

PECULIARITIES OF TOTAL HIP ARTHROPLASTY IN PATIENTS WITH LOW BONE MASS

<https://doi.org/10.71165/lf70-xbx6>

AUTHOR

Stanislav Bondarenko - Institut des pathologies du rachis et des articulations, Kharkov, Ukraine

SUMMARY

Background: Total hip arthroplasty (THA) is frequently performed in elderly populations where the prevalence of systemic bone loss is high. Despite the clinical success of THA, the impact of undiagnosed osteoporosis and osteopenia on implant stability remains a significant concern, as these conditions may be underestimated due to infrequent preoperative bone mineral density (BMD) screening.

Objective: This review aims to evaluate the incidence of low bone mass in THA candidates, analyze the patterns of periprosthetic bone remodeling, and examine the efficacy of modern uncemented acetabular components in patients with compromised bone quality.

Key Points: Research indicates that 21–32% of patients with severe osteoarthritis also have osteoporosis. Low BMD is associated with increased migration of uncemented components and higher risks of intraoperative periprosthetic fractures. Postoperative bone remodeling studies show significant BMD reductions in Gruen zone 7 and periacetabular regions within the first three years. While porous tantalum and titanium implants are designed to enhance biological fixation through biomimetic porosity and low Young's modulus, their performance in osteoporotic bone is less understood. Increased bone resorption and proinflammatory cytokines in these patients may elevate implant micromobility beyond the 150µm threshold, potentially leading to fibrous tissue formation instead of osseointegration.

Conclusion: Low bone mass significantly influences both intraoperative risks and long-term implant survivorship. Although highly porous acetabular designs offer theoretical advantages for biological fixation, further clinical and experimental studies are required to establish definitive protocols for managing THA in patients with reduced BMD.

KEYWORDS

Arthroplasty, Replacement, Hip; Osteoporosis; Bone Density; Acetabulum; Osseointegration

Incidence of osteoporosis and osteopenia among patients undergoing total hip arthroplasty

Total hip arthroplasty (THA) is one of the most common and clinically successful surgeries in the world [7]. In the United Kingdom, the average age of patients undergoing this procedure is 69.8 years for women and 67.6 for men. In 90% of patients, the indication for surgery is osteoarthritis, and 60% of patients are women [8]. The situation is very similar in the United States, where most patients are aged 55-74 (accounting for 57% of the total number of total hip arthroplasty procedures) [9].

This means that the majority of THA patients are women over 55 years of age. Therefore, we need to consider the incidence of osteoporosis and osteopenia among this patient population. In a clinical study conducted in the United States, 25% of women who underwent THA had latent osteoporosis [10]. Researchers in Finland obtained similar results: of the 53 postmenopausal women who underwent cementless THA, 28% had osteoporosis and 45% had osteopenia [11]. It is estimated that 21–32% of patients in the world with severe osteoarthritis have osteoporosis [12], but figures are probably underestimated due to insufficient evaluation of bone tissue in patients before THA. A survey of 433 orthopaedic surgeons in Switzerland, Austria, New Zealand, Macedonia and Estonia found that 60% of respondents considered it important to take BMD into account before performing THA, but only 4% actually prescribed bone densitometry [13].

In prospective clinical studies, it has been found that low mineral density leads to aseptic loosening of the stem [14] and acetabular component [15]. Continuous acetabular component loosening was recorded within 3–12 months post cementless hip arthroplasty in women with low bone mineral density (BMD), but only within the first three months for those with normal BMD [15]. Similar results were obtained by researchers from China [16]. According to some scientists, loosening of the acetabular component can lead to late loosening of the implants [17].

In addition to postoperative complications, patients with low BMD may also suffer intraoperative complications, the main one being intraoperative periprosthetic fracture of femur, the incidence of which is 0.3–7.8% [18]. Intraoperative fracture of the acetabulum is rare (0.29% in the United States) [19].

In osteoporosis patients undergoing THA, US surgeons use both cemented and uncemented fixation for the acetabular component [20]. However, cemented fixation is the gold standard in elderly patients [21]. Some researchers believe that new porous acetabular components can improve the longevity of uncemented fixation [20].

