

# Osteoporosis: The New Paradigm

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## ABSTRACT

Osteoporosis is one of the common diseases. Due to the serious complications, which cause disabilities and significant deterioration of the quality of life, it also presents a large public health problem, as well as a financial burden for the patients, their families, and the whole of society. The common clinical practice widely applied for >20 years has been based on the paradigm introduced on the hypothesis that osteoporosis is the consequence of decreasing bone mass due to increasing bone reabsorption over bone formation which makes bone prone to fractures. Based on that, bone densitometry has been introduced as a “golden” diagnostic standard and pharmacotherapy, with the goal of reducing bone reabsorption, has been introduced as a standard treatment. However, despite various drugs, the problem of osteoporosis is not solved or decreased. Also, complications such as drug adverse events and fractures after long-term pharmacotherapy presents a serious problem. Additionally, recent scientific research showed that osteoporosis is much more complex than was thought. So, clinical experience as well as scientific evidence clearly indicate the need for a significant change in clinical approach by introducing a new paradigm. According to the fact that osteoporosis is caused by the deterioration of bone matrix and bone architecture under the influence of various genetic, biomechanical, and biochemical factors, the new paradigm needs to be based on the principles of personalized and integrative medicine with the goal of improving biomechanical and metabolic balance, with stimulation of bone and cartilage regeneration, and thus improvement of the functional capacity of the musculoskeletal organ as a whole.

**Keywords:** Bone histomorphometry, Bone strength, Magnetic resonance therapy, Osteoporosis, Osteoporotic fractures.

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## INTRODUCTION

Osteoporosis is a big medical problem because of serious complications. The common complications of osteoporosis include hip and vertebral fractures that frequently cause permanent disabilities and a decrease in quality of life for patients and their families. Also, they are a significant burden for the national economies. That is partly the consequence of inadequate clinical practice due to insufficient knowledge of skeleton biology. A common opinion is still that osteoporosis, as well as osteoarthritis, is a consequence of aging and that symptomatic and partial therapy is all that can be done. Awareness of the importance of prevention is very poor and the promotion of prevention is still missing. Even though the interest in skeleton pathology significantly increased during the last few decades, skeletal biology has not yet been incorporated into the standard education of medical doctors. There is still no osteology as a clinical discipline that would attend to the musculoskeletal system as a whole, as one complex organ which actually it is. The fact that bones are renewed every 10 years through the process of remodeling while adjusting to the biomechanical and metabolic needs of the body in the dynamic balance with cartilage, muscles, tendons, ligaments, and fascia, working as a whole, is still unknown to the majority of people. Thus, to improve the treatment and increase awareness of prevention it is important to educate not only medical professionals but also the general population.

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Osteoporosis was defined as a disease by consensus in 1994 at a known medical conference. It was considered that osteoporosis is the consequence of increasing bone reabsorption over bone formation which reduces bone mass and makes bone prone to fracture. Based on that paradigm, a low bone mineral density (BMD) was introduced as a “golden” diagnostic standard and pharmacotherapy with the idea of suppressing bone reabsorption became a common clinical practice. However, there is a number of evidences showing that such clinical practice widely applied for >20 years, did not solve or decrease the problem of osteoporosis, therefore creating the need to be changed. Furthermore, there is no improvement in the prevention of complications. In 2016, the World Health Organization released data on global health estimates showing estimated global deaths by cause for the period of 2016–2060. Data

shows a worldwide growing trend in deaths caused by musculoskeletal illnesses and related disorders.

"Data on the fragility fractures in the largest five countries in Europe shows that in 2017 new fragility fractures are estimated at 2.7 million with an annual cost of €37.5 billion and a loss of 1.0 million quality-adjusted life years. Total fragility fractures are estimated to increase from 2.7 million in 2017 to 3.3 million in 2030, while the resulting annual fracture-related costs are expected to increase by 27%. Worldwide, osteoporosis causes >9 million fractures per year meaning that every 3 seconds fragility fracture occurs."<sup>1,2</sup> Thus, despite available various drugs widely recommended, the problem of osteoporosis was not solved or decreased. Additionally, adverse events of drugs and particularly fractures caused by long-term application of pharmacotherapy are a serious problem and a significant limitation of pharmacotherapy.<sup>3</sup>

Another existent problem, regarding the diagnostic criteria of osteoporosis, is that about 50% of patients who experience fractures on minor trauma, which is the best evidence of osteoporosis, have normal BMD. So, densitometry is not a reliable method for the diagnosis of osteoporosis. Furthermore, scientific research based on bone histomorphometry shows significant diversities in the microstructure and dynamics of bone remodeling in patients with osteoporosis, which indicates that there are different pathogenetic mechanisms that reduce bone strength with a consequent increase in the risk of fractures.<sup>4-6</sup> Thus, osteoporosis is a much more complex multifactorial disease and it cannot be successfully treated in the same way in all patients, as was the usual practice until now.

