Follow us @BoneJointRes

Freely available online OPEN ACCESS

BJR

EDITORIAL

Subchondral physiology and vasculo-mechanical factors in load transmission and osteoarthritis

M. C. Beverly, D. W. Murray

From Botnar Research Centre, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences (NDORMS), Oxford, UK

Cite this article: *Bone Joint Res* 2021;10(9):571–573.

Keywords: Subchondral, Hydraulic, Physiology, Vessels, Choke valve, MRI

Intraosseous pressure

Although the blood supply of bone at rest has been well defined by Brookes and others,[1–3] this was always in static or post-mortem tissue. Denham[4] and Day et al[5] recognized that several times body weight was transferred across joints during activity. Joint surface pressures of many atmospheres have been measured. While activity appears to be the primary function of the skeleton, the way in which activity affects perfusion under joints has received little attention.[6,7]

Intraosseous pressure (IOP) has been studied in normal, avascular, and steroid-treated models, but only under static conditions.[8-14] IOP has been recorded in association with forage decompression for painful and osteonecrotic bone conditions.[15,16] Variation in IOP with drugs and on exsanguination has been found.[17,18] IOP was thought to be raised in osteonecrosis, arthritis, and bone pain. However, there has been difficulty in defining normal IOP and using it effectively for clinical purposes.[19]

It is perhaps surprising that IOP is thought to be a constant, measurable by needle insertion. No other solid organ has had internal pressure measured this way. Although IOP recordings vary considerably, they usually exhibit wave patterns synchronous with the arterial pulse, with respiration, and even with drug circulation time.[20] IOP measurements in healthy bone are associated with a proportional pulse pressure (PP), which suggests that IOP reflects conditions at the needle tip rather than being a constant throughout the bone.[21]

Needle clearance by the traditional Ficat method of flushing with saline damages the local circulation and causes a prolonged drop in IOP whereas, after clearance by aspiration, recovery is rapid. It is likely that the injection of saline into normal bone causes a fall in IOP due to blood, fat, saline, heparin, and bone fragments being injected back into the delicate vascular tree.[22] Previous work which showed a raised IOP in ischaemic bone may have been measuring a raised IOP caused by the injection itself.[16]

Proximal arterial occlusion causes a drop in IOP and loss of the associated pulse pressure, whereas proximal venous occlusion significantly raises IOP with preservation of the PP.[21] The difference in pressure between the IOP with a proximal venous clamp in position, then with a proximal arterial clamp, gives a measure of perfusion achievable in the cleared volume at the needle tip.[20] This novel biological concept does not appear to have been considered previously or applied elsewhere. In osteonecrotic or avascular bone the pressure difference is small, while in healthy bone the range is greater.[20] This principle may be applied elsewhere, for example in compartment syndromes by using a proximal tourniquet.[8] Irrespective of the initial needle pressure in a compartment, where the proximal venous to arterial occlusion difference is large, there is a wide perfusion range achievable at the needle tip. If the subtraction difference is small, perfusion at the needle tip is limited and decompression is more urgently required.

Load transmission

Although it has previously been suggested that bone might be hydraulically strengthened, early studies did not support this but their methods were far from physiological. For example, dried grease-saturated bone was used.[5,23] When IOP is studied with physiological loading in an animal model and in vitro, loading causes an instantaneous and proportional increase in subchondral IOP. During proximal arterial occlusion, the rise in IOP is reduced, and with proximal venous

Correspondence should be sent to Michael C. Beverly; email: michael.beverly@btinternet.com

doi: 10.1302/2046-3758.109.BJR-2021-0031.R1

Bone Joint Res 2021;10(9):571–573.

occlusion there is a greater rise. With loading of one body weight the subchondral IOP is much higher than arterial pressure. In the animal model simultaneous recordings made at the femoral head, femoral condyle, and proximal tibia show an IOP rise at all sites when loaded. Saline injections at those sites show that pressure is transmitted through the length of a bone but not across the joints.[7,24] In the perfused in vitro model, cyclical loading to simulate walking causes marked fluctuation in IOP against a falling background.[25] Together these studies suggest that the subchondral bone is slightly flexible and that forces applied to the joint are transferred through the subchondral region partly by hydraulic pressure within a contained environment. These pressures can be very high.[5] It is to be expected that there might be modifications to the subchondral circulation to prevent capillary and fat cell damage.

