INTRODUCTION: The motion of intracortical fluid flow, which arises under mechanical loading, has been proposed to be an important mediator for regulating bone mass and morphology (1). Although the distribution of loading induced fluid parameters, i.e., the contributions of pressure, pressure gradient, velocity, and fluid shear stress, are not yet clear, bone fluid flow driven by loading may be necessary to explain the adaptive response of bone, which is coupled with load-induced strain magnitude or independent with matrix strain per se (2). We have previously shown that intracortical fluid flow is induced not only by bone matrix deformation, but by the intramedullary (IM) pressure generated during loading (3). These studies may only partially examine the fluid flow generated adaptive mechanism, because the loading of bone results not only in intracortical fluid flow (including the driven sources from matrix deformation and IM pressure), but also matrix strain, which makes it difficult to correlate the specific fluid components with the strain and stress in the matrix. While our previous data has demonstrated that bone fluid flow and its associated streaming potential product can be significantly influenced by the dynamic IM pressure (4), the fluid stimulus can be controlled quantitatively, the hypothesis of fluid induced bone adaptation was evaluated in an avian ulna model using IM fluid loading in the absence of bone matrix strain.

METHODS: Under the general isoflurane anesthesia, the left ulnae of total eight adult, one year old male turkeys were functionally isolated via transverse epiphysial osteotomies in loading (N=4) and sham control (N=4) groups. The metaphyses were then covered with stainless steel caps and well sealed with PMMA. Pins inserted transcutaneously through the caps and clamped with a pair of clamps prevented from internal and external mechanical loading. The bone was harvested from the sham control bone of a turkey subjected to 4 weeks of disuse. The contralateral control shows very little evidence of bone turnover (R). Disuse caused increasing of intracortical porosity (L).

RESULTS: In the animal group subject to sham disuse alone, cortex showed a significant decrease in cross sectional area, which is coupled mostly by intracortical resorption or increasing of porosity area, with reduced 6.1±4.2% compared to the area of contralateral control (Fig. 1). While bone loss was primarily through intracortical porosity and secondarily endosteal resorption, no bone resorption was identified at the periosteal surface in any animal. With IM pressure generated a spatial fluid pressure gradient distribution through the cortex, fluid loading (n=4) resulted in bone mass maintained at the middle of the cortex and endosteal surface, and resulted in new bone formation at the periosteal surface (12.2±4.2%) (Fig. 2). Interestingly, these remodeling experiments have shown nonuniform spatial distribution at endosteal and periosteal surfaces (Fig. 2). The sham control showed 4.1±3.0% of total bone loss (n=4) in porosity and surface resorption.

DISCUSSION: In the absence of matrix deformation, the adaptive response was significantly induced by fluid flow loading by means of IM hydraulic pressure. The results demonstrated that low magnitude of IM pressure could initiate a spatial fluid flow in bone and thus stimulated bone adaptive response. This suggests that oscillation of IM pressures will influence the perfusion of bone tissue in many ways. For example, IM pressure induced by circulation alone is on the order of 18 mmHg (2.38 kPa), which will provide basic nutritional supply and fluid pressure gradients to the bone. If resting or active IM pressures, (i.e., aging, bed rest and micro gravity) will influence the fluid perfusion in bone and may substantially stimulate remodeling. IM pressure loading can increase and improve this perfusion process. Moreover, it assumes that there is fluid pathway directly connected between marrow cavity and intracortical porous space, e.g., Haversian canal, lacunae-canaliculi, and even micropores, which may play a role in regulating fluid transportation and perfusion in bone. However, the mechanism that how cell respond to fluid loading, e.g., via pressure and/or fluid shear stress, is still remained unknown. Nevertheless, these experiments may yield new insights into the mechanisms, at least in the tissue level, by which bone fluid flow initiates and controls bone morphology and lead to a new strategy to control bone mass and morphology without the need for bone deformation. If bone is loaded at proper mechanical signal, i.e., magnitude and frequency, it may provide a useful treatment strategy to enhance bone mass.

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