Respectively, there is more than enough evidence that indicates the necessity of introducing a new paradigm and changing clinical practice in accordance with the new paradigm.

### **The New Paradigm to Diagnosis and Treatment of Osteoporosis on the "4P Principles" (Predict, Prevent, Personalize, and Participate)**

The new paradigm is based on the fact that the human body is constantly rebuilding and remodeling during its lifetime by the activity of cells that produce specific proteins. Thus, the entire skeleton is renewed over the course of 10 years. Bone cells osteoclasts resorb bone tissue and osteoblasts produce specific collagen tissue creating osteoid, which makes bone matrix and gives bone flexibility. That process is coordinated by specific bone cells, osteocytes, which give the signals to osteoclasts and osteoblasts to remodel bone microarchitecture, according to the biomechanical and metabolic needs of the body in the dynamic balance with cartilage, muscles, tendons, ligaments, and fascia.

Due to the fact that all parts of the musculoskeletal system work as a whole, like different musical instruments in a symphonic orchestra, a holistic approach is needed. The load caused by gravity is distributed to the entire musculoskeletal system, but in the case of biomechanical imbalance caused by skeleton deformities, such as spinal and foot deformities, hip dysplasia, sport, sedentary lifestyle, etc., certain parts of the musculoskeletal organ will be exposed to overload which

will cause damage to that tissue. Often, cartilage is damaged first since it is most exposed.

Due to the fact that chondrocytes have a small potential for regeneration, the cartilage is gradually replaced by fibrotic scars. In the beginning, there is no pain because there are no nerves in the cartilage. But, in time deterioration of cartilage properties decreases its capacity to absorb the load which extends the overload to tendons, synovial membranes, ligaments, and bone, causing chronic inflammation of joints followed by chronic pain and other complications.

Biomechanical imbalance also disturbs bone microarchitecture and thus causes osteoporosis, because it changes signals that muscle contractions send to osteocytes which coordinate the activity of osteoclasts and osteoblasts in remodeling the bone microarchitecture to resist the load.

Metabolic, biochemical, and hormonal balance as well as genetic factors have also a significant influence on the skeleton, particularly on bone, but on cartilage as well.

Thus, for example, there is clinical evidence showing that diabetes is an independent predictor for severe osteoarthritis.<sup>7</sup> Also, it is well known that premature menopause, most hormonal diseases, and some chronic inflammatory diseases negatively influence bone remodeling, decreasing bone strength.

Therefore, osteoporosis is caused by the deterioration of the bone matrix and bone architecture under the influence of various genetic, biomechanical, and biochemical factors. Due to the fact that there is large variation among people related to genetics, biochemical, and biomechanical factors, treatment needs to be based on a personalized approach.

It is also important to recognize that bone strength primarily depends on the quality of the osteoid, the collagen tissue which creates the bone matrix, as well as on bone architecture. So, a fracture as the major complication of osteoporosis is a consequence of low bone strength, independently of bone mass.

Thus, taking into consideration all mentioned above, it is clear that the definition of osteoporosis, as well as clinical practice, needs to be changed, in accordance with the new paradigm, and define it as a chronic bone disease caused by deteriorated bone strength, with consequently increased risk of fracture.<sup>8-10</sup>

In addition, it is important to know that drugs that are frequently used in the treatment of osteoporosis such as bisphosphonates, selective estrogen receptor modulators (SERM-s), and denosumab, suppress not only the activity of osteoclasts but also osteoblasts and thus could negatively influence the quality of the bone matrix, with the consequence of decreasing bone strength. That could explain the poor effect of pharmacotherapy, and fractures after long-term use of those drugs.

### **What should be the Goals of the Treatment of Osteoporosis?**

According to the new paradigm, the goal of successful treatment should be the prevention of fracture by increasing bone strength, primarily by stimulating the rejuvenation

of bone matrix and improving bone architecture. In order to achieve these goals, the following principles need to be followed:

- Considering that the quality and function of the musculoskeletal organ depends on the quality of all of its parts, the holistic concept is always needed. That means that it is necessary to evaluate the skeleton as a whole and treat all parts of the musculoskeletal system, trying to improve mobility and biomechanical balance.
- Due to significant variability among humans regarding genetic, biochemical, and biomechanical factors, the treatment needs to be based on the principles of personalized medicine.
- Due to the fact that there is no effective therapy able to achieve complete restitution of the skeleton, but there are treatments that can prevent the most of complications, prevention is the key.

### The “BaR” Concept, the New Guidelines for Clinical Approach to Osteoporosis

The acronym “BaR” comes from the initial letters for biomechanics and biochemical balance and regeneration. It is based on a holistic and personalized approach with a focus on early prevention. It includes a combination of methods with the goal to improve biomechanics and metabolic balance, by stimulating the regeneration of cartilage and bone tissue and providing good microarchitecture by regular exercise.

