Analysis Of Signal-to-noise Ratio On Cortical Bone Of The Ovariectomized Rats At Primary Stage By Using MRI With Swift Technique

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Introduction: Osteoporosis is a skeletal disorder characterized by compromised bone density and quality and an increased fracture risk. Bone quality is affected by bone architecture, turnover, accumulated damage, and mineralization (1). Estrogen replacement therapy reportedly increases the collagen content in bone as well as physiologic collagen cross-linking; previous studies suggest that the deteriorated bone quality associated with decreased estrogen levels causes bone fragility (2). Postmenopausal osteoporosis is the most common form of osteoporosis, and early diagnosis and treatment may prevent the increased risks of bone fracture and death, as well as QOL deterioration. Previous studies have focused on developing methods to assess bone quality. In recent years, Sweep Imaging with Fourier Transform (SWIFT) (3, 4) has been used to image tissues with an extremely short T2 relaxation time such as bone. In the SWIFT technique, the TE is able to be set to nearly 0, and excitation and signal acquisition are performed simultaneously; this enables signal detection and imaging of tissues with extremely short T2 relaxation times (3). The purpose of this study was to analyze the signal by conducting MRI using the SWIFT technique and to predict the water content changes within the tibial cortical bone of an ovariectomized (OVX) rat during the early postoperative period.

Methods: Twelve-week-old female Sprague-Dawley (SD) rats (N = 64) were used. The rats were housed in our institution’s animal facility in accordance with guidelines in the Guide for the Care and Use of Laboratory Animals published by the National Institutes of Health. The rats were randomized into sham or OVX experimental groups. This study was approved by our institutional review board for animal experiments. The subjects were killed using intraperitoneal sodium pentobarbital at 2, 4, 8, and 12 weeks postoperatively. The tibias were extracted. Imaging was performed with a high magnetic field MRI unit for animal experiments (Varian MRI system 7.04 Tesla [T], Agilent Technologies Inc., Palo Alto, California, USA) and a transmit/receive surface coil (3 × 3 cm diameter). The tibias were imaged using the SWIFT technique and the proton density weighted image (PDWI). Six regions of interest (ROIs), including all areas of the cortical bone, were set in the cortical bone in the proximal one-third of the tibial cortical bone with the same transected image. The signal intensity (SI) in ROIs was measured and averaged. The signal-to-noise ratio (SNR), defined as the ratio between the mean SI to the background noise standard deviation, was calculated (5). The tibial BMD was measured using DEXA (DCS-600EX-ⅢR, Aloka Co., Ltd., Tokyo, Japan). The tibial cortical BMD was measured using μCT (micro focus 2D/3D, ScanXmate-E090S40, Comscantecno Co., Ltd., Kanagawa, Japan). Tetracycline hydrochloride was administered dorsal subcutaneously immediately preoperatively to distinguish the new cortical bone
area. Forty specimens that were not decalcified were randomly selected at 2, 4, 8, and 12 weeks postoperatively. The specimens were stained with Villanueva bone stain and prepared at a location identical to that using MRI. The cortical bone histomorphometric characteristics were measured as follows: porosity area (Po. Ar), cortical area (Ct. Ar), and new bone area (New B. Ar). Measurements were expressed as the mean ± standard deviation. Two-way analysis of variance (ANOVA) and the Pearson correlation test were used. P < 0.05 was considered statistically significant.

**Results:** The cortical bone SNR was not significant by PDWI and was significantly higher in the OVX group than in the sham group at 8 and 12 weeks postoperatively by SWIFT (P < 0.05) (Fig. 1). The tibial BMD was lower in the OVX group than in the sham group at all points evaluated (P < 0.001) (Fig. 2a). The Cortical BMD was lower in the OVX than in the sham group at all points evaluated (Fig. 2b). The cortical BMD was correlated significantly with the SNRs at SWIFT (P = 0.037), but the relationship was weak and had a positive correlation coefficient (R2 = 0.066) (Fig. 2c). Po. Ar/Ct. Ar was larger in the OVX group than in the sham group at all weeks postoperatively and decreased in a time-dependent manner in both groups (P < 0.001) (Fig. 3a). New B. Ar/Ct. Ar was significantly smaller in OVX specimens than in sham specimens at 8 and 12 weeks postoperatively (P < 0.05) (Fig. 3b). New B. Ar/Ct. Ar correlated significantly with SNRs at SWIFT (P < 0.001), and the relationship was strong with a positive correlation coefficient (R2 = 0.430) (Fig. 3c).

**Discussion:** The cortical bone signals obtained using PDWI detected mainly water signals with a millisecond T2 component. However, the absence of any significant difference suggested that the changes were not considerable. The SNR findings based on the SWIFT technique suggested that it was mostly bound water that increased, particularly at 8 and 12 weeks postoperatively. The increased porosity area in OVX rats also supports an increase in cortical bone water content. However, porosity area decreased with time in both sham and OVX rats. The SNR using the SWIFT technique increased with time while porosity area decreased gradually, suggesting that bound water mainly increased. The cortical BMD exhibited only a weak positive correlation with the cortical bone SNR using the SWIFT technique; therefore, it determined using SWIFT may reflect bone quality that cannot be assessed using BMD alone. New bone is believed to have high water content. The positive correlation between the new bone area and the cortical bone SNR detected using SWIFT potentially indicates that in OVX rats, the early postoperative period is primarily characterized by increased bound water. In conclusion, this study revealed an increased SNR in the tibial cortical bone in OVX rats during the early postoperative period detected by MRI using the SWIFT technique. This may reflect a possible increase of bound water in the cortical bone and qualitative changes within the cortical bone in OVX rats. In OVX rats, MRI using the SWIFT technique may depict early changes in cortical bone quality.

**Significance:** In clinical practice, it is probably to be able to evaluate osteoporosis at primary stage non-invasively using MRI with SWIFT method.
(a) sham-PDWI
--- OVX-PDWI

(b) sham-SWIFT
--- OVX-SWIFT

SNR

Time after surgery (wks.)

a: $P < 0.001$, b: $P < 0.01$, and c: $P < 0.05$
vs. the sham group

**Fig. 1**

(a) sham
--- OVX

(b) sham
--- OVX

(c) $R^2 = 0.066$

**Fig. 2**

BMD (mg/cm$^2$)

Cortical BMD (mg/cm$^2$)

Cortical BMD (mg/cm$^2$)

Time after surgery (wks.)

SNR
Fig. 3

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a: $P < 0.001$, b: $P < 0.01$, and c: $P < 0.05$ vs. the sham group