Considering how commonplace and mundane bone healing may seem superficially, in reality it is the end result of a very intricate and highly regulated series of events. In a process honed over millions of years of evolution, a somewhat precarious balance of biology and biomechanics leads most often to solid union. Our collective clinical experience suggests that there is a wide range of conditions under which bone will heal, and the individual response remains highly variable. This generally reflects patient-specific characteristics, such as age, comorbidities, and recognized risk factors for nonunion. It is common knowledge throughout the orthopedic community of surgeons and researchers that a healthy teenager will heal much faster than an elderly diabetic smoker. This applies equally well to routine fracture healing as well as the regenerate bone characteristic of distraction osteogenesis, with which we are all familiar. Orthopedic surgeons constantly strive to reduce the healing time of bone and to minimize the incidence of delayed union and nonunion. Delayed union and nonunion are still relatively common, and this may be due, at least in part, to the local mechanical conditions being applied in and around the region of regenerate bone. Given that all of us are tremendously interested in maximizing the healing potential of bone and are looking for the best methods to optimize the process, how can we tip the balance in our favor?

The process of bone healing inevitably reflects a complex interplay of biology and biomechanics, and when these two elements are in harmony, bone healing proceeds uneventfully.[1] The mechanical environment is regarded as an equal contributor in the Diamond Concept of Fracture Healing, in concert with osteogenic cells, growth factors, and osteoconductive scaffolds.[2] However, we believe and have argued elsewhere that the biomechanics can actually be considered of paramount importance because the mechanical environment most likely orchestrates the nature of the biologic response.[1] Under most circumstances, when the biology and biomechanics act in symphony, bone heals readily and predictably. However, despite our knowledge and best practices, in some situations, the conditions are such that union is at best tenuous. Again, we must ask ourselves what can we do to consistently tip the balance in favor of the most rapid and predictable clinical course toward solid union? The answer may come from a novel approach called Reverse Dynamization (RD), a counter-intuitive biomechanical process compared to conventional dynamization. Under the principles of RD, the mechanical environment of the fracture site is manipulated during the early stage of healing to allow micromotion and promote callus formation and then changed to more rigid fixation to encourage progression toward union [Figure 1].

Our discussion here will now focus on how and why the RD method provides the mechanical leverage to minimize the risk of delayed and nonunion, while potentially accelerating bone healing and remodeling.

There can be no doubt that the mechanical environment plays a crucial role in the rate and quality of bone healing. How much, how long, and the type of motion that should be allowed for ideal bone healing remain unknown. Decades of experimental and clinical research has identified interfragmentary movement (IFM) as one of the key mechanical factors influencing the outcome of the healing process. IFM is the movement occurring between fracture fragments in response to physiological and external loading of the fractured limb. There are two main factors that influence IFM: (i) the rigidity of the implant stabilizing the fracture and (ii) the surface area of the fracture fragments. These factors determine the tissue strain, and the amount of callus formed is, in turn, dependent on the magnitude of IFM.[3-5] The maximal volume of callus is generated when there is controlled motion (IFM) between the fragment ends in the immediate postfracture period, and micromotion in the region of 1 mm or less has generally been recommended.[6-8] The strain theory suggested by Perren and Cordey[9] involves the concept of fracture strain or the amount of deformity or motion (IFM) that occurs at a fracture gap as a result of fixation stability. If the fracture strain is <2%, the conditions of absolute stability are met, and this should result in primary bone healing. However, fracture strain between 2% and 10% should lead to a condition of relative stability, and fracture healing would instead proceed through secondary bone healing, first forming a cartilaginous template. If the strain at the fracture site is >10%, fibrous tissue will most likely form and lead to nonunion. An integral concept is that further movement once callus has formed may actually be considered counterproductive, leading to failure of the callus to join the main fragments on either side of the fracture.[10-13] Kenwright and Gardner[14] previously demonstrated that excessive motion after callus has formed...
Despite this knowledge, for decades, orthopedic surgeons have failed to recognize how to properly manipulate the mechanical environment to encourage bone healing. Most accepted treatment protocols, instead, attempt to maintain rigidity during the initial 4–6-week early period using external fixators, locked intramedullary (IM) nails, or plates. Further manipulation of the local mechanical environment is considered only after the fracture has not demonstrated adequate progression toward union, and surgeons only then introduce limited motion in an attempt to dynamize the fracture site. Dynamization is the term most often used when IFM is increased by changing from stable to more flexible fixation. Ilizarov himself was an advocate of this approach, and many of us have adhered to this principle for many years as we gradually dismantle frames and increase the load on the regenerate bone itself. However, this approach has already been evaluated in several clinical trials and has consistently failed to demonstrate any benefits from dynamization, specifically for fracture healing with IM nails. It appears highly unlikely dynamization in the traditional sense contributes towards fracture healing in any meaningful way.[15–20]