Bone tissue remodelling around the implants after THA

Bone remodelling around the stem after uncemented THA is well studied, but loss of bone tissue is not always detected. A recent study found a decrease in BMD in Gruen zones 1, 5, 6 and 7 within 13.3 years for several types of uncemented stems [22] (Fig. 1a). In patients with osteoporosis or osteopenia at 2 years of follow-up, a 23% reduction in BMD was found in Gruen zone 7 after uncemented THA [23].

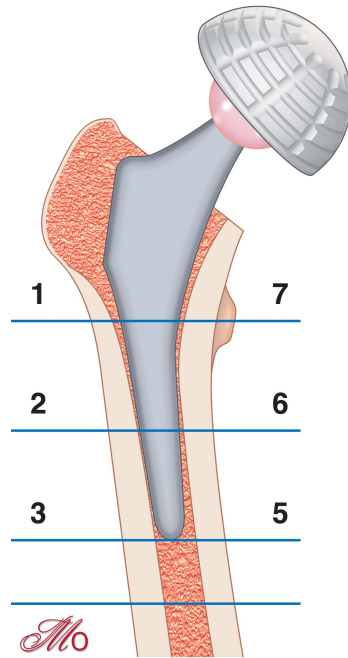


Figure 1. Gruen zones in the proximal femur (a). Adapted from (a) Alm J.J., et al., 2009 [23]; (b) Mueller L., et al., 2006 [28].

Another 10-year study (80 women aged 55–75 years) found that the greatest bone loss occurred in Gruen zone 7 after exactly 2 years, but the bone gradually recovered to baseline status 10 years after surgery [24]. The authors did not report any osteoporosis or osteopenia in their patients, but the exclusion criterion was the absence of metabolic bone disease. Therefore, it is likely that the results obtained are typical of normal bone tissue.

The most long-term study found that 20 years after THA, BMD increased by 11.19% in Gruen zone 7 and by 22.14% in Gruen zones 5 and 6 [25]. This study was performed in a small number of patients (8 women and 6 men, aged 66.2–82.3), with osteoporosis as an exclusion criterion. One possible conclusion is that bone loss does not positively correlate with length of implant survivorship in cases of normal bone tissue. We have not found similar studies of patients with low BMD.

Given the results of studies into the structure of the proximal femur of osteoarthritis patients with normal BMD [26] and reduced BMD [27], bone remodelling around the implants appears to occur in different ways. Patients with osteoarthritis or osteoporosis have architectural microdifferences in the subchondral bone of the femoral head [26]. The combination of osteoarthritis and osteoporosis decreases BMD and the strength of the femoral head [27].

The best clinical outcomes after THA are seen in patients with a high density of bone tissue in the acetabular area [29]. This reduces the risk of acetabular loosening, so it is important to analyse the remodelling of bone tissue around the acetabular cup at different times after THA. All these studies involved a small number of patients with uncemented acetabular cups. Quantitative computed tomography (QCT) (see Table 1) was used to estimate bone tissue density around the acetabular cups.

Authors	Number of patients	Follow-up	Changes in BMD of cancellous bone relative to the cup
[28]	26	1,1 years	↓ 18 % ROI 3 ↓ 30 % ROI 2 ↓ 35 % ROI 1
[29]	54 hips	3 years	↓ 52 %
[30]	26	1,28 years	↓ 20-33 %
[31]	23	2,2 years	↓ 43 % ROI 1 ↓ 53 % ROI 2
[32]	25	1, 3, 10 years	At three years : ↓ 37 % ROI 3 ↓ 60 % ROI 1 ↓ 71 % ROI 2 No change between Year 3 and 10

Interestingly, a study by Kress et al. [2011] found that there were no changes in BMD around the acetabular cups between 3 and 10 years of follow-up [32]. Similar results were obtained [24] for the stem. Bone remodelling of the acetabulum and proximal femur after THA is likely to follow a similar pattern.

Age may be a risk factor for loss of cancellous bone in ROI 3 around the cup [29], but upon analysing these studies, we find that the greatest bone loss occurs in ROI 1 and 2 (dorsal and ventral) within the first three years after surgery (Fig. 1b).

