Rapid increase of marrow fat content and decrease of marrow perfusion in females underwent bilateral oophorectomy: An magnetic resonance based longitudinal study of lumbar vertebra

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INTRODUCTION: Bone structure and quality are dependent on bone blood flow, cellular metabolism and structural matrix. Both men and women experience an increase in marrow fat content and a decrease in bone marrow perfusion as bone mineral density (BMD) decreased and osteoporosis develops. It is known that bilateral oophorectomy causes systemically reduced BMD [1, 2]. The temporal relationship between reduced BMD and reduced marrow perfusion, and increased bone marrow fat, and how quickly these change take place after female sex hormone depletion, however, remain unknown. Using MR spectroscopy (MRS) and dynamic contrast enhanced (DCE) MRI techniques, we undertook this longitudinal patient study to investigate the temporal relationship between BMD, marrow fat content and bone marrow perfusion in females underwent bilateral oophorectomy.

MATERIALS AND METHODS: In total there were six female patients with a mean age of 49.5 yrs (range: 45-54 yrs). All the patients had menorrhagia, with uterine fibroid in five cases and adenomyosis in another case. Hysterectomy plus bilateral salpingo-oophorectomy were carried out in all cases, and all the patients had uneventful recovery following the surgery. All the six patients had BMD measurement and MRS measurement at baseline and three months post surgery; while five patients completed DCE MRI measurement at baseline and three months post surgery. At nine months post surgery, five patients completed BMD measurement and MRS measurement, while four patients completed DCE MRI measurement. At 21 months post surgery, four patients completed MRS measurement, three patients completed BMD measurement and two patients completed DCE MRI measurement.

For BMD measurement, L3 vertebra trabecular BMD was measured using a clinical multi-detector CT scanner. QCT Torso Phantom (Image Analysis Inc, Columbia, USA) was used as the external reference. QCT 5000^{TM} Bone densitometry software (Image Analysis Inc.) was used for calculating BMD values. MRI was performed on a 3 Tesla clinical MR imaging system (Philips, Best, The Netherlands). A surface coil was placed under the lumbar spine region as the radiofrequency receiver and the body volume coil was used as the radiofrequency transmitter. Sagittal images of lumbar spine were obtained to exclude spine disease such as fracture or metastasis, and to guide positioning of a volume of interest within the L3 vertebral body for use at ^{1}H MR spectroscopy as well as DCE MRI. The width **(w)**, depth **(d)**, and height **(h)** of the L3 vertebral body were measured on MR images to define a volume of interest. A volume of interest with dimensions $\mathbf{w}/2 \cdot \mathbf{d}/2 \cdot \mathbf{h}/2$ cm^3 was located centrally in the vertebral body. After local shimming and gradient adjustments were performed, data were acquired at a spectral bandwidth of 1000 Hz and with 512 data points, and 64 non–water suppressed signals were obtained by using a point-resolved MR spectroscopic sequence (TR/TE=3000/25). MR spectroscopic data were analyzed at an off-line computer (Precision 650 Workstation; Dell, Austin, Tex). Water (4.65 ppm) and lipid (1.3 ppm) peak amplitudes were measured to determine vertebral marrow fat fraction (FF), which was defined as the relative fat signal amplitude in terms of a percentage of total signal amplitude (water and fat) and calculated according to the following equation: fat content = $[\mathbf{I}_{fat}/(\mathbf{I}_{fat} + \mathbf{I}_{wat})] \cdot 100$, where $\mathbf{I}_{fat}$ and $\mathbf{I}_{wat}$ are the peak amplitudes of fat and water, respectively. No correction for relaxation losses was applied. For DCE MRI, after obtaining an axial T1-weighted image of L3 vertebra. A dynamic short T1-weighted gradient echo sequence single slice MR series was obtained in the axial plane using the following parameters: TR=4.2 msec, TE=2.3 msec, flip angle=12,slice thickness=10 mm, matrix = 300×74, in-plane resolutio=1.00mm×2.03 mm, NEX=1. Temporal resolution was approximately 0.9 second/ acquisition. A bolus of gadoteric acid (Dotarem; Guerbet, Roissy, France) at a concentration of 0.6 mmol per kg body weight was injected at a rate of 2.5 mL/sec with an MR injection system (Spectris, Medrad, Pittsburgh, PA) through a 21G intravenous catheter inserted into an antecubital vein. The injection was followed by a 20-mL saline flush. Dynamic MRI started after the first 50 image acquisitions Dynamic MRI images were processed on a workstation (Viewforum, Philips Medical System, Best, The Netherlands). Regions-of-interest (ROIs) was drawn over the cancellous part of the L3 vertebra. Signal enhancement over time was recorded, and plotted as a time-signal intensity curve. From this time-signal intensity curve, two MR perfusion indices were analyzed, namely, maximum enhancement (E^{max}) and enhancement slope (E^{slope}), both of them relating to the first rapidly rising part of the curve. Maximum enhancement was defined as the maximum percentage increase of signal intensity from baseline. Enhancement slope was defined as the rate of enhancement between 10% and 90% of the maximum signal intensity difference between maximum signal intensity (I_{max}) and baseline signal intensity (I_{base}) [1]

RESULTS: Due to the small sample size of this study, statistical analysis was not carried out, instead, results are presented descriptively in this report. There was no spine fracture or metastasis or other spine diseases in the patients. The longitudinal results of BMD, FF, E^{max}, and E^{slope} results are show in table 1. The results showed reduced BMD, increased marrow FF, and reduced bone marrow perfusion occurred in synchrony. There was a sharp decrease of BMD, a sharp increase of marrow FF, and a sharp decrease of E^{max}, and E^{slope} during the initial 3 months post bilateral oophorectomy. BMD and marrow perfusion continues to decrease, and marrow FF continues to increase, though at a slower rate, during the later follow-up period.

Table 1. Bone mineral density (BMD), marrow fat fraction, and marrow maximum enhancement (E^{max}) and enhancement slope (E^{slope}) changes after bilateral oophorectomy.

	change between 0-3 months	change between 3-9 months	change between 9-21 months
BMD	- 12.0±6.9% (n=6)	- 4.0±3.6% (n=5)	- 2.9±4.9% (n=3)
Fat fraction	92.2±46.3% (n=6)	28.8±23.3% (n=5)	14.1±16.6% (n=4)
E^{max}	- 23.0 ±3.9 % (n=5)	- 12.4 ±5.9% (n=4)	- 19.7±2.3 % (n=2)
E^{slope}	- 44.9±7.7% (n=5)	- 22.3±10.2% (n=4)	- 29.4±0.6% (n=2)

DISCUSSION: this is the first study investigated longitudinal changes in BMD, marrow fat fraction, and marrow perfusion in lumbar spine in human subjects. Our results demonstrated a sharp increase of marrow fat fraction and a rapid bone marrow perfusion decrease during the initial 3 months post bilateral oophorectomy. BMD and bone marrow perfusion continues to decrease, and bone marrow fat content continues to increase, though at a slower rate, during the later follow-up period of 21 months.

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References: 1. *Griffith JF, et al. Radiology. 2010;254:739-46. 2. Wang YX, et al. J Magn Reson Imaging 2008; 28:1515-1518*