Improved T1 Weighted Dynamic Contrast Enhanced MRI to Probe Microvascularity and Assessment of Spine Bone Marrow

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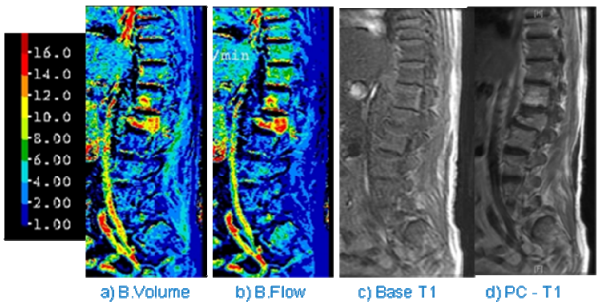
Introduction:

Dynamic Contrast Enhanced MR Imaging (DCE-MR) offers noninvasive characterization of the vascular microenvironment[1] and the assessment of bone marrow diseases have not been fully investigated unlike in cerebrovascular imaging. Present clinical evaluations for initial diagnosis, assessment of treatment response, and follow-up of patients with primary and metastatic tumors are inadequate, often depend on changes in tumor size and present with non-specific lesions. Routine MR imaging of the spinal marrow can be markedly limited in differentiating between tumors and non-tumoral processes, hyper and hypovascular tumors, viable from non-viable tumor, and pathological from non-pathological fractures and treatment related changes of the marrow. Recently, DCE-MR Imaging of Bone Marrow study has shown variations in bone marrow time-intensity curves between ages, sex subgroups, and among spinal levels[2]. Measuring the changes in tumor hemodynamics would give insight into tumor heterogeneity[3]. We aimed to develop an imaging biomarker to facilitate the decision-making process and establish a robust technique to unravel the complexity of tumor vasculature that may aid in therapeutic management of spine bone marrow patients employing the improved T1 weighted DCE MR algorithm[1].

Methods: MR imaging of the lumbar spine were performed in 22 Spine bone marrow tumor patients with age ranging from 45 to 76 (mean=59) on a 1.5T GE scanner using an 8 channel Cervical-thoracic-lumbar (CTL) surface spinal coil and were histopathologically proven. All subjects were divided into three different groups: patients with hyper-vascular tumors (10), hypo-vascular tumors (9), and without tumor (3) in the spine. MRI studies of lumbar spine included axial T1, T2, and saggital T1, T2, IR, DWI, followed by T1 w DCE and PCT1. T1 weighted DCE MR images were obtained with 3D fast SPGR sequence with following MR parameters: no of phases = 35, TR= 4-5 sec, TE=1-2 sec, slice thickness = 4-5 mm with no gap, flip angle =20, FOV=34-36 cm and matrix size of 256x256 in the sagittal plane. The first five time points were acquired to establish a pre-contrast baseline. At the fifth acquisition, Gd-DTPA in a dose of 0.1 mmol/kg of body weight was administered at a rate of 2-3.5 ml/s with the help of a power injector.

Analyzing tracer behavior on voxel to voxel basis, the effective change in T1 relaxation rate was determined by following algorithm before converting MR signal intensities into Bone Marrow Concentration Time curve. The MR signal was modeled in terms of T1 weighted effects of Gd-DTPA and the value of K defined as the pre-contrast medium steady state residue was optimized to bone marrow time-intensity curves.

$$c(t) = \begin{cases} \frac{1}{\alpha} \ln\left[\frac{(S_c(t) - K)}{(S_0 - K)}\right] & \text{provided} \quad \begin{matrix} S_c(t) - K > 0 \\ S_0 - K > 0 \end{matrix} \end{cases}$$



We have developed in-house software for evaluation and generation of Spine Bone Marrow maps - Blood volume and Blood Flow, Uptake curve maps – Upslope and Down slope, Enhancement maps - Peak and Relative map. The perfusion indices, Bone Marrow Blood Volume (Fig-a) and Bone Marrow Blood Flow maps (Fig-b) were generated by deconvolving arterial input function to calculate the residue. The uptake curve maps, the Upslope ([Smax – S_0]/Trise) and enhancement peak maps ([Smax-S_0]/ S_0×100%) were calculated, where Smax - maximum signal intensity; S_0 - baseline value; Trise - Bolus enhancement rise time. Marrow base T1 and Post Contrast T1 are shown as Fig c & d respectively.

Results and Discussion

To evaluate the functional parameters, we placed three similar small ROIs (20–35 pixels) at the tumor as well on the normal site and the third ROI was placed on the normal radiated region that underwent radiation therapy. The ratios of these three were subjected to statistical evaluation that showed a significant differences ($p<0.02$) in the tracer kinetic pattern, found between hyper (> 1) and hypovascular tumor groups (<1). These Spinal Bone marrow maps correlated well with histopathological findings that were confirmed by biopsy specimens. It also showed that there are no significant enhancements in the bone marrow without tumors.

Clearly, the generated maps visually appreciate the distinct regions fulfilling the characteristics of hyper vasculature and its heterogeneity when compared to tumor, normal and normally radiated regions. Furthermore, this improved technique offers insight into discrimination between normal marrow and pathologically replaced marrow with the range of colors identifying the highest BV and BF values and accurately characterizes the lesions as hyper or hypovascular. And even with susceptibility artifact from orthopedic hardware. The maps also distinguished pathological and osteoporotic fractures, and indicate a favorable utility of DCE in clinical work up of patients with spinal compression fractures. We propose that this simple and robust T1-Weighted Dynamic Contrast Enhanced non-invasive technique improves the accuracy of perfusion metrics and enables visual appreciation that could characterize marrow heterogeneity and differentiate between different conditions that affect the marrow pathophysiologically. This model lays the groundwork and necessitates further investigation on the utility of DCE in larger population bone marrow patients. Early detection and treatment response assessment may enhance the decision process towards improving patient management for change in treatment strategy or adjuvant treatments if any, would have an enormous impact on patient care.

References 1) Pauliah et al., MRI, 2007, 25(9):1292-1299. 2) Shih et al., Radiology, 2004, 233:121-128 3) Daldrup-Link HE et al Eur Radiol. 2007, 17(3): 743–761.