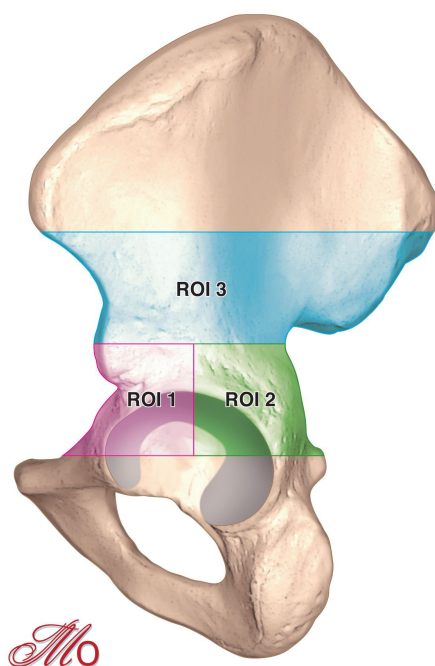


Figure 1. zones around the acetabular cup (b). Key to regions of interest (ROI): ROI 1 - ventral cup, ROI 2 - dorsal, ROI 3 - cranial. Adapted from (a) Alm J.J., et al., 2009 [23]; (b) Mueller L., et al., 2006 [28].

It remains unclear whether bone remodelling after THA in patients with reduced BMD differs from the results obtained by these authors. But given that bone loss can range from 20 to 60% in the first three years (see Table 1), the risk of post-THA complications increases in case of reduced BMD in this zone.

Authors	Number of patients	Follow-up	Changes in BMD of cancellous bone relative to the cup
[28]	26	1,1 years	↓ 18 % ROI 3 ↓ 30 % ROI 2 ↓ 35 % ROI 1
[29]	54 hips	3 years	↓ 52 %
[30]	26	1,28 years	↓ 20-33 %
[31]	23	2,2 years	↓ 43 % ROI 1 ↓ 53 % ROI 2
[32]	25	1, 3, 10 years	At three years : ↓ 37 % ROI 3 ↓ 60 % ROI 1 ↓ 71 % ROI 2 No change between Year 3 and 10

Particular features of modern uncemented acetabular cups and their use in patients with low bone mass

Modern uncemented components are designed to improve biological fixation. This means a stable press-fit of the cup in the acetabulum, with bone ingrowth into the acetabular cup.

More and more studies show the advantages of porous implants for uncemented fixation [34–37].

Porous acetabular components are designed to mimic native bone structure. They have a porosity of 60-80% [38], which is similar to that of cancellous bone (75-90%) [33]. A certain pore size (more than 500µm) and shape are important for bone ingrowth and subsequent biological fixation [39–41]. In addition, the material from which the cup is made can also induce osseointegration. In particular, tantalum induces the differentiation of osteoblasts (cells that form bone tissue) from osteoprogenitor cells [42,43].

An important issue is the survival of acetabular cups in patients with low bone mass (osteopenia or osteoporosis). In general, the pore distribution in these implants mimics normal bone tissue [38], but in patients with osteoporosis, the lower number of trabeculae mean they are spaced further apart [44]. The development of porous materials is aimed not only at improving osseointegration, but also at reducing the risk of stress-shielding [45]. However, the mechanism of action is not understood when the bone has an osteoporotic structure. Furthermore, in patients with osteoporosis or osteopenia, bone elasticity is lower compared to normal bone [46]. Porous implants have a low Young's modulus which is as close as possible to that of normal cancellous bone. It is not known which acetabular component best suits the physical characteristics of the bone tissue in the hip of a patient with low bone mass.

Most modern uncemented acetabular components have a press-fit design, allowing a gap of less than 1 mm between bone and cup [37].

This is especially important in cases of osteoporosis since it provides biological fixation and long-term survival of the implant. At this distance, micromobility of the implant (40-70µm) induces bone ingrowth. Increasing the micromobility to 150µm leads to the formation of fibrous tissue [47]. In an experimental study in dogs, it was found that 500µm micromobility causes fibrous cartilage to form on hydroxyapatite-coated titanium implants 4 weeks after implantation [48], which in turn suppresses the formation of bone tissue. Patients with low bone mass have an increased rate of bone metabolism, which means an increase in bone resorption and possibly an increase in the distance between cup and bone. This, in turn, increases micromobility. Thus, in women with postmenopausal osteoporosis and in patients with rheumatoid arthritis, high blood levels of TGF-β [49], a

proinflammatory cytokine that activates the differentiation of osteoclasts (bone resorbing cells) from precursors through RANKL and increases bone resorption, have been confirmed [50].

