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Great debates in trauma biomechanics

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Summary:
At the 2021 annual meeting of the Orthopaedic Trauma Association, the Basic Science Focus Forum hosted its first ever debate-style symposium focused on biomechanics and fracture repair. The 3 subjects of debate were "Mechanics versus Biology—Which is 'More Important' to Consider?" "Locked Plate versus Forward Dynamization versus Reverse Dynamization—Which Way Should I Go?" and "Sawbones versus Cadaver Models—What Should I Believe Most?" These debates were held because fracture healing is a highly organized synergistic response between biological factors and the local mechanical environment. Multiple studies have demonstrated that both factors play roles in governing bone healing responses, and the causal relationships between the 2 remain unclear. The lack of clarity in this space has led to a spectrum of research with the common goal of helping surgeons make good decisions. Before reading further, the reader should understand that the questions posed in the debate titles are unanswerable and might represent a false choice. Instead, the reader should appreciate that the debates were held to gain a more thorough understanding of these topics based on the current state of the art of experimental and clinical studies, by using an engaging and thought-provoking format.

Keywords: biomechanics, trauma, debate, discussion

1. Debate 1: Mechanics Versus Biology—Which is "More Important" to Consider?

1.1. The Case for Mechanics

Mechanics are almost always under the surgeon's control, whereas many factors related to biology are often outside clinical control. For example, it is known that shear strain and excessive axial strain are detrimental for bone healing.[1–3] Consequently, there has been tremendous interest in maximizing the healing potential of bone by optimizing the mechanical environment. The most important mechanical factor is interfragmentary movement between the fracture fragments, and its magnitude is dependent on fixation stiffness, weight-bearing, and muscle forces. Many aspects of the biology of fractures, such as patient age, medical comorbidities, and local traumatic damage, are outside of surgical control. Understanding these various factors are of course important because they decrease the chance of fracture healing, but typically we do not yet have effective techniques to improve biological issues.

We do, however, have a better understanding of mechanical "rules" that will lead to good clinical outcomes. For example, placing a lag screw across a simple fracture and protecting the lag screw with a neutralization plate will lead to fracture healing. Similarly, placing a buttress plate on a partial articular fracture on the correct side will promote healing, and avoiding varus malalignment of a subtrochanteric femur fracture will provide a mechanically advantageous environment for healing. Our understanding of biology of fracture healing is not nearly as well advanced, so we do not have analogous simple rules for how to appropriately create good biology in many situations.

1.2. The Case for Biology

The complex biology of fracture healing has been studied extensively for over a century and has, in fact, been described in intricate detail. For instance, we know that bone healing has several discrete but overlapping phases, with repair occurring either by primary (intramembranous ossification) or secondary (endochondral ossification) bone healing processes.[4] The specific cells, genes, and molecular pathways involved during each bone healing phase have already been identified.[5–7] These processes unfold in a highly organized fashion, where a broad spectrum of growth factors, as well as the timing and spatial relationship of their introduction, is required to interact with one another to achieve successful and predictable bone healing.

The hematoma/inflammatory phase initiates the process during the first 7 days, and mesenchymal, endothelial, and immune cells are recruited indiscriminately into the nascent fracture hematoma; there they become embedded and begin forming the extracellular matrix that quickly evolves into granulation tissue. Among those cells are macrophages and T cells, which secrete specific cytokines that catalyze the healing response. Subsequently, from the adjacent periosteum, bone marrow, and muscle, recruited progenitor cells migrate into the fracture site to initiate repair. These progenitors differentiate

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into either osteoblasts or chondrocytes, which will then form bone by intramembranous or endochondral ossification, respectively. The reparative phase follows and lasts anywhere from 1 to 6 weeks. During intramembranous ossification, bone is directly formed from osteoprogenitor cells without first forming a cartilaginous template to create hard callus. By contrast, during endochondral ossification, progenitor cells differentiate into chondrocytes to form a cartilaginous intermediate that becomes calcified and is eventually replaced by bone. During this process, chondrocytes hypertrophy and undergo apoptosis, the extracellular matrix calcifies, and blood vessels invade the matrix. This calcified cartilage is then resorbed and replaced by woven bone formed by osteoblasts. Finally, in the remodeling phase, osteons remodel newly formed woven bone and the immediately adjacent fracture ends, which gradually matures into lamellar bone. This last phase can take anywhere from months to years to fully complete, ultimately recapitulating normal anatomy, often closely restoring the shape and structure of the original bone.