Anatomy

Burkhardt[26] described normal bone histology and identified some features which might be pressure related, but there are no histological studies that look specifically for evidence of hydraulic pressure load transfer. The subchondral bone plate, capillaries, and trabeculae are relatively delicate. Much of the subchondral tissue is composed of large thin-walled adipocytes or haemopoetic tissue. Orthopaedic surgeons are aware that bone fat is essentially oily or fluid at body temperatures. Soft tissues would be capable of transferring pressure without suffering damage, provided that they are enclosed or contained and supported. The fine subchondral capillaries first described by Hunter (Hunter's mesentery) immediately below healthy cartilage are proportional in number to the thickness of the cartilage.[27] About a centimetre below that in the subchondral plane, there are previously undescribed radiating vessels, best seen on water bright MRI images running parallel to the articular surface.[28] The marks are present in all water bright MRI joint scans but are best seen in the subchondral plane of the upper tibia in axial slices. Radiological opinion is that the marks are vascular. Histologically their position and orientation matches that of the axial plane radiating vessels. The vessels are present in the first subchondral upper tibial slice, peak at 6 mm to 10 mm depth, and are absent by 16 mm depth. Histologically, where the vessels penetrate the cortex near the articular margin, there are complex distortions which could, under load, act as choke valves to prevent loss of blood from the cancellous interior.[29] Collectively these structures tolerate high pressures and pass the load by hydraulic pressure onto the larger trabeculae which converge onto the cortical shaft, transferring force along the shaft to the joint at the other end. There the reverse occurs, passing force from the shaft through the trabeculae, generating pressure in the subchondral region to support the joint surface.[28]

Osteoarthritis

There is an inverse relationship between the number of MRI marks and Kellgren-Lawrence grade of osteoarthritis, both medially and laterally.[28] While cause and effect remain to be separated, the relationship between vascular disease, osteoarthritis (OA), and osteoporosis is of orthopaedic interest.[30–32] Vasculomechanical mechanisms may explain other orthopaedic phenomena, for example the generally mutually exclusive nature of osteoporosis and OA. Several studies have suggested a link between subchondral bone health and OA.[33–35] However, it may be that the softer subchondral bone of the osteoporotic patient flexes proportionately more and is thereby better perfused than the harder sclerotic bone found in OA.

In conclusion, we present a novel understanding of joint physiology and subchondral bone circulation. At rest, subchondral cancellous bone behaves as a perfused tissue with IOP being mainly due to arterial supply rather than venous back pressure or tissue turgor. A single measure of IOP is variable and meaningless, reflecting only conditions at the needle tip. The difference in IOP with proximal venous and arterial occlusion possibly offers a better method for assessing perfusion at the needle tip. A substantial proportion of the load applied to a joint is transmitted through hydraulic pressure to the trabeculae. Subchondral tissues and vascular structures are designed to support hydraulic forces. Vessels are lost in early OA, suggesting that vasculo-mechanical physiology in the subchondral region may play a role in the development of OA. Our proposition opens the door to novel means of research, diagnosis, surveillance, and prognosis and in due course potentially better treatments for OA.

Twitter

Follow the authors @OOEC_Oxford

Supplementary material

Illustrations to expand on the editorial text.

References

1. **Barclay AE**. Micro-arteriography. *Br J Radiol*. 1947;20(238):394–404.
2. **Brookes M**. An anatomy of the osseous circulation. *Bone*. 1986;3:32–35.
3. **Brookes M**, **Revell WJ**. Blood Supply of Bone: Scientific Aspects. Springer Science & Business Media. 2012.
4. **Denham RA**. Hip mechanics. *J Bone Joint Surg Br*. 1959;41-B:550–557.
5. **Day WH**, **Swanson SA**, **Freeman MA**. Contact pressures in the loaded human cadaver hip. *J Bone Joint Surg Br*. 1975;57-B(3):302–313.
6. **Tondevold E**, **Bulow J**. Bone blood-flow in conscious dogs at rest and during exercise. *Acta Orthopaedica Scandinavica*. 1983;54(1):53–57.
7. **Beverly M**, **Mellon S**, **Kennedy JA**, **Murray DW**. Intraosseous pressure during loading and with vascular occlusion in an animal model. *Bone Joint Res*. 2018;7(8):511–516.
8. **Beverly M**, **Murray D**. An interpretation of intraosseous perfusion physiology and the effect of steroids. *J Exp Orthop*. 2020;7(1):34.
9. **Arnoldi C**, **Reimann I**, **Mortensen S**, **et al**. The effect of joint position on juxta-articular bone marrow pressure. Relation to intra-articular pressure and joint effusion--an experimental study on horses. *Acta Orthop Scand*. 1980;51(6):893–897.
10. **Azuma H**. Intraosseous pressure as a measure of hemodynamic changes in bone marrow. *Angiology*. 1964;15(9):396–406.

