RHEUMATOLOGY

Review

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Marrow fat may distribute the energy of impact loading throughout subchondral bone

Peter A. Simkin[1]

Abstract

Most students of articular mechanics consider impact loads to be compressive forces that are borne by an intraosseous, trabecular scaffold. The possible role of marrow fat, which comprises about 75% of the structure, is generally ignored, and the potential contribution of type 1 collagen, the prototypic tensile protein, is not considered. Here, I question the evidence underlying these omissions and reject the conclusion of exclusive trabecular compression. Instead, I suggest that impact loading pressurizes the fat in subchondral compartments, and those pressures stretch the elastic trabecular walls, which are thereby subjected to tensile loading. The load-driven pressure pulses then diminish as they pass from each compartment to its adjoining neighbours. The resulting pressure gradient distributes the burden throughout the subchondrium, stores energy for ensuing recovery and subjects individual trabeculae only to the net pressure differences between adjacent compartments.

Key words: bone mechanics, subchondrium, marrow fat, trabeculae, sacrificial bonds, impact loading, hydraulic, tensile, type 1 collagen, poroelastic

Rhuematology key messages

- Weight-bearing human joints safely manage seemingly excessive burdens during normal ambulation.
- Load-induced pressure within subchondral compartments imparts tensile stress to the trabecular walls.
- Adjoining compartments share the load through a descending pressure gradient.

REVIEW

Introduction

Subchondral bone is a load-bearing tissue divided into compartments by elastic, bony trabeculae and largely filled with marrow fat. Under load in a materials-testing machine, the typical epiphyseal specimen remains undamaged when loading stress (compression) causes up to 5% strain, that is, it may be reduced to 95% of its initial height under load, but it will rebound to 100% when the load is removed. Under higher loads, the pressure becomes excessive and the bone yields irreversibly. This point of incipient crushing has often been reached when loading pressures in megapascals (MPa) reach only 2 MPa (2 MPa = 15 000 mmHg or 20 atmospheres) [1]. In contrast, loading pressures *in vivo* have been found as high as 18 MPa during everyday activities as simple as rising from a chair or descending a staircase [2, 3].

[1]Division of Rheumatology, University of Washington, Seattle, WA, USA

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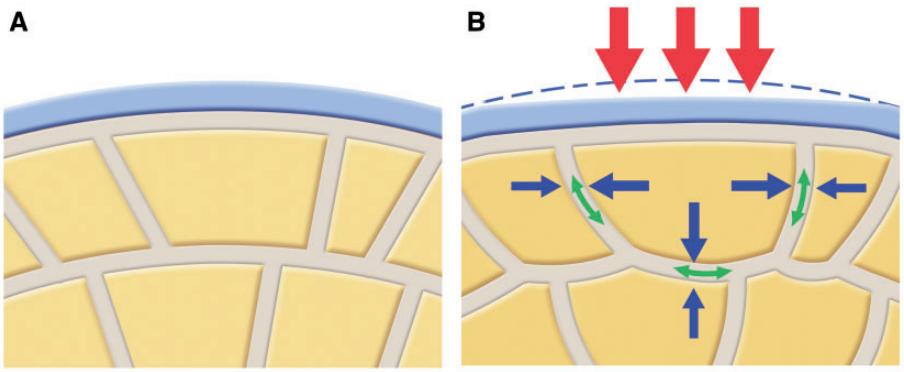
Correspondence to: Peter A. Simkin, Division of Rheumatology, Box 356428, University of Washington, Seattle, WA 98195-6428, USA.
E-mail: psimkin@uw.edu

How can this difference be reconciled? Students of trabecular mechanics have long recognized that synovial joints appear to be grossly overloaded, but the discordance between normal loading pressures *in vivo* and biomechanical capacity *in vitro* remains unexplained and understudied [4].

I believe that the answer lies in the marrow fat. In the femoral head, Pansini *et al.* [5] found the marrow to be 90% fat (93% in men and 87% in women), without significant variation over the 4 decades between 20 and 60 years of age. The small, resected specimens employed in most stress–strain studies provide minimal restraint of fat, and therefore present a distorted view of this most abundant of all subchondral constituents. Rather than being an inert non-participant, or a simple shock absorber, marrow fat may play a central role as a shock distributor that transduces the striking energy burdens imposed by normal impact loading on weight-bearing human joints [6] (Fig. 1).