Since there is no method by which we can measure bone strength, the diagnosis of osteoporosis should be done on individual clinical assessment based on knowledge of bone biology, not only by densitometry, as it is common practice.

The most important is to recognize the main pathogenetic mechanism and introduce the treatment according to that. Also, it is important to recognize diseases and medical conditions known to have a negative impact on bone structure and bone strength. Considering that in most cases it is not possible to cure the disease and completely reconstitute bone structure, it is important to start with the prevention of osteoporosis as soon as possible.

In order to fulfill this objective, it is important to provide good biochemical and biomechanical balance, reduce pain, and improve mobility because mobility is very important for bone remodeling. It is also important to stimulate the rejuvenation of the bone matrix by stimulating osteoblast activity with available treatments such as MBST—therapeutic magnetic resonance, as well as provide better architecture by regular exercises, such as “Tae Do.”

Due to the fact that MBST—therapeutic magnetic resonance as well as “Tae Do” exercise have no negative effects and there is no risk for patients, they are also recommended as primary prevention regardless of BMD in all diseases and conditions that are known to have a negative impact on bone strength, such as menopausal women, patients on corticosteroid therapy, rheumatic

and autoimmune diseases, patients on dialysis and after transplantation, diabetic patients, people suffering from chronic bone, and joint pain. Also, they are recommended for all people with low mineral density and all seniors above the age of 60. In most cases, it is recommended to do the “Tae Do” exercises every day and repeat the microbiology stimulating therapy (MBST) cycles once 1 year.

### What is “Tae Do”?

“Tae Do” is a special program of exercise based on the principles of the Korean martial art taekwondo. It consists of controlled movements with energy-directed contractions of the muscles which send signals to bone cells on how to remodel the bone microstructure to resist the load and thus improve bone strength.<sup>11</sup> The basic principle of martial arts is using the energy of mind and body to achieve the most efficient way of mobility. Thus “Tae Do” exercises influence the entire system of controlling and executing a motion, from the brain through the nervous system to the musculoskeletal system. In that way, “Tae Do” improves balance and reduces the risk of falls, but also improves bone microarchitecture sending signals to bone cells by intermittent, rhythmic muscle contractions. An additional advantage of the Tae Do program is that it consists of 13 simple movements that can be easily learned and practiced at home. The exercises are done in a sitting position, with maximum movement control so that everyone can adapt them to their abilities.

### Nuclear Magnetic Resonance Therapy—MBST

Nuclear magnetic resonance therapy is based on the well-known technology used in diagnostics, but compared to diagnostic magnetic resonance it uses much lower energy which is adjusted for the treatment. It is developed and patented in Germany under the brand MBST. The field strengths used by MBST devices are from 0.4 to 2.35 mT and 17–100 kHz in the magnetic resonance frequency. Since 1999, when MBST was introduced in clinical practice, a number of studies were conducted *in vitro* on cell cultures but also *in vivo* on animal models that confirmed the regeneration of the cartilage and stimulation of bone formation. Additionally, clinical studies done on a large number of patients as well as clinical experience demonstrated long-term therapeutic effects in osteoarthritis and osteoporosis.<sup>12–31</sup> Recent scientific studies also explained the intracellular mechanism, showing that therapeutic magnetic resonance (MBST) activates cells by affecting the circadian clock oscillation in a light-independent manner. Moreover, it changes the redox status of the cells and modulates the expression of HIF-1- $\alpha$ , also involved in the circadian system.<sup>32</sup>

Besides the unique therapeutic effect of stimulating tissue regeneration by influencing cellular activity, an additional advantage of this method is that it has no side effects.

The use of the MBST treatment program also needs to be based on personalized assessment in order to achieve maximum effect as a number of different treatment programs are currently available with this technology.

## CONCLUSION

Related to the clinical approach to osteoporosis it is important to understand that there is a certain limitation in the clinical evaluation of osteoporosis because of the fact that there is no possibility of measuring bone strength. That is the problem not only in diagnostics but also in the clinical evaluation of therapeutic effects.

Since measurement of bone strength is currently not possible, reliable evidence of successful osteoporosis treatment might be based on other indirect parameters, that is, monitoring of bone resistance to the strong force that usually happens in severe trauma. However, patients cannot be exposed to controlled double-blind, prospective, placebo-clinical studies based on purposely exposing patients to accidents with potential fracture trauma.

Nevertheless, taking into consideration all scientific and clinical data, it can be concluded that regardless of the mentioned limitations, there is enough evidence confirming the advantages and justifying the introduction of the new paradigm in the clinical approach to the skeleton, which is not limited only to a particular technology or a treatment and can be easily advanced with new therapeutic options and technologies in the future.

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