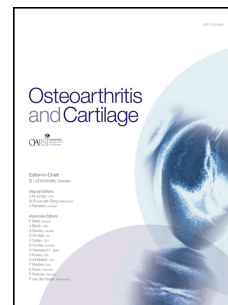


Journal Pre-proof

Subchondral bone — a welcome distraction in OA treatment

Richard M. Aspden, DSc



PII: S1063-4584(22)00652-5

DOI: <https://doi.org/10.1016/j.joca.2022.02.617>

Reference: YJOCA 5016

To appear in: *Osteoarthritis and Cartilage*

Received Date: 1 February 2022

Revised Date: 10 February 2022

Accepted Date: 23 February 2022

Please cite this article as: Aspden RM, Subchondral bone — a welcome distraction in OA treatment, *Osteoarthritis and Cartilage*, <https://doi.org/10.1016/j.joca.2022.02.617>.

This is a PDF file of an article that has undergone enhancements after acceptance, such as the addition of a cover page and metadata, and formatting for readability, but it is not yet the definitive version of record. This version will undergo additional copyediting, typesetting and review before it is published in its final form, but we are providing this version to give early visibility of the article. Please note that, during the production process, errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

© 2022 Published by Elsevier Ltd on behalf of Osteoarthritis Research Society International.

1 **Editorial**

2 **Subchondral bone — a welcome distraction in OA treatment**

3 **Richard M. Aspden, DSc**

4

5 Aberdeen Centre for Arthritis and Musculoskeletal Health

6 Institute of Medical Sciences

7 School of Medicine, Medical Sciences and Nutrition

8 Foresterhill

9 Aberdeen AB25 2ZD

10 UK

11 Email: r.aspden@abdn.ac.uk

12 Of the 291 conditions studied by the Global Burden of Disease study in 2010, hip and knee
13 osteoarthritis (OA) together ranked as the 11th highest contributor to global disability (as measured
14 by years lost to disability)¹. Despite how common it is, how many are affected, and the history of the
15 disease, therapeutic interventions are limited. The earliest descriptions distinguishing OA from
16 rheumatoid arthritis and gout depicted it as a whole-joint disorder associated with inflammation^{2,3}.
17 In the last half of the twentieth century, however, OA became characterized as a cartilage disorder
18 attributed to ‘wear and tear’. Accordingly, during this time, nearly all the research focused on
19 cartilage. While it is fair to say that we now understand far better the complexities and subtleties of
20 this remarkable tissue — its physiology, structure, and function — back then we were no closer to
21 finding a cure for OA. Indeed, by far the most momentous advance in treatment was low-friction
22 arthroplasty, pioneered by John Charnley, in which the whole joint is effectively removed. More
23 recently, it has been proposed that we should consider the joint as an organ^{4,5}; in this sense, we
24 have come full circle.

25 Understanding the interplay between cartilage and the underlying bone that supports it is
26 fundamental to understanding the joint. We then need to add innervation, vascularization, and the
27 other tissues intimately involved, including adipose, fibrous capsule, and synovium. This makes ‘the
28 joint’ at least as complex as any other organ in the body, and one that is frequently underestimated
29 and undervalued. And, of course, every joint is slightly different. So, what is going on in the bone in
30 OA?

31 Studies in patients with hip OA have identified an increased bone mineral density not only in the hip
32 but also in the distal radius, vertebrae, and calcaneus⁶. Scintigraphy has shown increased bone
33 formation in OA joints⁷. Laboratory studies have found alterations in the bone matrix and in
34 osteoblast behaviour. In the hip, we found an increase in cancellous bone volume of about 60%, but
35 this was associated with a reduced mineralization⁸. In addition, although the subchondral bone plate
36 was thicker, it too was less well mineralized⁹.

37 Osteophytes are outgrowths of bone and cartilage found in many patients at the margins of
38 diarthrodial joints or as outgrowths in the central portions of the articular space¹⁰. They form by
39 endochondral ossification¹¹. Together, these and other observations have led to the suggestion that
40 OA is a dysregulated growth process rather than one of degeneration³. These changes in bone
41 metabolism also lead to changes in the morphology of the joint. They can be quantified in 2D and 3D
42 using statistical shape modelling^{12,13}, and work is in progress to use these measures in disease
43 monitoring¹⁴.

44 Have there been any advances in therapeutic approaches to the whole joint? In this issue of
45 Osteoarthritis and Cartilage, Jansen et al. report on the changes occurring in subchondral bone over
46 a period of 2 years from undergoing distraction of the knee joint for OA. Distraction, using an
47 external fixation frame, separates the tibia and femur by 5 mm over a period of 4 days and holds the
48 joint in that position for 6 weeks. The authors have previously presented evidence that in young
49 patients (under 65 years of age) with tibiofemoral OA, 6 weeks of joint distraction results in an
50 increase in cartilage thickness that is still evident at 10 years, albeit somewhat reduced from the
51 initial distracted thickness¹⁵.

52 Baseline assessment of the bone, using CT, suggested that the subchondral bone plate was
53 thickened in the most-affected compartment (MAC), and that the subchondral bone density was
54 increased compared with the least-affected compartment (LAC). One year after distraction therapy,
55 the authors found that the subchondral bone in the MAC had thinned and become less dense. After
56 a further year, these properties were more-or-less unchanged.

