INTRODUCTION: Osteoporotic fracture fractures and stress fractures are thought to be attributed to the acculsion and coalescence of bone microdamage (mdx) (1, 2). These fractures are usually prevented by bone remodeling processes that are targeted to areas of mdx (3, 4). Osteocyte apoptosis that occurs in areas of damaged bone may act as a localizing signal for osteoclastic resorption and subsequent repair (5, 6). Factors affecting how and where this mdx accumulates and is repaired include age, sex, load strain-mode (compression, tension, shear), and the amount of previous strain-mode-specific adaptation (7-9). Hormones such as estrogen (est.) also play a significant role by regulating apoptosis of osteocytes, osteoblasts, and osteoclasts (10, 11). To better understand the events that proceed fragility fractures and the impact of est. on this process, we utilized the ral varexotomicy (ovx) fatigue loading model (12) to test the hypothesis that the lack of est. would lead to a higher amount of mdx accumulation following a single bout of fatigue loading and 18 days of healing time. In addition, we hypothesized that there would be stronger strain-mode correlations with specific mdx types in est. deficient animals due to less repair of fatigue damage.

RESULTS: Fig. 2 highlights the results of the mdx quantification. Intra-group medial ("M") vs. lateral ("L") comparison showed a significant difference in the coarse linear mdx in the OVX-EST group with a higher crack density in the medial cortex. In the OVX group, there was a significant med./lat. difference in the DMI and DD with the lat. cortices having more mdx (see p values superimposed on bars in Fig. 2). The inter-group comparison showed that the OVX-EST group had statistically significantly more mdx in all subtypes except for coarse linear microcracks in the lat. ("L") cortex, and DMI which was higher in the OVX group (see p values above bars in Fig. 2).

DISCUSSION: Our hypothesis that there would be more mdx accumulation in est. deficient animals (consistent with clinical findings in postmenopausal women who suffer fragility fractures) was only true for the DMI. This is an interesting finding in light of previous studies including our own work showing no association between DMI and repair-directed remodeling (13, 14). Therefore it is possible that the reduction in osteoclast apoptosis by est. deficiency (11) and the increase in osteocyte apoptosis due to damage (6) and est. withdrawal (10) that early est. deficiency leads to a paradoxical increase in osteoclastic repair of damage in our 5 m.e. rats. If the rats were older and/or est. deficient for a longer period of time prior to fatigue loading (>7 days as in the present study) it is feasible that other mechanisms such as increased porosity and decreased robusticity and bone mineral density could lead to a greater mdx burden that would overwhelm repairing capacity such as seen in long term osteoporosis. It is also notable that DMI was not only larger in the est. deficient animals but there was also a significant med./lat. strain-mode difference found as well consistent with previous reports of this being a tension specific form of mdx (1, 7). These findings could mean that est. may protect against this subtle form of mdx and its accumulation in est. deficiency may lead to a continuing decline in bone tissue mechanical properties contributing to fragility fractures.


[Supported by OREF 01-024]