Ontologically, one of the primary purposes of early callus is to stabilize the fracture by providing provisional mechanical stability at the fracture site and limiting further movement. Considering what is known and well-established regarding early callus formation, perhaps, it would be most logical to instead allow limited motion during the immediate postfracture period and then restrict motion completely after abundant callus has already formed, rather than dynamizing and allowing motion. With this knowledge, it was postulated that to achieve the most rapid union, a fracture site should be allowed early micromotion to encourage callus formation, and mechanical conditions should subsequently be modulated to produce a rigid environment to prevent any disruption of vascularization, thereby optimizing the potential for rapid bone healing.

To that end, over the past decade, the revolutionary concept of RD has been slowly gathering momentum.[1,21–24] With this strategy, the mechanical environment of the fracture site is manipulated during the early stage of healing in an attempt to accelerate progression toward union. The fracture is initially stabilized less rigidly to allow micromotion and encourage callus formation. Once callus has formed, stabilization is converted to a rigid configuration, and the fracture is then allowed to remodel. A growing body of basic science research supports this RD tactic;[1,21–24] however, to date, there is only limited evidence confirming its clinical efficacy. For example, studies in rat models have demonstrated early modulation (7-14 days) of the mechanical environment significantly accelerates bone healing, which is achieved by first stabilizing the defect under conditions of low stiffness and then by imposing high stiffness.[21] In contrast, a study by Claes et al. in the same animal model found that early dynamization (7 days), whereby initially high stiffness fixation is followed by low stiffness fixation, was very detrimental to bone healing.[25]

To better define the optimal clinical parameters for RD, one of us (Dr. Vaida Glatt) is now very actively coordinating a series of research projects at various sites around the globe. As the originator of the concept of RD, she continues to investigate this response in a rat model from her own laboratory at the University of Texas Health Science Center, San Antonio. Under her direction, an interesting set of both large animal (dog) and clinical studies is being organized together with Dr. Alexander Gubin at the Ilizarov Center in Kurgan, to investigate RD as a method to accelerate the consolidation of regenerate bone. In addition, with her input, further studies in an animal (goat) model are already underway at Ohio State University under Dr. Christopher Lobst, in collaboration with Drs. Mikhail Samchukov and Alexander Cherkashin from Texas Scottish Rite Hospital for Children in Dallas, using RD as a method to promote bone healing and remodeling in an osteotomy site. Preliminary results from this study are very promising, demonstrating improved and accelerated outcomes using this regimen.

It is very evident that successful regeneration and healing of bone rely on a synergy between the various biological factors and mechanical forces, governed by the timing and spatial relationship of their introduction. Optimizing the nature of these mechanical cues and the biological responses to them at various levels is most important, as this will determine the type and the amount of tissue formed, thereby controlling the rate of the healing process. The initial results from various investigations have been very positive, and it will be interesting to see what the studies
now planned or already underway will reveal. Regardless, we remain optimistic that RD will hold the key that finally tips the balance in favor of more rapid and reliable union, including both fractures and regenerate bone.

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