Demonstrable BOLD Effect in Human Bone Marrow

David K.W. Yeung[1], James F Griffith[2], Heather T Ma[3,4], and Alvin F.W. Li[2]

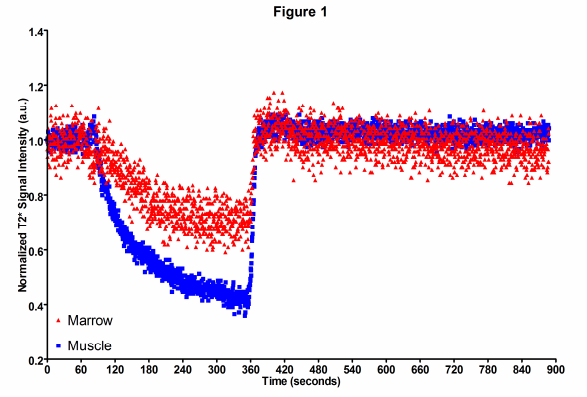
[1]Imaging and Interventional Radiology, Prince of Wales Hospital, Shatin, HKSAR, Hong Kong, [2]Imaging and Interventional Radiology, The Chinese University of Hong Kong, Shatin, HKSAR, Hong Kong, [3]Department of Electronic and Information Engineering, Harbin Institute of Technology, China, People's Republic of, [4]Imaging and Interventional Radiology, The Chinese University of Hong Kong, HKSAR, Hong Kong

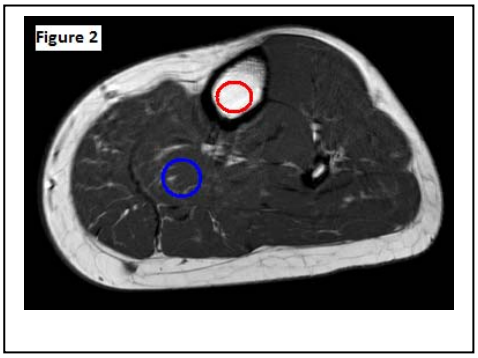
Background: Osteoporosis is the most common metabolic bone disease affecting humans. This silent disease is characterized by a general bone loss and deterioration in bone quality leading to bone fragility and an increased risk for fractures. Despite much research, what actually triggers rapid bone loss in some people is still largely unknown. One aspect of bone research that has recently attracted much attention is the relationship between bone marrow vasculature and bone modelling. However, only few methods are available to study blood supply in bone and the purpose of this study was to verify whether BOLD MRI technique may be employed to study bone marrow oxygenation status in healthy subjects.

Introduction: BOLD imaging has been shown to be useful for studying muscle oxygenation in patients with peripheral arterial occlusive disease (1). This technique employs a T2* imaging sequence to track deoxymyoglobin concentration changes following cuff-induced ischemia in the lower limb (2,3). The femoral artery carrying blood to the lower limb may be occluded using a thigh air-cuff wrapped round the mid-thigh and blood flow interruption causes a rise in muscle deoxymyoglobin level leading to a drop in T2* signal intensity because of magnetic susceptibility effects. The rapid T2* signal increase in muscle after cuff deflation is due to a disproportionate inflow of oxyhemoglobin during reactive hyperemia. Our hypothesis is that blood supply disruption in bone may also lead an accumulation of deoxyhemoglobin and its effect on bone marrow susceptibility may give rise to T2* signal changes. To the best of our knowledge, this effect has not been demonstrated in bone marrow. Our aim in this study was to verify whether a BOLD effect may be detected in the tibia marrow of healthy subjects following air-cuff induced ischemia.

Materials and Methods: Ethical approval was granted to perform this study on healthy subjects. Fifteen volunteers (8 females, 7 males; mean age 44 years) were recruited to undergo BOLD imaging of the lower limb using a 3T whole-body scanner (Achieva TX, Philips Healthcare). An eight-channel SENSE knee coil was used for signal reception and a T2*-weighted sequence (TR/TE 372/40 ms; slice thickness 5 mm; NEX 1; FOV 250 mm; dynamic measurements 500; scan time 180 s) was applied to acquire one axial slice located 20-25 cm away from proximal side of the air-cuff placed at the mid-thigh level. Distance between air-cuff and imaging plane was kept as far as possible to minimize air-cuff induced susceptibility effects. Cuff inflation was done using a sphygmomanometer (Spacelabs Healthcare, Redmond, WA) to interrupt blood flow one minute after BOLD imaging began. Air-cuff pressure applied was 50 mmHg above each subject's systolic pressure and air pressure was maintained until 6 minutes into the dynamic scan. After release of air-pressure, BOLD scan continued for a further 9 minutes. ROIs were drawn to obtain dynamic T2* signal intensity time-series from the soleus muscle and tibia marrow of all subjects.

Results: Muscle T2* signal intensity of all subjects showed a similar pattern: progressive fall in intensity after cuff inflation and a rapid signal rise when pressure was released. In 12 out of the 15 subjects, a progressive fall in T2* signal intensity in the tibia marrow could also be observed. The noise level from the marrow was much higher compared to muscle data and the unacceptably high noise level might account for the failure to detect meaningful signal changes in 3 subjects. Figure 1 shows an example of muscle and marrow T2* signal progression when an air-cuff paradigm was applied to the left thigh. Figure 2 shows the locations of the ROIs drawn on T1-w anatomical image of a female volunteer.





Conclusion: Our initial results have demonstrated the presence of a detectable signal change in the tibia marrow of healthy subjects. The observed marrow T2* signal intensity had a much higher noise level but it exhibited a similar pattern of signal change as that of muscles. We postulate that the observed signal variation was due to an accumulation of deoxyhemoglobin in the marrow after blood flow was interrupted. Since deoxyhemoglobin is paramagnetic, it affects the magnetic susceptibility of bone marrow leading to a T2* signal change. However, our initial finding needs to be further validated using other detection means such as high-field proton MRS or using animal models to investigate the origin of this signal change (4).

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