We also know that more general aspects of host physiology can have a tremendous influence on the outcome of fracture healing and that this can be influenced by many factors.[8] These factors may be local, secondary to extensive comminution, bone loss, and devascularization, or this compromise may be systemic, in those patients who are elderly, malnourished, smokers, or osteoporotic. Based on our considerable knowledge of bone biology, one could easily support the argument that the biology of fracture healing is far better understood than the mechanics involved. Admittedly, the mechanics can be simplified into rules that are often applied with some confidence in most fractures. Biology and mechanics are complementary forces that are intimately bound to one another, reflecting a delicate balance within a symbiotic relationship. As our appreciation of the biology involved is maturing, we can now work toward developing implants and specific mechanical treatment regimens to actively manipulate the fracture healing response and optimize the process in ways that enhance this response even under the most adverse conditions.

2. Debate 2: Locked Plate Versus Forward Dynamization Versus Reverse Dynamization—Which Way Should I Go?

Primary bone healing requires a rigid/static fixation, whereas secondary healing necessitates flexible fixation. As expected, whenever fixation is either too flexible or too rigid, healing might fail. Numerous studies have attempted to optimize bone healing through the process of dynamization, transitioning from a rigid to a more flexible configuration.[2,9–15] However, the results of these studies have been inconclusive, and the ideal level of stiffness of a fixation construct or interfragmentary motion across fracture sites is unknown. It is important to consider that the ideal level of stiffness is different for each fracture pattern (such as simple vs. comminuted, transverse vs. oblique) and each bone characteristic (osteoporotic vs. not, cortical vs. cancellous, diaphyseal vs. metaphyseal, etc). Bone healing may be improved by dynamization, where micromotions are deliberately introduced between bone fragments. Forward dynamization (FD) refers to the process of making a given fracture fixation construct less rigid over time while reverse dynamization (RD) refers to an intervention that makes a construct more rigid. The specific means by which either of these is accomplished depends on the type of fracture fixation used. When applied improperly, dynamization can be detrimental to the healing process.[16–21] Therefore, its use remains controversial.

2.1. The Case for Locked Plating

Locking plates represent a solution for some challenging fractures that nonlocking plates cannot fix successfully; however, they can also be the source of new challenges in some cases. For example, locked plating can be a useful tool for osteoporotic fractures, metaphyseal fractures, short articular segment fractures, and periprosthetic fractures. This design works in these cases because it does not rely on congruency between the plate and the bone and does not require plate/bone compression—both of which are reliant on good bone quality. Conversely, locking plates have introduced some new and unforeseen failure modes, such as tear-out of (still locked) implants from osteoporotic bone, screw perforation into the joint, and early implant breakage due to excess construct stiffness and stress concentration at the fracture site.

Several take-home points must be considered for the effective use of locked plate constructs. First, the fracture must be reduced before the screws are locked into the plate. Second, challenging cases that include osteopenia and short-segment fixation are prime applications of locking technology, but the use of these implants is not ubiquitous. The utility of locking implants must be weighed against the impact on construct stiffness and strain of the native bone, which is not always quantifiable in the clinic. Further work is required to understand how to optimize plate design and construct stiffness to ensure satisfactory fracture healing in different anatomic locations and under different conditions.

2.2. The Case for Forward Dynamization

FD fixation constructs typically include fixation with an intramedullary nail using interlocking screws placed in a dynamic hole.[22] Most of the contemporary femoral and tibial intramedullary nail designs have an oblong hole with an option of placing the interlocking screw in a dynamic mode. This approach is particularly useful in transverse fracture patterns, where the length will not change with loading. FD is usually achieved by converting a static construct into a dynamic construct. FD reduces the stress on the implant and results in increased compressive axial motion and loading of the bone. This technique can be used as a solution to delayed union and nonunion of long bone fractures and can also be considered when the cause of delayed union/nonunion is the fixation construct being too stiff.[23] Conversely, FD of plating constructs can lead to weakening of the stability of the fixation, which may cause failure of the fixation.

