Preliminary Results on Bone Perfusion Measurement using Dynamic Contrast Enhanced Ultrashort TE Imaging

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Purpose: Dynamic Contrast Enhanced (DCE) MRI has been applied for micro-vascular characterization of various tissues such as brain lesions and tumors [1]. Typically it requires the measurement of dynamic MRI signal over the region of interest using fast gradient echo sequence. So far its application to bone perfusion characterization has been limited to bone marrow studies [2,3] due to the lack of detectable signal from cortical bone, which has extremely short T_2 of around 300 to 500 μs and therefore cannot be detected by conventional gradient echo sequences with typical echo times of 1 ms or longer. As a result, there are no MR techniques available to directly assess bone perfusion for non-invasive study of bone physiology and metabolism. Ultrashort TE (UTE) sequences with TEs as short as 8 μs offer an opportunity to measure signal from cortical bone [4,5]. In this preliminary study we report on dynamic UTE imaging of cortical bone of healthy volunteers using a clinical 3T MR scanner. The dynamic data are processed through usual Tofts kinetic model, and pharmacokinetic parameters (K^{trans}, k_{ep} and v_p) are reported.

Materials and methods: MRI: MR experiments were performed on a Sigma HDx 3T scanner (GE Healthcare, Milwaukee, WI, USA). Dynamic data were acquired on three healthy male volunteers (38 to 68 years old), focusing on the tibia. A 3-inch diameter surface coil was used to improve signal to noise ratio (SNR). A 2D UTE sequence was optimized in order to obtain a good compromise between SNR, spatial resolution and temporal resolution. The following MR parameters were used: TE = 8 μs, TR = 20 ms, FA = 35º, BW = 250 kHz, FOV = 15 cm, 320 readout points, 711 radial projections, number of excitation (NEX) = 2, 10 mm slice thickness. Data were reconstructed onto a 512x512 square matrix. Using this sequence a 30 s temporal resolution was achieved. Acquisition was run 10 times pre injection and up to about 40 min post-injection of a clinical double dose (0.2 mg/kg) of a usual low molecular weight Gd contrast agent (GD-BOPTA; Multihance®; Bracco Imaging SpA, Mila, Italy). Kinetic Analysis: Classical Tofts model was applied to process the data with K^{trans}, k_{ep}, v_p and the bolus arrival time (BAT) as free parameters. An ROI was drawn on the arterial compartment (tibial artery) in order to derive a patient base arterial input function (AIF) that was fed into the model. MRI signal was converted into Gd concentration using usual SPGR signal equation considering a 1.4 s blood baseline T_1 and a 220 ms tibia baseline T_1, which was measured using a saturation recovery UTE technique [5]. Hence time vs. concentration curve can be obtained and processed through this model. We used a custom-made fitting algorithm coded under Mathematica (Wolfram Research Inc., IL, USA). A particularity of our algorithm is that it treats both kinetic model and MRI signal model together, allowing propagating MRI noise all the way to the pharmacokinetic parameter estimates, thus providing of estimation of the pharmacokinetic parameter uncertainty and correlations.

Results: Fig.1. shows representative UTE images obtained pre-injection a) and at the peak of bone enhancement b). Using a local coil for MR detection improves SNR but also implies non-uniform detection sensitivity which is evidenced on 1.a). For a better visualization of details average pre-injection data were subtracted from the post injection image on 1.b). The AIF and bone ROIs are emphasized in 1.b) with a red arrow and a red ellipse respectively. Bone SNR was of 29 pre injection and peaked at 34 about 3 min after injection. Fig. 2 displays the corresponding kinetic analysis. K^{trans} and k_{ep} were estimated with a reasonably low error. On the other hand v_p and the BAT exhibit large standard deviation (much higher than data SNR) because of a strong correlation between those two free parameters through the model (0.983 correlation coefficient).

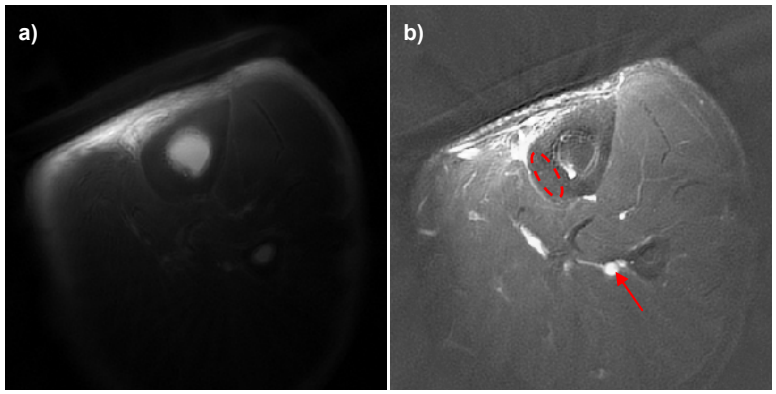

Figure 1: UTE images of tibia. a) pre-injection image
b) peak bone enhancement image subtracted from averaged baseline signal

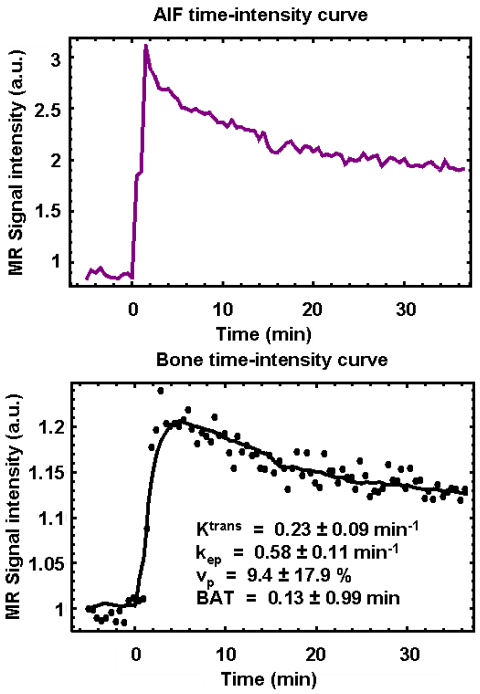

Figure 2: Kinetic analysis

Discussion and Conclusion: The importance of skeletal perfusion on bone health is apparent from a large number of studies which have shown a direct relation between bone perfusion and bone remodeling activity [2,3,6]. It would be tremendously helpful to have non-invasive methods to obtain measurements that are relevant for bone hemodynamics. As far as we know, this is the first study on direct bone perfusion assessment using DCE-MRI. Comparable studies performed using nuclear medicine [6] use more sophisticated model to describe the contrast agent kinetic and thus direct comparison of extracted parameters is not possible. Future studies will include optimization of the bone perfusion model, e.g considering three compartments (blood, interstitial fluid and water bound to collagen matrix), and apply this model to healthy volunteers as well as patients with osteoporosis (OP) to study bone physiology providing a heretofore unavailable opportunity to characterize bone diseases.

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References: **[1]** Tofts PS, et al., *J Magn Reson Imaging*, 1999; 10(3): p. 223 **[2]** Griffith JF et al., *Radiology*, 2010 ; 254 :p.254 **[3]** Lee JH et al., *J Bone Joint Surgery*, 2009; 91-B: p.333 **[4]** Robson MD, et al. J Comput Assist Tomogr, 2003, 27: p. 825 **[5]** Du J, et al. *J Magn Reson*, 2010 (in press) **[6]** Hawkins RA, et al., *J Nucl Med*, 1992; 33(5): p. 633