

## Opinion Article

# Mechanical loading effect to the functional bone adaptation

Alexander D. Kokkinias<sup>1</sup>, Sophianos-Orpheus D. Kokkinias<sup>2</sup><sup>1</sup>Physiotherapist; <sup>2</sup>Technological Educational Institute of Athens, Faculty of Health and Caring Professions, Department of Physiotherapy, Athens, Greece

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**Abstract**

The loads on skeleton control bone turnover, rates of adapted remodeling and influence growth. Mechanical stimulus detected by osteocytes, is derived from muscle contraction or gravity forces. It is difficult to separate the effect of gravity from muscle contractions at bone mass. A great number of studies show that muscle contractions are present, significant and able to represent the large majority which causes the adaptive bone responses.

**Keywords:** Muscle, Mechanical stimulus, Forces of gravity, Loading, Bone adaptation**Introduction**

Bone growth and bone loss are caused by mechanical elastic bone deformation. Muscles cause the highest loads and the largest deformations in bone and these deformations help to control biological mechanisms that determine the strength of entire bone. One of the dominant dogmas in the field of functional bone adaptation mentions that morphology, structure and strength of bone are dependent on forces generated by muscle contraction. Bone mass, bone geometry and bone strength are adapted to the everyday requirements. Bone mechanical properties are adapted, according to the required mechanical function<sup>1</sup>.

It is known that bone cells are sensitive to mechanical forces<sup>2</sup>. Tissue deformation during loading through exercising activates bone cells, such as osteocytes and this activation causes a series of signaling events that eventually lead to enhanced structural bone adaptation<sup>3</sup>.

While it is widely accepted that bone adapts to mechanical requirements which is subjected to, the origin of mechanical requirements which provide the motivating stimulus for bone tissue, i.e. muscle contraction or force of gravity, have come under stricter control in recent years. There are real and potential therapeutic consequences that determine specific roles of muscle loads and forces of gravity in bone adaptation<sup>4</sup>.

Determining the precise character of physical stimulus that leads to bone response, it was possible to take advantage of the biology of the system with minimum stimulation. New treatments and exercises associated with bone health can be optimized in order to be harmonized with these discoveries<sup>1</sup>.

Decrypting the primary stimulus for adaptive bone response to a more macroscopic level (muscle forces or forces of gravity), will give the opportunity to design more effective physical activities and treatments, specifically

aimed at improving bone mass<sup>1</sup>.

It has not still been demonstrated whether muscle forces are the main stimuli for functional bone adaptation. Muscle forces and forces of gravity coexist in human skeleton supporting body weight. It is not possible to investigate the separate contribution of muscle forces and forces of gravity, because there are no specialized models that could help in this study<sup>1</sup>.

However, there are some human disuse models which have been already studied<sup>5</sup>. A study conducted throughout 90 days to investigate the effects of immobilization to the bone mineral and muscle mass, in which the participants were immobilized and with -6° head down lean. It was found out that the loss of muscle began directly and the loss of bone occurred one month later. Furthermore, on the 89th day when the test finished and people rose, the muscles rapidly started to recover size, while the bone was still getting lost. A decrease of the mineral of tibia through immobilization in bed was observed and this loss was diminished by exercise and drug treatment with pamidronate<sup>5</sup>.

Nevertheless, as already mentioned, a great number of studies show that muscle forces are present, significant and able to represent the large majority which causes the adaptive bone responses<sup>1</sup>.

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**Corresponding author:** Alexander D. Kokkinias,  
2 Kiriazi str., Kifissia Athens, 14562, Greece

**E-mail:** kokkiniasalex@gmail.com

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## Muscle loads and bone tissue: the effect of upper limbs

The upper limb has a considerable muscle mass but due to bipedal posture and support of the human body does not transmit weight to the ground, therefore it is not subject to the reaction forces of gravity<sup>1</sup>. A brief overview of studies that examined relationship between muscle strength, muscle mass and bone mass in several positions at upper limb, shows a stable, important and positive association between them<sup>6</sup>. It is obvious that increase and loss of bone mass reflects increase and reduction of muscle strength during human life, including this of upper limb<sup>7,8</sup>.

The results of these studies could be interpreted in many ways:

- i) stronger muscles pull the skeleton with greater strength and therefore bone must adapt to these forces
- ii) heavier and larger bones require more muscle strength to move, thus muscles have to adjust to greater bone mass
- iii) bone and muscle mass are controlled by separate genetic factors and their association is false<sup>1</sup>.

Despite the fact that above results don't prove a cause - effect relationship between bone mass and muscle strength - it is obvious that in big people with great dimensions there could be genes for big muscles and big bones<sup>9</sup> - more detailed studies have examined this relationship in order to find the underlying effects of muscle mass. A survey which was conducted in underage tennis players with MRI, tested the size of muscles and bones in the arm holding the racket and in the free arm<sup>10</sup>. It was found increase in muscle and bone mass in the arm which was holding the racket and which was exercising during the game compared with the inactive one<sup>10</sup>.

