanics, transient osteoporosis, and stress reaction. In many cases, BME is associated with pain; however, the pathophysiology of BME is not known (1). Some studies have demonstrated increased intraosseous pressure in BME that could lead to diminished blood flow and hypoxia, altered osteoblastic cytokine expression, and osteocyte necrosis (2). The pharmacokinetic modeling of bone perfusion using dynamic contrast enhanced-MR imaging (DCE-MRI) has been used to monitor disease activity in juvenile rheumatoid arthritis (3). In this study, we investigate perfusion kinetics of BME using DCE-MRI in a Dunkin-Hartley guinea pig model of osteoarthritis and in human subjects with BME from different causes.

Materials & Methods

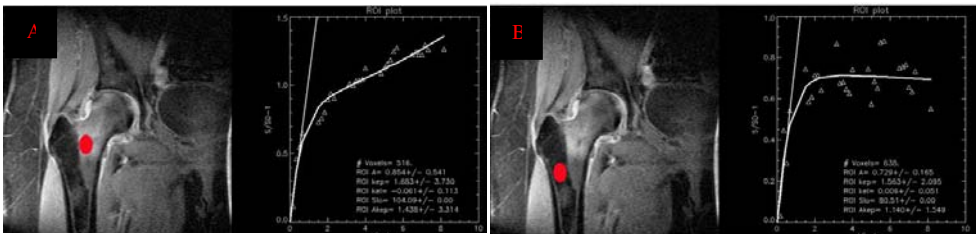
Animal studies The Dunkin-Hartley guinea pig was selected since it been shown to develop spontaneous knee OA over time and in a manner similar to the progression of OA in humans (4). Ten animals at 4 different ages (6, 9, 12, and 15 months) were studied. In preparation for MRI scanning, guinea pigs were anesthetized with isoflurane and placed in a 3.2 cm diameter inductively-coupled solenoidal coil. Scanning was performed on a 3T magnet (GE Medical Systems, Milwaukee, WI) using a fast spin-echo Short-Tau Inversion Recovery (STIR) sequence for BME detection, and a fast multi-planar gradient echo for blood flow analysis; time resolution varied from 4.6-9.6 seconds/image depending on whether 4-6 slices were acquired, respectively. A syringe attached to the central venous line was used to administer Gd-DTPA (0.65 cc/kg). Following on-line reconstruction, data was exported for analysis using in-house IDL software (RSI-Kodak, Boulder, CO). BME was assessed qualitatively on STIR images. Regions of interest (ROIs) drawn on the lateral aspect of the knee were selected as the control, since OA develops almost exclusively on the medial femorotibial joint.

Human studies MR imaging was performed on 13 adults with BME using a 1.5T magnet (Symphony; Siemens, Erlangen, Germany) and a surface coil. Prior to DCE-MRI, STIR [3500/17/150 (TR/TE/TI)] was performed to localize the largest focus of BME. DCE-MRI using the volumetric interpolated breath-hold examination sequence [5.50/2.89 (TR/TE); 10° (flip-angle), 350 Hz/pixel (bandwidth); 16cm (FOV); 5mm, slice thickness; one excitation; and 256 x 151, matrix] was performed before and during intravenous administration of 0.1mmol/kg of gadodiamide at 2cc/sec. DCE-MRI images were analyzed with customized IDL 6.1 software. Separate ROIs were placed on areas of BME and normal bone marrow, and signal intensity-time curves were generated. For both animal and human studies, pharmacokinetic modeling was performed using the two-compartment Brix model to generate rate constants A, k_{ep}, and k_{el}. A paired Student's t-test was used to compare kinetic parameters between normal and edematous marrow.

Results BME appeared in the medial tibial plateau of the guinea pig between 6 months and 9 months of age, prior to the development of cartilage lesions, and was not observed in the lateral side of the knee. Mean k_{el} was smaller in the medial femorotibial joint (p=<.001) and decreased as a function of age and severity of OA (Figure 2). In the human-subject studies, signal intensity-time curves show higher wash-in rate and lower wash-out in BME when compared with normal tissue (Figure 1); analysis of Brix model parameters shows higher mean A (p<.001), lower k_{ep} (p=0.05) and lower k_{el} (p=0.03) in BME compared to normal bone marrow (Table I).

Discussion and Conclusions This study provides insight into the significance and pathophysiology of BME. In the guinea pig model of OA, BME is observed in subchondral marrow of the medial tibia adjacent to the site of articular cartilage lesions but before these lesions are morphologically apparent. DCE-MRI shows both significantly increased A, consistent with increased perfusion, and decreased k_{el}, consistent with reduced contrast elimination, in BME compared to normal bone marrow. Future studies will compare kinetic perfusion parameters in BME from osteoarthritis and osteonecrosis with that from acute traumatic knee injury.

Figure 1. ROI in red on BME (A) and normal bone marrow (B) with respective signal intensity-time curves.



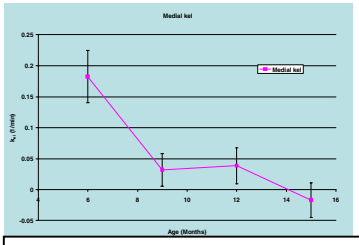


Figure 2. Graph shows decrease in k_{el} with increasing age of guinea pig.

Table I (mean±SD)	A	k_{ep}	k_{el}
BME	0.93± 0.44	2.9±1.5	-0.037±0.1.4
Normal Bone	0.34±0.19	5.5±4.7	0.02±0.21
p-value	<.001	.05	.03

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