INTRODUCTION:
The delayed repair mechanism in osteoporotic bone is poorly understood. The development of transgenic mice provides a powerful tool to investigate the functional role of the specific genes involved in bone repair. Previously published models of osteoporotic bone repair in mice have their limitations. The internal fixation model is challenged by its angular motion and the external fixation model is challenged by its decreasing holding power of the screws in osteoporotic condition. Mouse drill-hole healing model in normal bone was established by Dr. Campbell, which showed technically simple and highly reproducible, but it has not been applied in osteoporotic mice yet. The objective of this study was to develop a bone drill-hole healing model in osteoporotic mice.

METHODS:
Total 112 3-month-old female C57BL/6 mice were randomely divided into ovariectomy group (OVX) and sham-operated group (Sham). A cortical bone defect on right femur was created six weeks after OVX operation in all the mice. High resolution micro-CT (VivaCT 40, Scanco) was employed to in-vivo monitoring the repair process at day 0, 3, 7, 10, 14 and 21. Mice were sacrificed at each time point (n=8 at day 0, 3, 7, 10, 14 and n=16 at day 21). Mice callus and sera samples were collected for histology, mRNA expression, and mechanical testing.

RESULTS SECTION:
H&E staining showed that there were less granulation tissues at early stage, less woven bone and mineralized trabecular at middle stage and less organized cortical at late stage in OVX mice compared to Sham mice (Figure 1). In vivo microCT measurement showed OVX and Sham groups differed significantly in the pattern of the change in the bone volume over time in both defect region and intra-medulla space (P<0.05 for the interaction between time and group by the repeat measure ANOVA) (Figure 2). Bone formation marker P1NP was increased from baseline followed by a peak at day 10 and return back to baseline at day 21 in Sham mice. The profile was shifted right in OVX mice. Bone resorption marker CTX share the similar pattern to PINP. Estrogen receptor alpha (ER alpha) expression was higher in Sham mice compared to OVX mice while estrogen receptor beta (ER beta) expression was lower in Sham mice compare to OVX mice. Sham mice showed significant higher ultimate load and energy to failure compared to the OVX mice at day 21 (Figure 3).

DISCUSSION:
Bone drill-hole healing model is a simple way for investigating mice bone repair. Bone repair pattern in OVX-induced osteoporotic mice was altered, the altered ER alpha and ER beta expression may contribute to its underlying mechanism.

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REFERENCES: