

Skeletal muscle dynamics generated fluid flow in bone and its role in adaptation

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INTRODUCTION: Exercise such as muscle contraction appears to increase blood flow to the skeletal tissues, i.e., bone and muscle. These evidences imply that bone fluid flow induced by muscle dynamics may play an important role in regulating fluid flow through coupling of muscle and bone via microvascular system. We propose that musculo-dynamics induced by physiologic muscle contraction can significantly induce fluid flow and enhance perfusion in bone, which may act as a mediator in initiating and regulating osteonal adaptation. Using oscillatory pressurized marrow fluid flow stimuli, the physiological fluid stimulus was found to initiate new bone formation and reduce intracortical bone porosities caused by disuse, even in the absence of direct tissue strain [1]. The objectives for this work were to evaluate (a) the role of dynamic muscle contraction served as a dynamic pump in regulation of intramedullary pressure (ImP), (b) the response of cortical perfusion enhanced by dynamic muscle contraction, and (c) the in vivo adaptive response to dynamic skeletal muscle contraction adjacent to bone.

METHOD: *Experimental setting of muscle induced ImP:* An experiment with total of three 9-month old rats was performed. Rats were anesthetized using standard isoflurane inhalation. A micro cardiovascular pressure transducer was inserted through the catheter and sealed with a cap. An electronic muscle stimulator was connected to the electrodes and musculo contraction was applied to the skeletal muscle adjacent to the right femur with frequencies of 1, 2.5, 3.5, 20, 25, 35, 45 and 60 Hz with the same electrical magnitude.

Intracortical perfusion tracing: Before the animal was sacrificed, convective filtration in the intracortical capillary was evaluated using fluorescent microspheres. The histomorphometric analyses of these slides were examined using a fluorescent microscope and quantified using Osteomeasure.

In vivo study: A hind limb suspension (HLS) rat model is developed to generate interstitial fluid flow in femur via dynamic muscle contraction. HLS preparation was performed in 8 female rats, 6 months old (n=4 experimental, n=4 control). Daily fluid flow loading was administrated by a low voltage, extremely small current and battery powered electronic muscle stimulator at left femur with frequency of 10 Hz, 5 min/day, for 3 weeks.

RESULT: Skeletal muscle contraction significantly generates fluid pressure in the marrow cavity, in which low magnitude muscle contraction increased the ImP on the order of 8+/-1.4 mmHg (1 Hz), 8.7+/-0.5 mmHg (2.5 Hz), 9.3+/-4.7 mmHg (25 Hz), and 1.8+/-0.1 (45 Hz). Heart rate alone induced 2 mmHg ImP.

Muscle contraction improved short term perfusion in bone. Fluorescent tracer in the experimental bone was stained in the Haversian region and was 3x greater than the control bone, in which the number of stained Haversian canals was 127+/-44 [14.3+/-4.6 (mm²)⁻¹ for normalized to bone cross sectional area] in loaded femur and 42.3+/-5.3 in the control. The perfusion in the tibia at the loading site was also increased from 36.7+/-8.3 (control) to 58.5+/-18.0 (experimental). There was no strain in the lacunar-canalicular area with 30 s (0.2 micron in diameter) loading. Micro-CT images showed that 5 min, 10 Hz, 3 weeks of loading did not result in significant structural change in the experimental group.

Dynamic histomorphometry analysis indicated significant trabecular bone remodeling, in which the ratio of labeled vs. bone surface (LS/BS) has more than 50% increase in the experimental distal femur compared to contralateral control. Double labels have shown in the experimental group, but not in the sham control, in which mineral deposition rate (MAR) was at 1.5 $\mu\text{m}/\text{day}$. There is no significant evidence of bone resorption at the periosteal and endosteal surfaces in both experimental and sham control femurs after 3 weeks

DISCUSSION: These results suggest that dynamic fluid contraction in muscle may generate hyper-tension in the skeletal nutrient vessel and induce ImP, and may substantially influence the fluid flow in bone [2]. Physiologic and dynamic muscle contraction can serve as a non-invasive source for generating ImP, which can further drive fluid flow through bone. This may help to devise a biomechanical based intervention for treating osteoporosis, muscle atrophy, and accelerating fracture healing. [This work is kindly supported by the NIAMS (AR049286), US Army (USAMRAA) (DAMD-17-02-1-0218) and the Whitaker Foundation (RG-0024).]

REFERENCE: [1] Qin, Y-X. et al.: J Biomech, 36:1427-1437, 2003. [2] Winet, H.: Eur.Cell Mater. 6:1-10,10-1-2003.