Experimental studies have compared different types of porous metals used for modern acetabular components [51-53], but only under the conditions of normal bone tissue. At the same time, a large number of experimental studies have been performed on an oestrogen-deficient model (osteoporosis/osteopenia model) using the same titanium as for dental implants [54-57]. The simulated osteoporosis was found to inhibit the formation of cancellous bone tissue around the implant within 4–24 weeks after implantation.

This is important for understanding the osseointegration of acetabular components into the acetabulum, which is predominantly represented by cancellous bone tissue. However, given the large number of implants available, it remains unclear which is the best for patients with low bone mass.

Low bone mass in patients undergoing THA due to osteoarthritis is therefore an important factor influencing the occurrence of intraoperative (periprosthetic fractures, acetabular fractures) and postoperative (acetabular cup and stem loosening) complications. Implant survival in such patients may be reduced due to greater resorption of bone tissue around the implant, which leads to micromobility and loosening. In addition, there is an inhibition of bone ingrowth, which is an important condition for the osseointegration of porous acetabular components with a press-fit design. This is certainly important given that 21–32% of patients in the world with severe osteoarthritis, most of which undergo THA, have osteoporosis.

However, despite the clinically-proven negative effect of low bone mass on the success of uncemented THA, as well as on implant survivorship, there is a lack of studies that clinically or experimentally evaluate the benefits of using certain types of acetabular components in such conditions. Bone tissue ingrowth around the acetabular cup in such patients after THA has not yet been studied. However, it has been shown bone tissue loss in this area in patients with normal bone mineral density can reach 20–60% in the first three years after THA. Further studies are therefore needed into changes in bone mineral density around the acetabular components in patients with osteoporosis and osteopenia, to determine the feasibility of using highly porous acetabular components.