The success rate of FD is reported to be variable, between 24% and 99%.[24] Gap and/or comminution at the fracture site are factors that may play a role and have been shown to be negative predictors for FD.[22] The timing of dynamization also is important: Earlier intervention for dynamization (10–24 weeks after initial fixation) is more successful in achieving bony union than later in the follow-up period (>24 weeks).[25] It has been demonstrated that an interlocking screw in a dynamic hole works better than removing all interlocking screws from one end of the nail.[25] Another factor is the amount of callus at the fracture site. The presence of callus significantly increases the success of FD.[24,26,27]

The ideal case characteristics for successful FD are (1) stable fracture pattern and fixation construct (axial and rotational), (2) presence of callus, (3) absence of gap/comminution at the fracture site, (4) dynamization performed at 3–6 months after initial fixation, and (5) an interlocking screw in a dynamic hole rather

than removing all screws. Dynamization is a viable low-risk and low-cost treatment option for delayed union and nonunion in patients with stable fracture patterns, and stable fixation constructs and should be considered and offered to these patients.

2.3. The Case for Reverse Dynamization

RD is a counterintuitive process from FD. The scientific premise for RD is that early flexible fixation allows for micromotion, encouraging callus formation, while prolonged motion instead produces high tissue strains that disrupt neovascularization. Therefore, once substantial callus has formed, stabilization is best converted to a rigid fixation under which the soft callus is quickly converted to hard callus, leading to more rapid union.

Several animal models have supported the use of RD.[28–33] For instance, when rat osteotomies were initially stabilized using flexible fixation, then changed to more rigid fixation after 7 or 14 days, bone healing and remodeling was significantly accelerated.[28] However, when the regimen of FD was applied at 7 days, it was highly detrimental to bone healing.[34] Interestingly, the FD and RD regimens applied at 21 days had very similar results.[28,35] These findings are not surprising considering in studies that mimicked the late stage of healing, the fixator contributed very little to the overall stability. Instead, most of the load was transferred through intrafracture materials.[36,37] Separately, a goat 2-mm osteotomy model also confirmed that the RD regimen, flexible fixation for 3 weeks, followed by 5 weeks of rigid fixation, accelerated healing/remodeling of tibias compared with the static/rigid and dynamic/flexible fixation groups.[31] Although clinical data are limited regarding the benefits of RD, and most reports are unpublished or anecdotal, the initial results have been very positive, consistently demonstrating accelerated bone healing when the RD regimen is applied during the early phase of healing.

The fastest way to generate maximal callus is through early flexible fixation, and rapid conversion to hard callus requires rigid fixation to avoid neovascular disruption. By optimizing this process, the RD regimen provides a modern strategy to accelerate bone healing and tips the balance in favor of a more rapid and reliable bone union, thereby likely minimizing the incidence of nonunion. Implementing RD clinically will require development of implants specifically designed to allow surgeons to carefully manipulate their mechanical properties without the need for further surgery.

3. Debate 3: Sawbones Versus Cadaver Models—What Should I Believe Most?

3.1. The Case for Cadaveric Models

The current bias in existing research is toward using cadaver bone. In a review of 67 biomechanical studies for proximal humerus fracture implants, 87% of studies used cadaver bone, 7% were in sawbones, and 4% used animal bones.[38] This finding aligns with a recent review article, which outlined the parameters that should be considered when designing biomechanical experiments related to fracture fixation[39]: Biomechanical fracture experiments should re-create the in vivo situation; bone quality of the experimental bone should resemble the fracture population; cadaveric bone should be preferred to the available synthetic replica; fracture geometry should be carefully selected to avoid bias; and the load applied to the specimen should result in forces within the range of in vivo measured values.