Two simple models, here called open and closed, illustrate the potential mechanisms of marrow containment during articular load-bearing both *in vivo* and *in vitro*. Trabecular bone has been widely, and appropriately,

Fig. 1 How a compressive load may cause tensile stress in underlying trabecular walls



(**A**) Schematic subchondral compartment at rest. Light blue, hyaline cartilage overlies yellow, fat-filled compartments separated by light grey trabecular walls comprised primarily of calcific crystals bound to type 1 collagen. (**B**) The same compartment under load. Depression of the overlying cartilage has pressurized the fat, and that pressure (large purple arrow) induces tension (green double-headed arrows) within the elastic trabecular walls. The depressed walls, in turn, impinge on the adjacent and subjacent compartments, which also become pressurized but to a lesser extent (smaller purple arrows).

considered to be a poroelastic tissue; that is, it may be seen as a viscous fluid (marrow) within a porous, elastic matrix (trabeculae). To the extent that the marrow carries and distributes loading energy, the mechanics of such a system are hydraulic or closed. To the extent that the fluid escapes such a role and the energy goes directly into the trabeculae, the system will be open.

In the open model, marrow fat and water flow freely when the bone is compressed, and the stress is borne entirely by compression of the trabecular walls. Authoritative studies of articular mechanics have not found evidence of hydraulic support in small excised specimens and are therefore consistent with the open concept [7].

In contrast, the closed model presented in this hypothesis envisions a compartmentalized structure filled with incompressible fatty marrow that is too viscous to allow rapid flow past the series of plates and pores that obstruct its passage. There, the volume of each compartment remains constant as vertical compression produces bulging trabecular walls and floors (Fig. 1). Thus, the force of the impact is transmuted by marrow fat to become tensile stress throughout the strong, elastic, type 1 collagen within these barriers. Further, the injurious potential of impact-loading energy is mollified by a descending pressure gradient that sees each trabecular wall to be buttressed by a somewhat lower pressure on its more distal side.

In the structure suggested by this hypothesis, load-bearing joint members vary widely, and each of them possesses elements somewhere between those of the open and closed models. Young joints are seen as mostly closed, whereas older people's subchondral structure becomes progressively more open as remodelling fenestrates the trabecular walls [8]. The resultant perforations will increase the tissue connectivity and reduce its hydraulic resistance. In so doing, they reduce the capacity to distribute and store the energy imparted by loading impacts.

Previously, we and others have published experimental evidence of hydraulic support under load *in vitro* [9–11]. Some of that work interpreted the issue as one of hydraulic stiffening, but stiffened trabeculae would shift injurious impact stress to proximal articular cartilage and distal cortical bone. Instead, the present, closed model amounts to a compound hydraulic spring that accepts and stores impact energy. In so doing, it cushions all three: cartilage, trabecular bone and cortical bone. Here, I consider specific concerns about previous stress–strain methodology and present an alternative hypothesis based on pressure-loaded intraosseous fat and tension-stressed trabecular walls.

Problems of previous stress–strain studies *in vitro*

Small samples are vented

The wafer-shaped specimens used in many stress–strain studies have been 5 mm (< ¼ in) in thickness, while the alternative cylindrical samples are 5 mm in diameter [12]. These dimensions place all of the trabecular compartments at or near the severed surface and allow interstitial fluid (including fat) to escape freely during compressive loading. Clearly, this unconstrained fluid cannot be expected to bear weight, and the experiment exemplifies a nearly open, or unconfined, system [13]. By definition, loaded poroelastic matrices will distend, and their fluid pressure will rise unless that fluid can escape. In most small-sample studies, such escape is inevitable.

To obviate this concern, some investigators have confined cylindrical specimens within impervious sleeves. Unfortunately, this approach is vulnerable to new problems, including leakage around the cut margins and prevention of lateral expansion under load.

Bones studied *in vitro* are old

Essentially all studies of human bone mechanics use the willed bodies of elderly donors. As people age, their bones undergo continuous modelling and remodelling, which results in thicker, more rod-like trabeculae and wider apertures between adjacent compartments [8, 14, 15]. Both of these changes leave the bone more open, stiffer and less capable of pressurization under load. I feel that appropriate studies of potential hydraulics must use intact bones of younger individuals *in vitro* and intact, load-bearing joints of mature young animals *in vivo*.