An important observation concerning the role of muscle forces in bone mass is the clinical finding of newborns who are suffering from intrauterine neuromuscular paralysis and though they have normal bone length, they exhibit a severe reduction of cortical thickness and bone mass<sup>11,12</sup>. These infants often are born with multiple fractures at humerus and radius, which occurred before the birth<sup>11,12</sup>. Keeping in mind that both normal embryos and those with paralysis were grown in amniotic sac, in an almost "weightless" aqueous environment, it is unlikely that considerable forces of gravity were produced during pregnancy<sup>1</sup>. Only when muscle forces are eliminated, do bones become thin and fragile<sup>1</sup>.

These findings confirm that in developing skeleton muscle forces are the main stimulus that leads to bone adaptive response and not the forces of gravity<sup>1</sup>.

## Muscle loads and bone tissue: the effect of lower limbs

In several studies parts of skeleton that accept higher loads of muscle forces and forces of gravity, i.e. legs, were examined and it was concluded that muscle forces play the dominant role in bone mass regulation<sup>1</sup>.

In patients with partial hip replacement the forces

which applied to the joint were monitored telemetrically by positioning force converters inside the axes of prostheses<sup>13</sup>. Patients were asked to stand immovable in an upright position and then walk along a force platform for the purpose of: i) calculating telemetrically, by force converters into the prostheses, muscle forces and forces of gravity produced when the body standing upright or moving along the force platform ii) quantifying balance, walking and other biomechanical parameters. More than 70% of the forces, which were generated in the thigh bone during a normal cycle of walking, were developed from the action of the muscles and less than 30% of the forces came from the reaction of gravity on the patients body weight<sup>13</sup>.

However, these results fall short of determining the proportion of muscle forces applied in hip joint during a high-load exercise, in which the applied muscle loads increase significantly.

Experimental study in rats showed that daily replay of low intensity exercise, like jumps, for a period of eight weeks, could increase bone mass and muscle strength of lower limbs<sup>14</sup>.

Research results in young and aged rats with bones hypertrophy, who were divided into three groups according to age and were trained by jumping, running or sedentary lifestyle, showed that:

- a) in young rats who followed training program either jumping or running, tibia length as well as femur length and diameter increased<sup>15</sup>.
- b) in all age groups of rats tibia diameter was greater in those who were trained by jumping compared with those who followed sedentary lifestyle or workout by running<sup>15</sup>.

Therefore, muscle contractions are capable of causing functional adaptation and bone response.

## Muscle loads and bone tissue: results from genetic mice model studies

In a study conducted in normal and lacking myostatin mice it was found that those with the absence of myostatin had normal size, shape and bone mass in thigh bone (excluding enlarged trochanters and tubercles for muscle attachment) but the mass of isolated muscles was up to 3 (three) times bigger than that of non-mutant mice<sup>16,17</sup>.

To assess how much the major muscles of lacking myostatin mice were stronger than those of normal, their muscle contractile properties were tested and found to have significantly increased, showing an increase by 30% compared with those of normal mice and this increase remained proportional to the muscle size<sup>18</sup>.

In an experiment with four mice groups - two control groups, one normal group and one with lacking myostatin, both of these last groups exercised on a treadmill for 30 min / day, 5 days / week for 4 weeks - radius mechanical properties were measured and it was found that: whole bone structural properties of the lacking myostatin mice increased by 30% compared with those of the control group mice, while normal exercised mice showed only a minor, insignificant

increase in their bone structural properties compared with those of the control group<sup>19</sup>.

Consequently, exercising larger and stronger muscles entails larger and stronger bones.

In a study conducted with forty virgin female mice up to 14 weeks of age which of each animal was injected with Botox in the right posterior leg and with vehicle in the left posterior leg, after muscle inactivation, animals were randomly separated into two groups: 1) cage control and 2) tail suspended for six weeks and it was found that the skeletal effects of Botox-provoked muscle inactivation are not only due to the diminution of gravitational forces<sup>20</sup>. The retraction of gravitational forces of the posterior legs through tail suspension caused a loss of bone mass as a result of declined periosteal bone formation and increased endosteal bone resorption<sup>20</sup>. The increase in endosteal bone resorption was noticeable by a significant increase in medullary area and a decline in cortical area and cortical thickness<sup>20</sup>. Botox-provoked muscle inactivation on tail suspension worsened these skeletal modifications with both of retraction of gravitational forces and muscle inactivation had the biggest harmful influence on the skeleton, caused the least benefits in midshaft tibial bone mass, cortical area and cortical thickness, greatest benefits in midshaft tibial medullary area and lowest proximal tibial trabecular bone volume fraction<sup>20</sup>. These data demonstrate Botox-provoked muscle inactivation causes skeletal reactions further those associated with removed gravitational forces<sup>20</sup>. These results show that muscle has a direct influence on bone.

## Conclusions

Mechanical signals must be adequately strong and in significant rates to cause bone adaptation. It is possible to promote bone turnover, only when forces of gravity, that fulfill these criteria, are produced during physical activity.

Muscle forces are able to promote bone response and functional adaptation. Muscle forces usually provide a significant amount of applied force, thus, they contribute to the deformation of long bones. It remains to be seen whether muscle loads are the primary stimulus for functional bone adaptation.

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