REFERENCES

1. **Kloppenburg M, Berenbaum F.** Osteoarthritis year in review 2019: epidemiology and therapy. *Osteoarthr Cartil* 2020;28:242–8. [✉ https://doi.org/10.1016/j.joca.2020.01.002](https://doi.org/10.1016/j.joca.2020.01.002).
2. **Cross M, Smith E, Hoy D, Nolte S, Ackerman I, Fransen M, et al.** The global burden of hip and knee osteoarthritis: Estimates from the Global Burden of Disease 2010 study. *Ann Rheum Dis* 2014;73:1323–30. [✉ https://doi.org/10.1136/annrheumdis-2013-204763](https://doi.org/10.1136/annrheumdis-2013-204763).
3. **James SL, Abate D, Abate KH, Abay SM, Abbafati C, Abbasi N, et al.** Global, regional, and national incidence, prevalence, and years lived with disability for 354 Diseases and Injuries for 195 countries and territories, 1990-2017: A systematic analysis for the Global Burden of Disease Study 2017. *Lancet* 2018;392:1789–858. [✉ https://doi.org/10.1016/S0140-6736\(18\)32279-7](https://doi.org/10.1016/S0140-6736(18)32279-7).
4. **Reginster JY, Burlet N.** Osteoporosis: A still increasing prevalence. *Bone* 2006;38:4–9. [✉ https://doi.org/10.1016/j.bone.2005.11.024](https://doi.org/10.1016/j.bone.2005.11.024).
5. **Kanis JA, Diseases WHOC for MB.** Assessment of Osteoporosis at the Primary Health Care Level. WHO Collaborating Centre for Metabolic Bone Diseases, University of Sheffield Medical School; 2008.
6. **Crawford RW, Murray DW.** Total hip replacement: Indications for surgery and risk factors for failure. *Ann Rheum Dis* 1997;56:455–7. [✉ https://doi.org/10.1136/ard.56.8.455](https://doi.org/10.1136/ard.56.8.455).
7. **Learmonth ID, Young C, Rorabeck C.** The operation of the century: total hip replacement. *Lancet* 2007;370:1508–19. [✉ https://doi.org/10.1016/S0140-6736\(07\)60457-7](https://doi.org/10.1016/S0140-6736(07)60457-7).
8. National Joint Registry for England, Wales, Northern Ireland and the Isle of Man (NJR) 14th Annual Report, 2017.
9. **Wolford ML, Palso K, Bercovitz A.** Hospitalization for total hip replacement among inpatients aged 45 and over: United States, 2000-2010. *NCHS Data Brief* 2015;1–8.
10. **Glowacki J, Hurwitz S, Thornhill TS, Kelly M, Leboff MS.** Osteoporosis and Vitamin-D Deficiency among Postmenopausal Women with Osteoarthritis Undergoing Total Hip Arthroplasty. *J Bone Jt Surg - Ser A* 2003;85:2371–7. [✉ https://doi.org/10.2106/00004623-200312000-00015](https://doi.org/10.2106/00004623-200312000-00015).
11. **Mäkinen TJ, Alm JJ, Laine H, Svedström E, Aro HT.** The incidence of osteopenia and osteoporosis in women with hip osteoarthritis scheduled for cementless total joint replacement. *Bone* 2007;40:1041–7. [✉ https://doi.org/10.1016/j.bone.2006.11.013](https://doi.org/10.1016/j.bone.2006.11.013).
12. **Glowacki J.** Osteoporosis and Osteopenia in Patients with Osteoarthritis. *Orthop Rheumatol Open Access J* 2016;2. [✉ https://doi.org/10.19080/oroaj.2016.02.555590](https://doi.org/10.19080/oroaj.2016.02.555590).
13. **Maier GS, Kolbow K, Lazovic D, Maus U.** The Importance of Bone Mineral Density in Hip Arthroplasty: Results of a Survey Asking Orthopaedic Surgeons about Their Opinions and Attitudes Concerning Osteoporosis and Hip Arthroplasty. *Adv Orthop* 2016;2016. [✉ https://doi.org/10.1155/2016/8079354](https://doi.org/10.1155/2016/8079354).
14. **Aro HT, Alm JJ, Moritz N, Mäkinen TJ, Lankinen P.** Low BMD affects initial stability and delays stem osseointegration in cementless total hip arthroplasty in women: A 2-year RSA study of 39 patients. *Acta Orthop*, vol. 83, 2012, p. 107–14. [✉ https://doi.org/10.3109/17453674.2012.678798](https://doi.org/10.3109/17453674.2012.678798).
15. **Finnilä S, Moritz N, Svedström E, Alm JJ, Aro HT.** Increased migration of uncemented acetabular cups in female total hip arthroplasty patients with low systemic bone mineral density. *Acta Orthop* 2016;87:48–54. [✉ https://doi.org/10.3109/17453674.2015.1115312](https://doi.org/10.3109/17453674.2015.1115312).
16. **Liu J, Deng J, Han XS, Xu L.** Bone mineral density decreased is a high risk factor for uncemented acetabular cups migration in female total hip arthroplasty patients. *Zhongguo Gu Shang* 2017;30:33–7. [✉ https://doi.org/10.3969/j.issn.1003-0034.2017.01.008](https://doi.org/10.3969/j.issn.1003-0034.2017.01.008).