Bones differ in trabecular design

Studies of trabecular mechanics have often employed specimens taken from the proximal tibia. But no one site can represent all trabecular bones, since the inner architecture varies greatly between and within individual bones. For instance, as in other weight-bearing articulations, the concave (tibial) side of the knee has a well-formed subchondral plate and more open underlying trabeculae that are relatively thick and stiff. In addition, the marrow compartments are larger and more broadly connected, that is, more open, whereas those in the opposing femoral condyles are smaller and more tightly connected [16].

We found the hydraulic implications of such a different design to be striking in studies of hydraulic resistance to saline infusions in intact canine shoulder bones *in vitro* [17]. There, the mean resistance value was 2186 mmHg min/ml at a depth 9 mm beneath the surface of the convex humeral head, but only 284 mmHg min/ml at the same depth beneath the concave glenoid fossa; an 8-fold difference. If, instead, the mean resistance within 1X1X1 cm cubes resected from the same scapulae are compared with those in the intact humeri, the difference is 50-fold [17]. Hydraulic load distribution is most likely to be significant in the subchondrium of convex joint members, but concave specimens have been studied more often.

Living bones are pre-stressed

Weight-bearing sites are pressurized at rest in living human subjects, where mean baseline pressures were 25.1 mmHg in the tibial epiphyses of anesthetized children and ~20 mmHg in the metaphyses both of children and adults [18, 19].

In their useful review of the mechanical environment of bone marrow, Gurkan and Akkus listed 11 studies of mammalian intraosseous pressure in anesthetized animals, but epiphyseal (i.e. subchondral) data were lacking in all but one. They concluded that the usual medullary, resting pressure of ~30 mmHg was generally ~25% of the concurrent systolic blood pressure [20]. In living puppies, femoral condyle pressures rose further, with stresses as modest as an intraarticular saline injection or passive flexion of the knee [21] and ambulation-induced pressures that were higher still.

Unfortunately, but not surprisingly, there is a dearth of data regarding hydrostatic pressure in the epiphyses of young, normal human beings. A lone, but conspicuous, exception was a value of 1000 mmHg found recently by Beverly *et al*. [22] in the proximal tibia of an ambulating subject. Though limited, these findings, imply that the walls of subchondral compartments are pre-stressed by a continuous tensile stress, which rises further during active weight-bearing.

Pre-stressed mechanics may be analogous to those of a new tennis ball or an automobile tyre, where resilience is enhanced by basal pressurization, but goes flat when that pressure has been lost.

Note that the energy store of articular springs differs in that it is stored entirely in the elastic trabecular walls rather than the pressurized content (intraosseous fat). The coefficients of compressibility for triglycerides are equivalent to those of water and, like water, fat can be expected to transmit but not to store the energy of impact loading [23].

In reasoning analogous to that of this paper, Chen *et al*. [24] recently suggested that human vertebral bodies are strengthened under load by pressurized, intrinsic fat. We differ in that they felt the fat itself to be elastic, whereas I believe the requisite elasticity (as well as the strength of the structure) lies in the type 1 collagen of the trabecular walls.

Marrow viscosity is impaired by adipocyte lysis *in vitro*

Although the energy of impact loading is the essence of fracture risk, that risk will be reduced if marrow fat distributes the impact stress widely. In so doing, it enlists an expanded area of trabeculae to serve as shock absorbers and lessen the likelihood of fracture failures in the immediate subchondrium. To achieve this role, the normal, fatty marrow must resist load-driven displacement from its intertrabecular compartments. The nature of this resistance was studied by Metzger *et al*., who found fresh marrow to be highly viscous. When that marrow was restudied after being frozen and thawed, its viscosity fell by an order of magnitude. They attributed this change to failing integrity of the adipocyte membranes [25]. Since stress–strain studies have rarely been performed in fresh tissues, diminished viscosity has not been recognized previously as a factor contributing to under-recognition of hydraulic support. Nevertheless, many stress–strain studies do reveal a contributing element of viscosity through viscoelastic behaviour. Viscoelasticity is quantified through the related properties of creep and stress relaxation. In both, compressive loading pressurizes the underlying viscous intraosseous fluid. When the loading is arrested, that pressure persists, but it resolves as the fluid flows downhill into adjacent, less pressurized bone.

In studies akin to our work with hydraulic resistance, we examined stress relaxation in intact shoulder bones from normal dogs. Stress relaxation was readily demonstrated: its magnitude was directly related to the rate of loading, and here again it was greater (by a mean factor of 6-fold) in the humeral head than it was beneath the opposing glenoid fossa [26]. I believe that this finding reflects the same resistance to flow of indigenous fat that we found, to a lesser degree, in our studies with infusions of saline [17].

Implications

Osteoarthritis

With this analysis, I propose that load-driven pressurization of a functionally compartmentalized subchondrium plays an important role in the physiology of synovial joints. Serving as a compound hydraulic spring, each bone uses intertrabecular fat to distribute impact energy to trabeculae throughout the epiphysis. As it passes each trabecular baffle, the pressure pulse from every impact decreases and thereby establishes a gradient that descends away from the point of loading. Throughout the descent, the slender trabeculae are buttressed by the somewhat lower pressures in adjacent and subjacent compartments of bone; the overlying articular cartilage and the distal cortical bone are thereby cushioned against the full force of the impact; and spring-stored energy can be recovered to help drive subsequent articular activity [6]. Unfortunately, age and attrition progressively degrade the mechanism as the trabeculae thicken, connecting apertures enlarge, the normal isotropy is lost, and the structure becomes more and more open [8]. These changes, then, play a central role in the vicious cycle that is OA. Trabecular overload begets trabecular stiffness, which worsens overload. As this develops among the trabeculae, the cartilage and cortical bone must accept and dissipate more of each load, and the capacity to store and recover energy is depleted.

Nutrition of cartilage

In each synovial joint, the convex member has a larger surface area than does its concave mate. This means that the contact, loaded area migrates across the convex surface and leaves the non-contact area transiently without direct loading, but sharing in the pressurization of the entire epiphysis [27]. For instance, the entire convex femoral ball is pressurized as it turns within the concave socket. As it does so, the unloaded portion remains internally pressurized by the adjacent load. The resultant bone/cartilage difference may then drive delivery of nutrient solutes from the richly vascular subchondrium. This mechanism rests on the presence of a closed system. Ultimately, as the subchondrium becomes more open, the decreased pressure of loading will diminish this supply of nutrients and may contribute to the cartilagenous thinning of old age. This pressure-driven flow from bone into cartilage is analogous to that from cartilage into the joint space foreseen by Charles McCutchen in his model of weeping lubrication [28].

A metabolic role?

In this article, I have considered the apparent role of marrow fat within adipocytes as a transducer of load and energy in the mechanics of trabecular bone, but it is appropriate to recognize that most current interest in these cells involves their function as producers of adipocytokines [29, 30]. The present hypothesis suggests that adipocytes are normally subjected to cyclic pulses of load-driven hydrostatic pressure. If so, these surges may play an important, but as yet undetermined, role in the release of adipocytokines and the metabolism of normal and osteoarthritic joint members.

Sacrificial bonds

I have stressed the concept that compartmental pressurization will lead to tensile loading of trabecular walls. This point may be important for understanding of the radiographically invisible microcracks between the lamellae within the trabeculae of osteoarthritic bones [31]. The cause of these lesions is thought to involve rupture of the bonds between overlaying lamellar layers within the trabecular wall [32]. There, an inordinate tensile stress may overcome those bonds, with injurious slipping and subsequent thickening and stiffening within the wall [32]. This process, defined as sacrificial bonds and hidden length [33], remains one of the most exciting perspectives in the pathophysiology of OA. I believe it has not been accepted widely among students of bone structure and function because trabeculae have been seen as compressive rather than tensile members. The concept becomes more plausible when the stresses of loading are considered to be more tensile than compressive.

Type 1 collagen: the prototypic tensile protein

As exemplified by tendons and ligaments, those tissues where type 1 collagen is the predominant protein are those that are routinely subjected to tensile stress. There, this protein has been found to be remarkably strong under tension, but of little or no help under compression [34, 35]. I believe that the same principle applies to the type 1 collagen in trabecular bone. The pressure applied by the loaded fat drives this stress, and the intraosseous collagen resists it. Thus, by distributing energy widely to trabecular walls with impressive tensile strength, marrow fat may impart the value that has been needed to explain the capacity of load-bearing synovial joints.

Summary

In summary, this hypothesis presents a new paradigm to further explain the physiology of load bearing in synovial joints and to explore some of the pathophysiology of OA. It deals with intraosseous pressure, a fundamental property that is largely overlooked in current thinking and remains a challenge to the interested investigator. Further, it suggests that marrow fat, the most abundant constituent of epiphyses, may transduce impact energy into tensile stress which is ably borne by the type 1 collagen within calcified trabecular walls. If so, the subchondral trabeculae are not overburdened but function well within their capacity as they bear the pressures imparted by normal joint loading.

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