Muscle-based pharmacokinetic model for bone marrow perfusion study

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Introduction: Over the recent decade, dynamic contrast enhanced (DCE) MRI has been used to assess bone marrow perfusion and has proved useful in showing alteration in perfusion parameters in different disease and physiological states. However quantitative analysis of DCE-based pharmacokinetic models require 三 an arterial input function (AIF), which is variable due to many factors including examination technique. . As a result, quantitative analysis of bone marrow perfusion using standard AIF as a reference is limited. The purpose of this study is to characterize bone marrow perfusion parameters in a quantitative way by using adjacent muscle perfusion as an internal reference standard.

Methods: Eighty-two subjects (age 72.5±3.4 yrs) were studied. Area bone mineral density (BMD) of L3 level was measured by dual-energy X-ray absorptiometry (DXA). MR imaging was performed at 1.5T (Intera NT, Philips, Best, Netherlands). Axial T1-weighted (TR/TE, 450/11 ms; 4 mm thick) and DCE-MRI (2.7/0/95; prepulse inversion time, 400 ms; flip angle, 15°) data were acquired through the mid-L3 vertebral body region. A total of 160 dynamic images were obtained with a temporal resolution of 543 ms, resulting in a total interrogation time of 87 seconds.

A region of interest (ROI) was drawn manually for each muscle area and bone marrow area on this axial image (Fig.1) and a time-signal intensity curve generated by averaging signal intensity within the ROI. Target of interest (TOI) was the bone marrow. A muscle-based pharmacokinetic model was established by adapting a reference region-based model [1]. Erector spinae muscle signal was fitted to the model as

$$C_m(t) = A \cdot t \cdot \exp(-t \cdot B) + C[1 - \exp(-t \cdot D)] \cdot \exp(-t \cdot E)$$

where A, B, C, D, and E are density and time constants respectively. The muscle-based pharmacokinetic model for the TOI was finally formatted as

$$C_{TOI}(T) = R \cdot C_m(T) + R \cdot [(K^{trans,m} / V_{e,m}) - (K^{trans,TOI} / V_{e,TOI})] \cdot \int_0^T C_m(t) \cdot (\exp(-K^{trans,TOI} / V_{e,TOI})(T-t))dt$$

where $R \equiv K^{trans,TOI} / K^{trans,m}$, C_{TOI} and C_m were the concentration of the contrast agent (Gd-DTPA) in the TOI and erector spinae muscle; $K^{trans,TOI}$ and $K^{trans,m}$ are contrast agent extravasation rate constants for TOI and muscle; and $v_{e,TOI}$, $v_{e,m}$ are the extravascular-extracellular volume fractions for TOI and muscle, respectively.

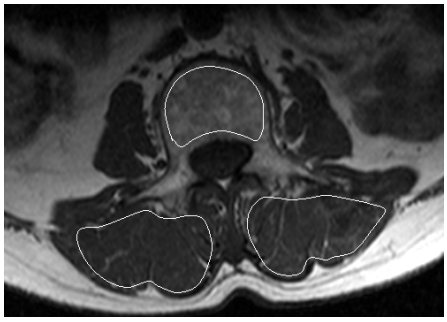


Fig 1. T1-weighted MR image in axial plane, with manually drawn ROI within L3 vertebral body and erector spinae muscle.

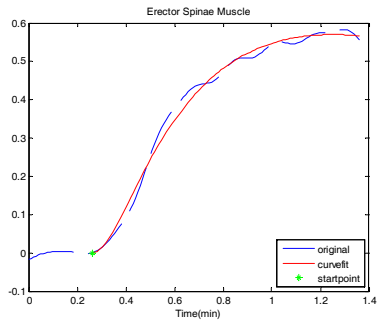
Results: ANOVA analysis was performed for the key parameters of different muscle groups.

Table 1: Muscle groups comparison by ANOVA

Group(n)	$K^{trans,TOI}$ (min^{-1})	$K^{trans,m}$ (min^{-1})	$V_{e,TOI}$	$V_{e,m}$
Normal(n=11)	0.369±0.129	0.303±0.101	0.191±0.245	0.186±0.286
Osteopenia (n=26)	0.334±0.110	0.310±0.116	0.146±0.214	0.114±0.177
Osteoporosis (n=39)	0.255±0.135	0.280±0.136	0.125±0.184	0.159±0.276
pvalue	0.009	0. 623	0. 637	0. 662

All statistical analysis was performed by using SPSS 16. Significant difference was only observed in the parameters of $K^{trans,TOI}$ among different BMD groups.

(a)



(b)

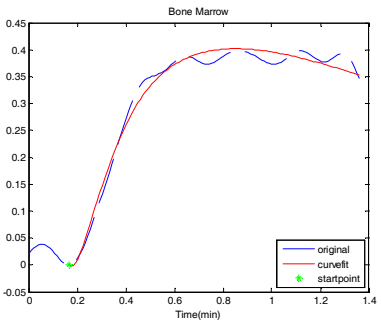


Fig 2. Curve fitting for DCE signals from erector spinae muscle (a) and bone marrow (b).

Discussion: First, this study established a muscle-based pharmacokinetic model for bone marrow DCE-MRI data, which avoided the negative influence of variable AIF values. The model provided a more reliable and robust analysis. Secondly, the parameters $K^{trans,TOI}$ and $v_{e,TOI}$ diminished with decreasing BMD, indicating an impaired perfusion of osteoporotic bone marrow. Such changes are most probably due to the reduced arterial permeability, an increase of marrow fat content and a corresponding reduction in marrow red cell mass in subjects with lower BMD. Thirdly, muscle perfusion indices did not significantly change among different BMD groups ($p>0.05$). Perfusion did not change in the paravertebral muscle in osteoporotic subjects though bone marrow perfusion was significantly reduced compared to normal subjects. In other words, the impaired perfusion function is only a function of the bone marrow and not of the adjacent musculature indicating a local rather than a systemic etiology, particularly since bone and paravertebral muscles share the same arterial supply.

Acknowledgement: This study is supported by the Research Grants Council of the Hong Kong Special Administrative Region, China (Project No. 465111), National Natural Science Foundation of China (81000647), Basic Research Foundation (Outstanding Young Investigator Track) of Shenzhen (JC201005260124A), and High-end Talent Oversea Returnees Foundation of Shenzhen (KQC201109020052A).

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