57 Distraction will result in unloading of the joint. It is well established that bone responds positively to
58 mechanical loading and that unloading leads to gradual bone loss. In that regard, the changes seen
59 are in the expected direction. Given that neither joint morphology nor knee alignment appear to
60 have been altered, it seems quite dramatic that 6 weeks of unloading, followed by 12 months of
61 reloading, can result in such long-term changes. Could it be that the increased thickness of cartilage

62 in the MAC is sufficient to realign the joint just enough to relieve the biomechanical stresses? Or is
63 5 mm of leg lengthening enough to induce small alterations in gait that have long-term effects? In
64 addition, distracting the joint could stretch the capsule and thus affect its metabolism. The authors
65 point out that other studies have found anabolic and catabolic changes resulting from joint
66 distraction. These may indicate a modification of the whole-joint metabolism, including not only
67 cartilage and bone but also synovial tissue activity that could lead to long-term joint repair¹⁶.

68 Could this approach to treating the whole joint be taken up more widely and used in older patients?
69 The surgery is not complicated, although avoiding infection tracking through the pins will be
70 important. The cost should be far less than a total knee replacement, and rehabilitation is almost
71 immediate — patients are sent home and told to weight bear until the fixator is removed. The
72 results presented in this journal provide further evidence for sustained and beneficial changes in the
73 joint, and suggest that this approach is worthy of serious consideration.

74

75 There were no other contributors to this editorial, and no funding was received. I have no conflicts
76 of interest to declare.

77

78 **References**

- 79 1. Cross M, Smith E, Hoy D, Nolte S, Ackerman I, Fransen M, et al. The global burden of hip and
80 knee osteoarthritis: estimates from the Global Burden of Disease 2010 study. *Ann Rheum*
81 *Dis* 2014;73:1323–1330.
- 82 2. Dobson GP, Letson HL, Grant A, McEwen P, Hazratwala K, Wilkinson M, et al. Defining the
83 osteoarthritis patient: back to the future. *Osteoarthritis and Cartilage* 2018;26:1003–1007.
- 84 3. Aspden RM, Saunders FR. Osteoarthritis as an organ disease: from the cradle to the grave.
85 *European Cells and Materials* 2019;37:74–87.
- 86 4. Loeser RF, Goldring SR, Scanzello CR, Goldring MB. Osteoarthritis: a disease of the joint as an
87 organ. *Arthritis and Rheumatism* 2012;64:1697–1707.
- 88 5. Radin EL, Burr DB, Caterson B, Fyhrie D, Brown TD, Boyd RD. Mechanical determinants of
89 osteoarthrosis. *Seminars in Arthritis and Rheumatism* 1991;21:12–21.
- 90 6. Nevitt MC, Lane NE, Scott JC, Hochberg MC, Pressman AR, Genant HK, et al. Radiographic
91 osteoarthritis of the hip and bone mineral density. The Study of Osteoporotic Fractures
92 Research Group. *Arthritis and Rheumatism* 1995;38:907–916.

- 93 7. Buckland-Wright JC, Macfarlane DG, Lynch JA. Sensitivity of radiographic features and
94 specificity of scintigraphic imaging in hand osteoarthritis. *Revue du Rhumatisme (English Ed)*
95 1995;62:145–265.
- 96 8. Li B, Aspden RM. Composition and mechanical properties of cancellous bone from the
97 femoral head of patients with osteoporosis or osteoarthritis. *Journal of Bone and Mineral*
98 *Research* 1997;12:641–651.
- 99 9. Li B, Aspden RM. Mechanical and material properties of the subchondral bone plate from
100 the femoral head of patients with osteoarthritis or osteoporosis. *Annals of the Rheumatic*
101 *Diseases* 1997;56: 47–254.
- 102 10. McCauley TR, Kornaat PR, Jee WH. Central osteophytes in the knee: prevalence and
103 association with cartilage defects on MR imaging. *American Journal of Roentgenology*
104 2001;176:359–364.
- 105 11. Gelse K, Soder S, Eger W, Diemtar T, Aigner T. Osteophyte development — molecular
106 characterization of differentiation stages. *Osteoarthritis and Cartilage* 2003;11:141–148.
- 107 12. Neogi T, Bowes MA, Niu J, De Souza KM, Vincent GR, Goggins J, et al. Magnetic resonance
108 imaging-based three-dimensional bone shape of the knee predicts onset of knee
109 osteoarthritis: data from the Osteoarthritis Initiative. *Arthritis and Rheumatism*
110 2013;65:2048–2058.
- 111 13. Gregory JS, Waarsing JH, Day JS, Pols HA, Reijman M, Weinans H, et al. Early identification of
112 radiographic osteoarthritis of the hip using an active shape model to quantify changes in
113 bone morphometric features: can hip shape tell us anything about the progression of
114 osteoarthritis? *Arthritis and Rheumatism* 2007;56:3634–3643.
- 115 14. Gregory JS, Barr RJ, Yoshida K, Alesci S, Reid DM, Aspden RM. Statistical shape modelling
116 provides a responsive measure of morphological change in knee osteoarthritis over 12
117 months. *Rheumatology (Oxford)* 2020.
- 118 15. Jansen MP, Mastbergen SC, MacKay JW, Turmezei TD, Lafeber F. Knee joint distraction
119 results in MRI cartilage thickness increase up to ten years after treatment. *Rheumatology*
120 *(Oxford)* 2021.
- 121 16. Watt FE, Hamid B, Garriga C, Judge A, Hrusecka R, Custers RJH, et al. The molecular profile of
122 synovial fluid changes upon joint distraction and is associated with clinical response in knee
123 osteoarthritis. *Osteoarthritis and Cartilage* 2020;28:324–333.