17. **Mjöberg B.** Is early migration enough to explain late clinical loosening of hip prostheses? *EFORT Open Rev* 2020;5:113–7. [🔗 https://doi.org/10.1302/2058-5241.5.190014](https://doi.org/10.1302/2058-5241.5.190014).
18. **Bottai V, Dell’Osso G, Celli F, Bugelli G, Cazzella N, Cei E, et al.** Total hip replacement in osteoarthritis: The role of bone metabolism and its complications. *Clin Cases Miner Bone Metab* 2015;12:247–50. [🔗 https://doi.org/10.11138/ccmbm/2015.12.3.247](https://doi.org/10.11138/ccmbm/2015.12.3.247).
19. **Haidukewych GJ, Jacofsky DJ, Hanssen AD, Lewallen DG.** Intraoperative fractures of the acetabulum during primary total hip arthroplasty. *J Bone Jt Surg - Ser A* 2006;88:1952–6. [🔗 https://doi.org/10.2106/JBJS.E.00890](https://doi.org/10.2106/JBJS.E.00890).
20. **Mears SC.** Management of Severe Osteoporosis in Primary Total Hip Arthroplasty. *Curr Transl Geriatr Exp Gerontol Rep* 2013;2:99–104. [🔗 https://doi.org/10.1007/s13670-013-0044-7](https://doi.org/10.1007/s13670-013-0044-7).
21. **Van Praet F, Mulier M.** To cement or not to cement acetabular cups in total hip arthroplasty: a systematic review and re-evaluation. *SICOT-J* 2019;5:35. [🔗 https://doi.org/10.1051/sicotj/2019032](https://doi.org/10.1051/sicotj/2019032).
22. **Brodt S, Matziolis G, Buckwitz B, Zippelius T, Strube P, Roth A.** Long-term follow-up of bone remodelling after cementless hip arthroplasty using different stems. *Sci Rep* 2020;10:10143. [🔗 https://doi.org/10.1038/s41598-020-67189-x](https://doi.org/10.1038/s41598-020-67189-x).
23. **Alm JJ, Mkinen TJ, Lankinen P, Moritz N, Vahlberg T, Aro HT.** Female patients with low systemic BMD are prone to bone loss in Gruen zone 7 after cementless total hip arthroplasty: A 2-year DXA follow-up of 39 patients. *Acta Orthop* 2009;80:531–7. [🔗 https://doi.org/10.3109/17453670903316801](https://doi.org/10.3109/17453670903316801).
24. **Karachalios T, Tsatsaronis C, Efrimis G, Papadelis P, Lyritis G, Diakoumopoulos G.** The long-term clinical relevance of calcar atrophy caused by stress shielding in total hip arthroplasty: A 10-year, prospective, randomized study. *J Arthroplasty* 2004;19:469–75. [🔗 https://doi.org/10.1016/j.arth.2003.12.081](https://doi.org/10.1016/j.arth.2003.12.081).
25. **Sessa G, Costarella L, Puma Pagliarello C, Di Stefano A, Sessa A, Testa G, et al.** Bone mineral density as a marker of hip implant longevity: a prospective assessment of a cementless stem with dual-energy X-ray absorptiometry at twenty years. *Int Orthop* 2019;43:71–5. [🔗 https://doi.org/10.1007/s00264-018-4187-1](https://doi.org/10.1007/s00264-018-4187-1).
26. **He Z, Chu L, Liu X, Han X, Zhang K, Yan M, et al.** Differences in subchondral trabecular bone microstructure and finite element analysis-based biomechanical properties between osteoporosis and osteoarthritis. *J Orthop Transl* 2020;24:39–45. [🔗 https://doi.org/10.1016/j.jot.2020.05.006](https://doi.org/10.1016/j.jot.2020.05.006).
27. **Chu L, Liu X, He Z, Han X, Yan M, Qu X, et al.** Articular Cartilage Degradation and Aberrant Subchondral Bone Remodeling in Patients with Osteoarthritis and Osteoporosis. *J Bone Miner Res* 2020;35:505–15. [🔗 https://doi.org/10.1002/jbmr.3909](https://doi.org/10.1002/jbmr.3909).
28. **Mueller L, Kress A, Nowak T, Pfander D, Pitto R, Forst R, et al.** Periacetabular bone changes after uncemented total hip arthroplasty evaluated by quantitative computed tomography. *Acta Orthop* 2006;77:380–5. [🔗 https://doi.org/10.1080/17453670610046299](https://doi.org/10.1080/17453670610046299).
29. **Zingler K, Haerberle L, Kress A, Holzwarth Ulrich, Raimund Forst, Mueller LA, et al.** Comparison of cortical and cancellous bone remodeling of the pelvis after press-fit cup total hip arthroplasty dependent on patient and prosthesis-specific characteristics: A computed tomography-assisted osteodensitometry study in vivo Katharina Zingler. *Biomed Tech* 2011;56:267–75. [🔗 https://doi.org/10.1515/BMT.2011.105](https://doi.org/10.1515/BMT.2011.105).
30. **Wright JM, Pellicci PM, Salvati EA, Ghelman B, Roberts MM, Koh JL.** Bone density adjacent to press-fit acetabular components: A prospective analysis with quantitative computed tomography. *J Bone Jt Surg - Ser A* 2001;83:529–36. [🔗 https://doi.org/10.2106/00004623-200104000-00007](https://doi.org/10.2106/00004623-200104000-00007).
31. **Mueller LA, Schmidt R, Ehrmann C, Nowak TE, Kress A, Forst R, et al.** Modes of periacetabular load transfer to cortical and cancellous bone after cemented versus uncemented total hip arthroplasty: A prospective study using computed tomography-assisted osteodensitometry. *J Orthop Res* 2009;27:176–82. [🔗 https://doi.org/10.1002/jor.20742](https://doi.org/10.1002/jor.20742).

