34th Annual International Conference of the IEEE EMBS
San Diego, California USA, 28 August - 1 September, 2012

# Perfusion and Bone Mineral Density as Function of Vertebral Level at Lumbar Spine*

Heather T. Ma, *Member IEEE,* Haiyan Lv, James F. Griffith, Alvin FW Li, David KW Yeung, Jason Leung, Ping-Chung Leung, Jing Yuan

***Abstract*—The objective of this study is to characterize perfusion and bone mineral density (BMD) in the lumbar spine as a function of level and anatomic location. Fourteen male subjects with healthy vertebral endplates were selected to avoid gender and endplate disease influence. The bone perfusion and BMD of different vertebral level (L1-L4) were measured by the dynamic contrast enhancement MRI (DCE MRI) and the dual-energy X-ray absorptiometry (DXA) respectively. Perfusion parameters showed a significant negative correlation with upper to lower vertebral levels while inverse observation was found for BMD. The results indicated that the perfusion and BMD are as function of vertebral level and anatomic location at lumbar spine. The BMD varying with vertebral level may be determined by the biomechanical usage at the lumbar spine, where the lower levels sustain more mechanical forces. Perfusion changes along the lumbar spine level suggested that the bone marrow component could be different when BMD varies, which needs further histological verification.**

## I. Introduction

The bone tissue, following Wolff's Law, adapts to various mechanical forces and loading patterns. Bone mineral density (BMD) is the most used measure to indicate the bone mechanical properties [1]. In recent decade, bone perfusion was employed to investigate the bone health [2,3] and bone properties under some diseases [4]. Dynamic contrast enhanced (DCE) MRI can provide a direct measurement of tissue perfusion in a living system, which can reflect the blood supply in a microenvironment. Bone perfusion measurement will be dependent on multiple factors, such as tissue blood flow, capillary capacitance and permeability etc. [5,6]. These factors can be assessed by semi-quantitative parameters directly from the perfusion characteristic curves [7] or by quantitative parameters from modeling [5].

As the largest segment of the movable part of the vertebral column, vertebral properties at lumbar spine are likely to differ among anatomic locations among vertebrae depending on level. The relationship between bone characteristics and specific anatomy site in lumbar spine has been investigated to a limited extent. Yoganandan et al found BMD difference among cervical and lumbar vertebrae in male subjects [8]. A decreased bone perfusion was reported in lower lumbar vertebra compared to upper lumbar segments [9]. However, no systematic study investigated the relationship between the variation in BMD and bone perfusion among lumbar vertebra.

The objective of this study is to characterize bone properties, in terms of perfusion and BMD, in lumbar spine as a function of level and anatomic location. Through the semi-quantitative and quantitative parameters, the BMD and site-specific bone microcirculation characteristics are compared among different levels of lumbar spine.

## II. Methodology

### A. Subjects

In order to avoid gender influence, only male subjects were selected. This study involved a reassessment of DCE-MRI raw data obtained in one previous study [2]. Due to the fact that the subjects were all elderly, to avoid other possible influential factors we further selected subjects based on the following criteria.

1. no clinical or imaging evidence of metabolic bone disease or severe vertebral fracture;
2. no low back pain history;
3. no imaging evidence of Modic changes for all lumbar spinal vertebra.

With the criteria, 14 subjects (age 72.1±4 yrs) in total were involved in this study. The study was approved by the Ethics committee, Chinese University of Hong Kong with all participating subjects providing written consent.

### B. Data acquisition

Area bone mineral density (BMD) of L1-L4 levels was measured by the dual-energy X-ray absorptiometry (DXA).

MR imaging was performed at 1.5T (Intera NT, Philips, Best, Netherlands). Sagittal T1-weighted (TR/TE, 450/11 ms; 4 mm thick) of the lumbar spine were obtained. Dynamic contrast enhancement MRI (DCE-MRI) data were acquired in the mid-lumbar sagittal plane. Dynamic MR imaging was performed using a short T1-weighted gradient-echo sequence

*Research supported by the National Natural Science Foundation of China under Grant NSFC 81000647 and Basic Research Foundation (Outstanding Young Investigator Track) from Shenzhen Science, Industry, Trade & Information Commission under Grant JC201005260124A.

Heather T. Ma and Haiyan Lv are with the Department of Electronic & Information Engineering, Harbin Institute of Technology Shenzhen Graduate School, Shenzhen, China. (Corresponding author: Heather T. Ma. Phone: +86-755-26033608; fax: +86-755-26033608; e-mail: tma@hitsz.edu.cn).