When comparing cadaver bone with synthetic bone, it is important to determine whether cadaver bone behaves like real bone. For example, a finite element analysis comparing human cadaveric femurs with synthetic femurs compared the biomechanical properties of each undergoing axial and torsional loading.[40] Synthetic bones were significantly stiffer with 2.3 times increased torsional stiffness and 1.7 times increased axial stiffness compared with the cadaveric samples. Another study evaluated fourth-generation composite sawbones compared with cadaver bones surgically stabilized for simulated femoral neck fractures.[41] After 20,000 load cycles, sawbones saw an average of 0.8 mm of migration compared with 2.2 mm for the cadaver bone. Although this difference may not be clinically significant, this study, along with others, found that sawbones failed in a different pattern than from cadaver bone.[42–45]

Head-to-head comparisons of synthetic bone versus cadaver bone have demonstrated that sawbones do not replicate the biomechanical behavior of real bone. For example, a study comparing proximal and distal placement of locking plates for two-part fractures of the proximal humerus was duplicated in cadaver and sawbones.[43] Results of the study were different based on the material. In the cadaver specimens, there were no differences found between the 2 constructs while in sawbones, there were statistically and clinically significant different stiffnesses between the 2 constructs.

In conclusion, whenever reasonably possible, use cadaveric bone for biomechanical studies. This is especially true when performing construct testing, when doing cyclic loading, and when evaluating osteoporotic conditions. It is important to ensure that failure modes of the test mimic those seen clinically.

3.2. The Case for Synthetic Bone Models

The irrefutable advantage of synthetic models is that they reduce the variability found in cadaveric bones. For example, one study performed the same protocol on cadaveric and synthetic proximal humeri, and the variability in several biomechanical variables was decreased by an order of magnitude.[43] While this is a valuable asset, the synthetic models in this study did not faithfully recapitulate the human condition, and therefore results must be interpreted carefully. Despite the reported differences in outcomes between the synthetic and human tissue, synthetic models are still used regularly.[46–49] Updates to synthetic bone designs have led to improved efficacy between cadaveric and synthetic models. In a series of studies, it was shown that fourth-generation sawbones replicate physiologic or near physiologic values in torsion, axial compression, lateral bending stiffness, and cancellous bone pullout strength.[50–52]

Synthetic models are also advantageous because they provide the opportunity to perform an experiment without concern for disease transmission. The use of cadaveric tissue requires various levels of institutional approval and requires a Biosafety level 2 laboratory space. To prevent disease transmission, the use of personal protective equipment is required, whereas synthetic bones can be used anywhere without the need for personal protective equipment, freezers for storage, or specialized training for the handling of the tissue.

Depending on the topic of an experiment, the inherent age bias of cadaveric specimens can lead to models that are not representative of clinical practice. In general, donors of cadavers typically represent the elderly population. Although this limitation is not applicable to studies modeling elderly populations (eg, fragility fracture repair), it is particularly important to consider

when planning experiments geared toward younger populations (sport injuries, high-energy trauma).

The future is bright for synthetic bone models in orthopaedic experimentation. Additive manufacturing techniques continue to revolutionize orthopaedics, and biomechanical testing is part of that. As materials and techniques continue to improve, the gap between cadaveric and synthetic models will shrink. When this gap closes, the benefits of synthetic bone will all be leveraged and the need for cadaveric specimens may become obsolete.

4. Conclusions

A great body of work has gone into understanding the role and interplay between mechanics and biology of fracture healing. Current evidence strongly supports the concept that bone healing/remodeling can be accelerated by optimizing the biological response through mechanical cues.[15,28,30,32,33,53] These cues are governed by the timing and spatial relationship of their introduction, determining the type and amount of tissue formed, thereby controlling the rate of healing. Unfortunately, we are a long way from really being able to predict or optimize fracture healing for each patient's injury. However, our heuristics for optimizing mechanics have evolved over many decades and have produced guiding clinical principles to optimize mechanics. Violating these principles will typically lead to poor outcomes, but following them will almost always lead to union.

Regardless of what model or substrate is used for experimental tests, the reader should distinguish between statistically significant differences and clinically significant differences. Uniform results from benchtop tests often provide statistically different results that may not be clinically relevant. Finally, readers of biomechanical studies should be wary of conclusions that equate stronger constructs with better constructs. Stronger constructs often require more dissection. Comminuted fractures that require relative stability clearly do not require stronger stiffer constructs. Therefore, stronger is not always better.

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