11. **Hungerford DS**. Pathogenesis of ischemic necrosis of the femoral head. *Instr Course Lect*. 1983;32:252–260.
12. **Iwasaki K**, **Suzuki R**, **Okazaki T**, **Ikeda S**, **Inoue Y**, **Shimauchi R**. The haemodynamics of Perthes' disease. An intraosseous venographic study combined with measurement of the intramedullary pressure. *Int Orthop*. 1982;6(3):141–148.
13. **Jones JP**, **Ramirez S**, **Doty SB**. The pathophysiologic role of fat in dysbaric osteonecrosis. *Clin Orthop Relat Res*. 1993;296:256–264.
14. **Lemperg RK**, **Arnoldi CC**. The significance of intraosseous pressure in normal and diseased states with special reference to the intraosseous engorgement-pain syndrome. *Clin Orthop*. 1978;136:143–156.
15. **Arnoldi CC**, **Linderholm H**, **Müssbichler H**. Venous engorgement and intraosseous hypertension in osteoarthritis of the hip. *J Bone Joint Surg Br*. 1972;54-B(3):409–421.
16. **Ficat RP**. Idiopathic bone necrosis of the femoral head. *J Bone Joint Surg Br*. 1985;67-B(1):3–9.
17. **Gold EW**, **Fox OD**, **Weissfeld S**, **Curtiss PH**. Corticosteroid-induced avascular necrosis: An experimental study in rabbits. *Clin Orthop Relat Res*. 1978;135:272–280.
18. **Gosling DC**, **Sampson WF**, **MacLeod M**, **Hanby AM**, **Slapak M**. Susceptibility of the rabbit and the rat to steroid osteonecrosis--an experimental study. *Transplantation*. 1987;43(5):751–753.
19. **Salzman JG**, **Loken NM**, **Wewerka SS**, **Burnett AM**, **Zagar AE**, **Griffith KR**, **et al**. Intraosseous Pressure Monitoring in Healthy Volunteers. *Prehosp Emerg Care*. 2017;21(5):567–574.
20. **Beverly M**, **Murray D**. Factors affecting intraosseous pressure measurement. *J Orthop Surg Res*. 2018;13(1):187.
21. **Beverly M**, **Urban J**, **Murray D**. Factors affecting physiology of intraosseous pressure measurement. *Osteoarthritis and Cartilage*. 2016;24:S343.
22. **Taylor CC**, **Clarke NM**. Amputation and intraosseous access in infants. *Brit Med J*. 2011;342:d2778.
23. **Swanson SA**, **Freeman MA**. Is bone hydraulically strengthened? *Med Biol Eng*. 1966;4(5):433–438.
24. **Beverly M**, **Marks BE**, **Murray DW**. Subchondral pressures and perfusion during weight bearing. *J Orthop Surg Res*. 2020;15(1):1.
25. **Beverly M**, **Murray D**. An in vitro model to explore subchondral perfusion and intraosseous pressure. *J Exp Orthop*. 2019;6(1):1.
26. **Burkhardt R**. Bone Marrow and Bone Tissue: Color Atlas of Clinical Histopathology: Springer-Verlag. Berlin Heidelberg New York. 1971.
27. **Hunter W**. Of the structure and disease of articulating cartilages. 1743. *Clin Orthop Relat Res*. 1995;42(317):3–6.
28. **Beverly M**, **Stamm G**, **Hamilton TW**, **Murray DW**, **Pandit HG**. Upper tibial MRI vascular marks lost in early knee osteoarthritis. *J Orthop Surg Res*. 2018;13(1):281.
29. **Beverly M**. The Role of Subchondral Circulation in the Physiology of Load Transmission [DPhil in Musculoskeletal Science]. Oxford: University of Oxford. 2019.
30. **Hart DJ**, **Mootoosamy I**, **Doyle DV**, **Spector TD**. The relationship between osteoarthritis and osteoporosis in the general population: the Chingford Study. *Ann Rheum Dis*. 1994;53(3):158–162.
31. **Dequeker J**, **Aerssens J**, **Luyten FP**. Osteoarthritis and osteoporosis: clinical and research evidence of inverse relationship. *Aging Clin Exp Res*. 2003;15(5):426–439.
32. **Im GI**, **Kim MK**. The relationship between osteoarthritis and osteoporosis. *J Bone Miner Metab*. 2014;32(2):101–109.
33. **Shao LT**, **Gou Y**, **Fang JK**, **et al**. Parathyroid hormone (1-34) ameliorates cartilage degeneration and subchondral bone deterioration in collagenase-induced osteoarthritis model in mice. *Bone Joint Res*. 2020;9(10):675–688.
34. **He Z**, **Nie P**, **Lu J**, **et al**. Less mechanical loading attenuates osteoarthritis by reducing cartilage degeneration, subchondral bone remodelling, secondary inflammation, and activation of NLRP3 inflammasome. *Bone Joint Res*. 2020;9(10):731–741.
35. **González-Chávez SA**, **Pacheco-Tena C**, **Quiñonez-Flores CM**, **Espino-Solis GP**, **Burrola-De Anda JI**, **Muñoz-Morales PM**. Positive transcriptional response on inflammation and joint remodelling influenced by physical exercise in proteoglycan-induced arthritis: An animal study. *Bone & Joint Res*. 2020 May 16;9(1):36–48.

Author information:
- M. C. Beverly, MBBS, FRCS, FRCS(Orth), DPhil, Researcher, Botnar/NDORMS, University of Oxford, Oxford, UK.
- D. W. Murray, MA DM FRCS, Professor of Orthopaedics, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences (NDORMS), University of Oxford, Oxford, UK; Nuffield Orthopaedic Centre, Oxford, UK.

Author contributions:
- M. C. Beverly: Conceptualization, Investigation, Writing - original draft.
- D. W. Murray: Supervision, Writing - review & editing.

Funding statement:
- No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article.

Open access funding:
- Open access funding for this study was self-funded.

Acknowledgements:
- We acknowledge support from the Wellcome Trust (Grant 12425), Barbara Marks, and the staff of the Oxford Orthopaedic Engineering Centre and Botnar Research Centre.