32. **Kress AM, Schmidt R, Vogel T, Nowak TE, Forst R, Mueller LA.** Quantitative computed tomography-assisted osteodensitometry of the pelvis after press-fit cup fixation: A prospective ten-year follow-up. *J Bone Jt Surg - Ser A* 2011;93:1152–7. <https://doi.org/10.2106/JBJS.J.01097>.
33. **Nouri A, D. P, We C.** Biomimetic Porous Titanium Scaffolds for Orthopedic and Dental Applications. *Biomimetics Learn. from Nat., InTech*; 2010. <https://doi.org/10.5772/8787>.
34. **Meneghini RM, Ford KS, McCollough CH, Hanssen AD, Lewallen DG.** Bone Remodeling Around Porous Metal Cementless Acetabular Components. *J Arthroplasty* 2010;25:741–7. <https://doi.org/10.1016/j.arth.2009.04.025>.
35. **Engh CA, Hopper RH, Engh CA.** Long-term porous-coated cup survivorship using spikes, screws, and press-fitting for initial fixation. *J. Arthroplasty*, vol. 19, *J Arthroplasty*; 2004, p. 54–60. <https://doi.org/10.1016/j.arth.2004.06.004>.
36. **Small SR, Berend ME, Howard LA, Rogge RD, Buckley CA, Ritter MA.** High Initial Stability in Porous Titanium Acetabular Cups: A Biomechanical Study. *J Arthroplasty* 2013;28:510–6. <https://doi.org/10.1016/j.arth.2012.07.035>.
37. **Wiznia DH, Schwarzkopf R, Iorio R, Long WJ.** Factors That Influence Bone-Ingrowth Fixation of Press-Fit Acetabular Cups. *JBJS Rev* 2019;7:e2. <https://doi.org/10.2106/JBJS.RVW.18.00147>.
38. **Chen H, Han Q, Wang C, Liu Y, Chen B, Wang J.** Porous Scaffold Design for Additive Manufacturing in Orthopedics: A Review. *Front Bioeng Biotechnol* 2020;8:609. <https://doi.org/10.3389/fbioe.2020.00609>.
39. **Taniguchi N, Fujibayashi S, Takemoto M, Sasaki K, Otsuki B, Nakamura T, et al.** Effect of pore size on bone ingrowth into porous titanium implants fabricated by additive manufacturing: An in vivo experiment. *Mater Sci Eng C* 2016;59:690–701. <https://doi.org/10.1016/j.msec.2015.10.069>.
40. **Perez RA, Mestres G.** Role of pore size and morphology in musculo-skeletal tissue regeneration. *Mater Sci Eng C* 2016;61:922–39. <https://doi.org/10.1016/j.msec.2015.12.087>.
41. **Ran Q, Yang W, Hu Y, Shen X, Yu Y, Xiang Y, et al.** Osteogenesis of 3D printed porous Ti6Al4V implants with different pore sizes. *J Mech Behav Biomed Mater* 2018;84:1–11. <https://doi.org/10.1016/j.jmbbm.2018.04.010>.
42. **Liu X, Song X, Zhang P, Zhu Z, Xu X.** Effects of nano tantalum implants on inducing osteoblast proliferation and differentiation. *Exp Ther Med* 2016;12:3541–4. <https://doi.org/10.3892/etm.2016.3801>.
43. **Kang C, Wei L, Song B, Chen L, Liu J, Deng B, et al.** Involvement of autophagy in tantalum nanoparticle-induced osteoblast proliferation. *Int J Nanomedicine* 2017;12:4323–33. <https://doi.org/10.2147/IJN.S136281>.
44. **AlAnouti F, Taha Z, Shamim S, Khalaf K, Al Kaabi L, Alsafar H.** An insight into the paradigms of osteoporosis: From genetics to biomechanics. *Bone Reports* 2019;11:100216. <https://doi.org/10.1016/j.bonr.2019.100216>.
45. **Wang S, Zhou X, Liu L, Shi Z, Hao Y.** On the design and properties of porous femoral stems with adjustable stiffness gradient. *Med Eng Phys.* 2020;81:30–38. <https://doi.org/10.1016/j.medengphy.2020.05.003>
46. **Osterhoff G, Morgan EF, Shefelbine SJ, Karim L, McNamara LM, Augat P.** Bone mechanical properties and changes with osteoporosis. *Injury* 2016;47:S11–20. [https://doi.org/10.1016/S0020-1383\(16\)47003-8](https://doi.org/10.1016/S0020-1383(16)47003-8).
47. **Gao X, Fraulob M, Haiat G.** Biomechanical behaviours of the bone-implant interface: A review. *J R Soc Interface* 2019;16. <https://doi.org/10.1098/rsif.2019.0259>.
48. **Søballe K, Hansen ES, B.-Rasmussen H, Jørgensen PH, Bünger C.** Tissue ingrowth into titanium and hydroxyapatite-coated implants during stable and unstable mechanical conditions. *J Orthop Res* 1992;10:285–99. <https://doi.org/10.1002/jor.1100100216>.

