Introduction: Recent clinical study has shown that vertebral marrow blood perfusion is significantly decreased in the osteoporotic subjects compared with those of the osteopenic subjects and normal bone density subjects, as demonstrated by MRI derived parameters of maximum contrast enhancement and contrast enhancement slope (1). In the current study we set out to investigate whether it was possible to repeat the clinical observations in the classic osteoporosis model of rat ovariectomy (OVX) with dynamic contrast enhanced MRI.

Materials and Methods: Eight female Sprague-Dawley rats of seven months old were used in this study (four for OVX and four as controls). These animals were housed 2-3 animal per stainless steel cage at 22°C temperature and with a 12-h light and 12-h dark cycle, and received a standard rat chow and water ad libitum. For MRI, studies were performed on a 1.5-T clinical whole-body imaging system (Philips Medical Systems) with a maximum gradient strength of 30 mT/m. Rats were anaesthetized, and the tail vein cannulated with a heparinised catheter. A surface Coil-(Micro 4.7) was put under the rat lumbar spine region as the radio frequency receiver and the body volume coil was used as the radio frequency transmitter. A sagittal plane through mid section of the lumbar spine was prescribed (Fig1). For dynamic scan, the MR parameters were as follow: short T1-weighted gradient echo sequence, TR=4 msec, TE=1.4 msec, Flip angle 15, slice thickness=5mm, Average=1, matrix =128*51. MRI contrast agent was Gd-DOTA, a dose of 0.3mmol/kg (0.15 ml for a 250 gram rat) was injected after initial baseline 60 seconds (Viewforum; Philips Medical System). Region of interest (ROI) was drawn over lumbar vertebra bodies.

Dynamic MRI images were processed in the radiologic workstation (Viewforum; Philips Medical System). Region of interest (ROI) was drawn over lumbar vertebra L6-L2 and the vertebra cortex was excluded in ROIs, the signal change over time was recorded (Fig 2). Two perfusion indexes of the time–signal intensity curve were measured—namely, maximum enhancement and enhancement slope. Maximum enhancement, or ME, was defined as the maximum percentage increase in signal intensity from baseline (Ibase). Enhancement slope, or ES, was defined as the rate of enhancement between 10% and 90% of the maximum signal intensity difference between maximum signal intensity (Imax) and Ibase. Both indexes are derived from the first-pass phase of signal intensity enhancement and are considered to represent arrival of contrast agent material into the arteries and capillaries and its diffusion into the extracellular space.

CT assessment of bone mineral density and MRI assessment of blood perfusion were performed at baseline prior to surgery and 4 weeks post OVX. The experimental protocol was approved by the local Animal Experiment Ethics Committee.

Results: Despite the small animal number, the following results were shown four weeks post ovariectomy.

1) OVX rats increased body weight by 18% (significant compared with baseline and with the control animals, both P<0.05) while that of the control animals remains consistent.
2) OVX rats decreased vertebral BMD by 7.7% (significant vs control, P<0.05)
3) OVX rats decreased MRI maximum enhancement by 25.6% (significant vs control, P<0.05 and vs baseline P<0.01)
4) OVX rats decreased MRI enhancement slope by 39% (significant vs control, P<0.01 and vs baseline P<0.001)

Discussion: This pilot study demonstrated it is possible to repeat the clinical observations that decease of vertebra bone mineral density is associated with decease of vertebra blood perfusion in the classic rat osteoporosis model of OVX with dynamic contrast enhanced MRI. That MRI can non-invasively detect blood flow changes of rat spine in vivo opened a new field for research. Further studies are being carried out in our laboratories to further validate our findings, to use pharmacokinetic modeling to qualify blood flow and vessel permeability in the rat vertebra (2), and to observe pharmaceutical and diet intervention on rat spine bone mineral density and blood perfusion.

References:

Decease of vertebra bone mineral density is associated with decease of vertebra blood perfusion: dynamic contrast enhanced MRI study in rat ovariectomy model

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