James F. Griffith, Alvin FW Li, David KW Yeung, and Jing Yuan are with the Department of Diagnostic Radiology and Organ Imaging, The Chinese University of Hong Kong, Hong Kong, China.

Jason Leung and Ping-Chung Leung are with the Jockey Club Centre for Osteoporosis Care and Control, The Chinese University of Hong Kong, Hong Kong, China

(2.7/0/95; prepulse inversion time, 400 ms; flip angle, 15°). 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 bolus of gadoteric acid (Dotarem, Guer-Guerbet, Aulnay, France) at a concentration of 0.15 mmol per kilogram body weight was injected via a power injector (Spectris; Medrad, Indianola, Pa) at a rate of 2.5 mL/s through a 20-gauge antecubitial vein intravenous catheter (Angiocath; Infusion Therapy Systems, Sandy, Utah). Injection was followed by a 20-mL saline flush. Dynamic MR imaging started at the same time as contrast medium injection started ("time zero" or $T_0$).

### C. Data processing

Region of interest (ROI) was drawn manually on the T1-weighted MRI image, which was co-registered to the DCE images, to obtain the characteristic signal. The ROI was drawn encompassing the cancellous bone of vertebral body for L1-L4 levels (as shown in Fig.1). Signal intensity within the ROI was averaged to generate a time-signal intensity curve for each ROI, which was saved for off-line analysis.

DCE-MRI data was analyzed by semi-quantitative method and a pharmacokinetic model [10,11], respectively. $S_{max}$ was extracted from the raw characteristic perfusion signal, representing the maximum enhancement of the signal compared to the baseline (shown in Fig.2). The employed pharmacokinetic model is as follows:

$$\frac{S(t)}{S_0} = 1 + A\frac{k_{ep}\left(e^{-k_{ep}t} - e^{-k_{el}t}\right)}{k_{el} - k_{ep}}. \quad (1)$$

where $S_0$ is the baseline signal intensity before contrast injection; $S(t)$ is the signal intensity change with time after contrast injection; A is the amplitude of contrast uptake; $k_{ep}$ is the rate constant for contrast extraction from interstitial space into the plasma; $k_{el}$ is the eliminating rate constant of the contrast from the body. Quantitative perfusion parameters were obtained by fitting the original signal from $T_0$ to the end by the model using the least square method (shown in Fig.2).

In total, fifty six ROIs were analyzed. Analysis of variance method (ANOVA) was employed to evaluate differences in parameters among levels. Pearson correlation was performed to investigate linear relationship between variables. Statistical analysis was performed using statistical software (SPSS 16.0).

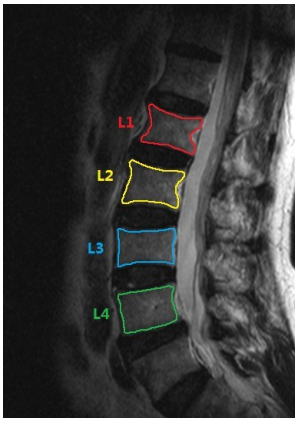


Fig. 1 ROI drawn in T1-weighted MR image in sagittal plane

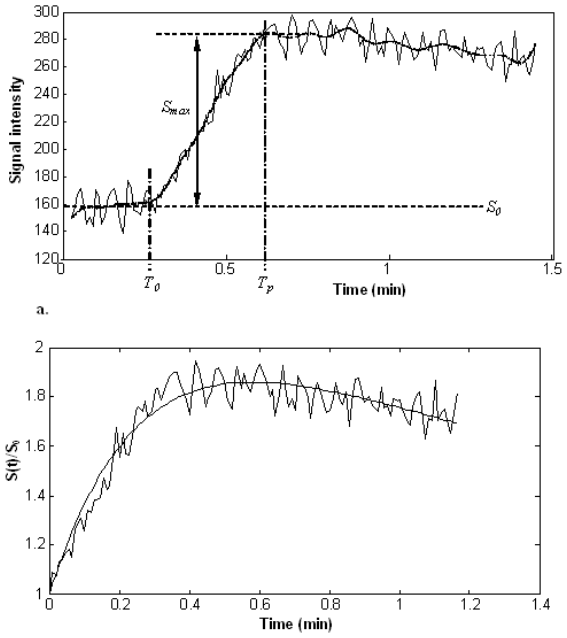


Fig. 2 Data processing on DCE data. (a) Filtering intensity signal and detecting characteristic points. (b) Curve fitting by pharmacokinetic model. The solid and smooth line is the fitting result.

