INTRODUCTION

There has been considerable interest in the cross-talk, and physicochemical signaling, between bone and cartilage in the initiation or progression of osteoarthritis (OA). This interest has been heightened by observations that 1) bone marrow edema and intraosseous hypertension are associated with bone pain and progression of cartilage lesions, and 2) that OA osteoblasts alter their cytokine expression profile associated with bone remodeling and cartilage degradation. The hypothesis of this study is that changes in perfusion in subchondral bone bear a functional relationship to bone remodeling and cartilage degradation and are a part of a physicochemical signaling mechanism to osteoblasts. We assess bone perfusion in the Dunkin-Hartley guinea pig with gadolinium-enhanced magnetic resonance imaging (Gd-MRI).

METHODS

The Dunkin-Hartley guinea pig displays changes of OA at about 12 months of age with increased subchondral bone thickness and increasing histological-histochemical (Mankin) scores in the medial tibial plateau. All procedures were approved by Weill Cornell IACUC. Magnetic Resonance Imaging (MRI) of the guinea pig knee joint was performed in animals 6, 9, 12, and 15 months of age. Central jugular venous lines were placed in order to ensure reliable venous access for MRI perfusion studies. Guinea pigs were anesthetized using isoflurane and placed in a custom-designed apparatus with a 7 turn, 3.2 cm diameter inductively coupled solenoidal coil tuned to 127.7 MHz.

We have utilized Gadolinium Diethyltriaminepenta-acetic Acid (Gd-DTPA) enhanced MRI in the Dunkin-Hartley model to assess perfusion and bone marrow edema in developing OA. Gd-DTPA enhancement has been validated by comparison to 99Tc-labeled nanocolloid scintigraphy. All studies were performed on a 3.0 Tesla GE MRI Scanner. MRI scans used for analysis were (1) a Fast Spin Echo-Short T1 Inversion Recovery (STIR) for edema visualization, and (2) a Fast Multi-Plane Spoiled Gradient Echo (FMPSGPR) for blood flow analysis. Following off-line reconstruction, data was exported for analysis using in-house software written to display and analyze the data using IDL 6.0 (RSINC/Kodak, Boulder, CO). Bone marrow edema was assessed by voxel intensity and by T2 maps.

The Brix two compartment tissue model describes the kinetics of exchange of Gd-DTPA. It is characterized by several rate and volume transfer constants (Figure 1). Perfusion data was analyzed using previously published in-house software yielding perfusion parameters based on the compartmental model of Brix. The perfusion parameters were analyzed based on regions of interest drawn at the medial and lateral tibial plateaus. The various rate constants can be determined mathematically from time-intensity plots. Decreases in \( k_{el} \) indicate outflow obstruction and reduced perfusion (Figures 2A and B).