

Original article

# Decrease with aging of the microcirculatory function of the lumbar vertebral marrow preceding the loss of bone material density and the onset of intervertebral discal degeneration: A study about the potential cause

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## Abstract

**Objective:** Using a dynamic computed tomographic perfusion (CTP) imaging method to explore the age-related distribution of the microcirculation perfusion function in the vertebral marrow, the bone material density (BMD), and the intervertebral discal degeneration (IDD). Further, to discuss a possible causation relationship between them.

**Methods:** One hundred and eighty-six people were randomly enrolled by stratified sampling and grouped by age:  $\leq 15$ , 16–25, 26–35, 36–45, 46–55, 56–65, 66–75, and  $\geq 76$  years old. The average CTP and BMD of the third and fourth lumbar vertebrae marrow were measured and the IDD incidence of the third-fourth vertebrae was assessed. The temporal–spatial distribution patterns of the age-related changes of the CTP, BMD, and IDD were described, and the correlations between them were calculated.

**Results:** The microcirculatory perfusion function of the vertebral marrow develops to maturity by 25 years and is maintained until age 35, then declines with aging. The BMD grew to a peak from 26 to 45 years old, then decreased yearly. The IDD showed a sudden increase after 45 years of age. The CTP [BF ( $r = 0.806$ ,  $P = 0.000$ ), BV ( $r = 0.685$ ,  $P = 0.005$ ) and PMB ( $r = 0.619$ ,  $P = 0.001$ )] showed strong positive correlations and CTP [TTP ( $r = -0.211$ ,  $P = 0.322$ ) and MTT ( $r = -0.598$ ,  $P = 0.002$ )] showed negative correlations with BMD. The CTP [BF ( $r = -0.815$ ,  $P = 0.000$ ), BV ( $r = -0.753$ ,  $P = 0.000$ ) and PMB ( $r = -0.690$ ,  $P = 0.000$ )] had strong negative correlations, and CTP [TTP ( $r = 0.323$ ,  $P = 0.126$ ) and MTT ( $r = 0.628$ ,  $P = 0.001$ )] had positive correlations with the incidence of IDD.

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**Conclusion:** The decrease with aging of the microcirculatory perfusion in the lumbar vertebral marrow preceded, and is a potential causative factor for the loss of BMD and the onset of IDD.

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**Keywords:** Lumbar spinal degeneration; Microcirculatory function; Hemodynamics; CT perfusion (CTP)

## Introduction

Currently the therapeutic emphasis in the field of lower back pain associated with lumbar vertebral degeneration is placed on disc surgery<sup>1,2</sup> and lumbar fusion.<sup>3,4</sup> Discal degenerative disease (DDD) and subsequent degenerative spondylosis associated unsteadiness is the downstream problem. Identifying the origin of DDD could be potentially helpful for preventing and/or relieving the disease. It has been suggested in previous studies that reduced blood supply to the vertebrae marrow is correlated with the increased incidence of intervertebral discal degenerative disease (IDD),<sup>5</sup> and loss of vertebral bone material density (BMD).<sup>6</sup> However, these studies achieved a “correlation” rather than proof of a causative relationship. This study aims to investigate the temporal–spatial distribution of the microcirculation of the vertebrae marrow, vertebral BMD and IDD in different age groups by an observational hemodynamics study using the computer tomography perfusion (CTP) technique. We expect to disclose the causation between circulation and pathology.

## Materials and methods

### *Patients*

The volunteer subjects enrolled in this study came from the medical examination center of the Southeast Hospital (Clinical School of the Medical College, Xiamen University) from January, 2011 to December, 2013. The exclusion criteria included: body height/weight ratio is more than 20% or less than 10% of normal reference standard, spinal development malformation, any history of spinal surgeries, any history of traumatic spinal fracture, and any disease (for e.g., metabolic disease, renal inadequacy, cardiac insufficiency, connective tissue disorder) or tumor that could potentially affect the spinal homogeneity and influence the results.

All subjects were enrolled by stratified sampling, and were divided into eight subgroups by age:  $\leq 15$ , 16–25, 26–35, 36–45, 46–55, 56–65, 66–75, and  $\geq 76$  years old. Each group was to be a set of 24

randomly selected subjects with an equal number of men and women. In actuality, the subgroup  $\leq 15$  years old did not enlisted volunteers from 1 to 9 years of age and was composed of only 18 subjects (9 males and 9 females) from 10 to 15 years old. At the final evaluation there were a total of 186 subjects.

The hospital ethics committee approved the study, and informed consents were obtained from the subjects in the study.

### *Computed tomographic examinations*

Many previous studies had used magnetic resonance tomography perfusion (MRP), mainly due to its being free of X-ray radiation. However, MRP, whether with contrast enhancement or arterial spin label (ASL) methods, has shortcomings. These include unsatisfactory acquisition speed and temporal and spatial resolution, magnetic insensitive to skeleton because of rare hydrogen protein in bone mine material, lower accuracy and reproducibility due to fluctuations of the magnetic field, inflow effect, and nephrogenic systemic fibrosis from Gadolinium-based contrast agents.<sup>7</sup> As opposed to the MRI, the advantages of computed tomography (CT) are its lower cost, excellent availability in the speed of acquisition and the temporal and spatial resolution. In addition, CTP allows the acquisition of successive multiple phases and provides functional information to better analyze bone and soft tissue. The functional analysis is more reproducible than that of MRI. The development of multidetector CT and recent technological advances reduce the radiation dose from examination that the patient is exposed to. The best example is the recent appearance of iterative reconstructions that reduces the dose by half with an equivalent image quality.<sup>8</sup> With these technological innovations and better control of the optimization of the acquisition parameters, it is now possible to obtain CT imaging with a dose almost equal to that of the standard X-ray assessment. In this study an advanced CT dose optimization and reduction scheme were used.<sup>9</sup>

We selected the third and fourth lumbar vertebral bodies as the region of interest (ROI) due to the

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