A $p$ value of less than 0.05 was considered statistically significant.

## III. Results

For perfusion quantification, parameters $S_{max}$ and $A*k_{ep}$ were chosen to indicate the perfusion blood volume and permeability surface area product per unit volume of vasculature. ANOVA analysis results are summarized in Table 1. The three investigated parameters showed statistically non-significant difference among vertebral levels. However a gradually increasing or decreasing trend from upper to lower lumbar levels was observed for BMD and perfusion parameters respectively. In other words, the lower lumbar vertebrae has higher BMD while lower bone perfusion. These changing trends can be better reflected by Fig.3.

TABLE 1 ANOVA Analysis Results

| Param | Level | N | Mean | Std | p-value |
|---|---|---|---|---|---|
| BMD | L1 | 14 | 0.79 | 0.19 | 0.756 |
| | L2 | 14 | 0.84 | 0.21 | |
| | L3 | 14 | 0.85 | 0.22 | |
| | L4 | 14 | 0.88 | 0.23 | |
| $S_{max}$ | L1 | 14 | 0.34 | 0.12 | 0.059 |
| | L2 | 14 | 0.30 | 0.12 | |
| | L3 | 14 | 0.26 | 0.11 | |
| | L4 | 14 | 0.22 | 0.09 | |
| $A*K_{ep}$ | L1 | 14 | 1.18 | 0.38 | 0.085 |
| | L2 | 14 | 1.02 | 0.42 | |
| | L3 | 14 | 0.86 | 0.47 | |
| | L4 | 14 | 0.79 | 0.45 | |

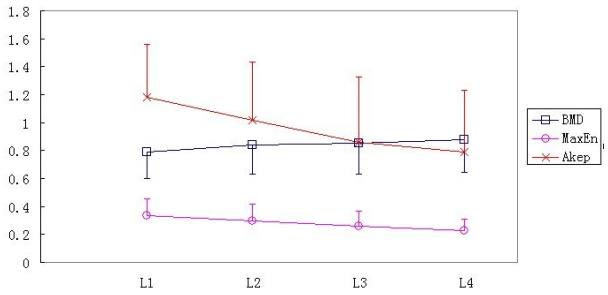

Fig.3 BMD and perfusion parameter changes along the lumbar spine (the error bar indicates the standard deviation).

Figure 3 reflects a good linear relationship between the three investigated parameters and the vertebral levels. Pearson correlation showed that perfusion parameters had statistically significant correlation with vertebral level while BMD showed non-significant correlation, which could be caused by relatively large standard deviation. The correlation coefficients were listed in Table 2.

TABLE 2 CORRELATION ALONG VERTEBRAL LEVELS

| Param | Correlation Coefficient | P-value |
|---|---|---|
| BMD | 0.145 | 0.288 |
| $S_{max}$ | -0.363 | 0.006 |
| $A*K_{ep}$ | -0.339 | 0.011 |

## IV. DISCUSSIONS

Perfusion function measured by DCE MRI is increasingly being employed to the study of bone marrow. Therefore, knowledge of variations in normal marrow contrast profiles is important. DCE MRI can provide a direct measurement of tissue perfusion in a living system, which can reflect the blood supply in a microenvironment. Previous study showed significant differences in perfusion parameters between upper and lower lumbar spine segments [9] but the comparison was not performed level by level. Our study showed a gradually decreasing trend along the lumbar spine although the difference among L1-L4 levels were not statistically significant. As bone perfusion varies for different vertebral level, same vertebral body should be investigated in cases of repeated measurements, therapy monitoring, and comparison among different studies.

Previous studies reported higher BMD [8] and lower perfusion [9] in lower lumbar vertebra. Current study basically confirmed their observations. Further we investigated both perfusion and BMD on the same group of subjects. As bone mineral content is adapted to the mechanical loading on the bone, it is expected that the lower lumbar vertebral bodies have higher BMD since they sustain more body weight.

Bone marrow perfusion under the DCE-MRI measurement is dependent on multiple factors, such as tissue blood flow, capillary capacitance and permeability, interstitial diffusion, interstitial space volume and venous return [5,12]. In Savvopoulou's study [9], the BMD was not measured and compared among different lumbar vertebra so the reduced bone perfusion in lower vertebral level cannot be well explained. In the current investigation we found an inverse trend for BMD change along the lumbar spine when compared to bone perfusion parameters. The denser mineral content in the bone could result in a reduced interstitial space volume, which can cause a decrease perfusion function.