49. **Sansone V, Pagani D, Melato M.** The effects on bone cells of metal ions released from orthopaedic implants. A review. *Clin Cases Miner Bone Metab* 2013;10:34–40. [✉ https://doi.org/10.11138/ccmbm/2013.10.1.034](https://doi.org/10.11138/ccmbm/2013.10.1.034).
50. **Li J, Ayoub A, Xiu Y, Yin X, Sanders JO, Mesfin A, et al.** TGF β -induced degradation of TRAF3 in mesenchymal progenitor cells causes age-related osteoporosis. *Nat Commun* 2019;10:1–15. [✉ https://doi.org/10.1038/s41467-019-10677-0](https://doi.org/10.1038/s41467-019-10677-0).
51. **Su KX, Ji P, Wang H, Li LL, Su LZ, Wang C.** In vivo study of 3D printed porous tantalum implant on osseointegration. *Hua Xi Kou Qiang Yi Xue Za Zhi* 2018;36:291–5. [✉ https://doi.org/10.7518/hxkq.2018.03.012](https://doi.org/10.7518/hxkq.2018.03.012).
52. **Wang H, Su K, Su L, Liang P, Ji P, Wang C.** Comparison of 3D-printed porous tantalum and titanium scaffolds on osteointegration and osteogenesis. *Mater Sci Eng C* 2019;104. [✉ https://doi.org/10.1016/j.msec.2019.109908](https://doi.org/10.1016/j.msec.2019.109908).
53. **Bandyopadhyay A, Mitra I, Shivaram A, Dasgupta N, Bose S.** Direct comparison of additively manufactured porous titanium and tantalum implants towards in vivo osseointegration. *Addit Manuf* 2019;28:259–66. [✉ https://doi.org/10.1016/j.addma.2019.04.025](https://doi.org/10.1016/j.addma.2019.04.025).
54. **Vidigal GMI, Groisman M, Gregório LH, Soares GDA.** Osseointegration of titanium alloy and HA-coated implants in healthy and ovariectomized animals: A histomorphometric study. *Clin Oral Implants Res* 2009;20:1272–7. [✉ https://doi.org/10.1111/j.1600-0501.2009.01739.x](https://doi.org/10.1111/j.1600-0501.2009.01739.x).
55. **Duarte PM, Gonçalves PF, Zaffalon Casati M, Sallum EA, Nociti FH.** Age-Related and Surgically Induced Estrogen Deficiencies May Differently Affect Bone Around Titanium Implants in Rats. *J Periodontol* 2005;76:1496–501. [✉ https://doi.org/10.1902/jop.2005.76.9.1496](https://doi.org/10.1902/jop.2005.76.9.1496).
56. **Du Z, Chen J, Yan F, Xiao Y.** Effects of Simvastatin on bone healing around titanium implants in osteoporotic rats. *Clin Oral Implants Res* 2009;20:145–50. [✉ https://doi.org/10.1111/j.1600-0501.2008.01630.x](https://doi.org/10.1111/j.1600-0501.2008.01630.x).
57. **Yamazaki M, Shiota T, Tokugawa Y, Motohashi M, Ohno K, Michi KI, et al.** Bone reactions to titanium screw implants in ovariectomized animals. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 1999;87:411–8. [✉ https://doi.org/10.1016/S1079-2104\(99\)70239-8](https://doi.org/10.1016/S1079-2104(99)70239-8).