However, the correlation of the vertebral level with BMD is not as significant as that with perfusion parameters. Other factors are possibly varied along the lumbar spine levels, such as the percentage of yellow marrow content, which was found an impact factor for bone perfusion in our previous studies [2]. This needs further investigation to be verified.

A limitation of the current study is the sample size. In order to minimize other factors influence (e.g. gender and disease), only 14 male subjects were included in current study. The standard deviations of the three investigated parameters were relatively large compared to their means. This could influence the statistical analysis results. As this is an on-going research, more reliable results will be provided later.

As a conclusion, our results confirmed previous findings in other studies and provided further details on perfusion and BMD changes along lumbar spine. Further investigation is still needed to provide more evidence on the perfusion change physiology.

## ACKNOWLEDGMENT

This study is supported by the National Natural Science Foundation of China (81000647) and Basic Research Foundation (Outstanding Young Investigator Track) from Shenzhen Science, Industry, Trade & Information Commission (JC201005260124A).

## REFERENCES

[1] Y. Jiang, J. Zhao, P. Augat, X. Ouyang, Y. Lu, S. Majumdar, H.K. Genant, Trabecular bone mineral and calculated structure of human bone specimens scanned by peripheral quantitative computed tomography: relation to biomechanical properties, *J Bone Miner Res.*, vol. 13, no. 11, pp. 1783-1790, Nov 1998.

[2] J. F. Griffith, D. K. Yeung, G. E. Antonio, et al. Vertebral bone mineral density, marrow perfusion, and fat content in healthy men and men with osteoporosis: dynamic contrast-enhanced MR imaging and MR spectroscopy. *Radiology.*, vol. 236, pp. 945-951, 2005.

[3] A. Biffar, G. P. Schmidt, S. Sourbron, M. D'Anastasi, O. Dietrich,M. Notohamiprodjo, M. F. Reiser, A. Baur-Melnyk., Quantitative analysis of vertebral bone marrow perfusion using dynamic contrast-enhanced MRI: initial results in osteoporotic patients with acute vertebral fracture, *J Magn Reson Imaging.*, vol. 33, no. 3, pp. 676-683, Mar 2011.

[4] Y. F. Zhang, Y. X. Wang, J. F. Griffith, W. K. Kwong, H. T. Ma, L. Qin, T. C. Kwok, Proximal femur bone marrow blood perfusion indices are reduced in hypertensive rats: a dynamic contrast-enhanced MRI study, *J Magn Reson Imaging.*, vol. 30, no. 5, pp. 1139-1144, Nov 2009.

[5] P. S. Tofts. Modeling tracer kinetics in dynamic Gd-DTPA MR imaging. *J Magn Reson Imaging.*, vol. 7, pp. 91-101, 1997.

[6] R. Luypaert, S. Boujraf, S. Sourbron, M. Osteaux, Diffusion and perfusion MRI: basic physics. *Eur J Radiol.*, vol. 38, pp. 19-27, 2001.
[7] T. T. Shih, H. C. Liu, C. J. Chang, S. Y. Wei, L. C. Shen, P. C. Yang. Correlation of MR lumbar spine bone marrow perfusion with bone mineral density in female subjects. *Radiology.*, vol. 233, pp. 121-128, 2004.
[8] N. Yoganandan, F. A. Pintar, B. D. Stemper, J. L. Baisden, R. Aktay, B. S. Shender, G. Paskoff, P. Laud, Trabecular bone density of male human cervical and lumbar vertebrae, *Bone.*, vol. 39, no. 2, pp. 336-344, Aug 2006.
[9] V. Savvopoulou, T. G. Maris, L. Vlahos, L. A. Moulopoulos, Differences in perfusion parameters between upper and lower lumbar vertebral segments with dynamic contrast-enhanced MRI (DCE MRI), *Eur Radiol.*, vol. 18, no. 9, pp. 1876-1883, Sep 2008.
[10] U. Hoffmann, G. Brix, M. V. Knopp, T. Hess, W. J. Lorenz. Pharmacokinetic mapping of the breast: a new method for dynamic MR mammography. *Magn Reson Med*., vol. 33, pp. 506-514, 1995.
[11] H. T. Ma, J. F. Griffith, D. K. Yeung, P. C. Leung, Modified Brix Model Analysis of Bone Perfusion in Subjects of Varying Bone Mineral Density, *J Magn Reson Imaging*., vol. 31, no. 5, pp. 1169-1175, May 2010.
[12] R. Luypaert, S. Boujraf, S. Sourbron, M. Osteaux. Diffusion and perfusion MRI: basic physics. *Eur J Radiol,* vol. 38, pp. 19-27, 2001.