2 Early and Late Mechanical Stability of the Cementless Bone-Implant Interface in Total Joint Arthroplasty

Elise C. Pegg, Stephen J. Mellon, and Harinderjit S. Gill

Introduction

The mechanical stability of an orthopedic implant is essential for optimal function and outcome. Implant design and theories about fixation have changed greatly over the years, but what does remain is a belief in the importance of achieving both primary stability and secondary stability.

> Primary stability: Mechanical fixation of an implant achieved at surgery
> Secondary stability: Bone growth directly onto the implant surface, enabling long-term fixation

The purpose of this chapter is to examine our current understanding of how these two stages can be achieved and the various influencing factors.

There are two main techniques used to achieve fixation of orthopedic components: application of polymethylmethacrylate (PMMA) to "cement" the implant into the bone and "cementless" fixation where bone ingrowth directly onto the implant is encouraged using bioactive implant coatings and a rough surface texture. Much of our understanding of primary and secondary stability stems from the early studies of these techniques; therefore, we will begin by discussing the history behind cementless fixation. We will then examine the current theories behind the mechanism by which primary and secondary stability is achieved and finally we will focus on how implant design can affect stability.

Development of Cementless Components

Fixation of early components for joint replacement was largely unsatisfactory; many components were press-fit into the bone and some experimented with screw fixation [1], but loosening remained a common complication [2]. In 1962, Sir John Charnley decided to employ PMMA cement for his low-friction arthroplasty hip [3], and following the success of the procedure, PMMA cement use in orthopedics became common. However, some issues were associated with PMMA cement. One of these was the high temperature resulting from the exothermic polymerization reaction; this could lead to necrosis of the bone in some cases [4]. In addition to this, in 1976, Harris et al. published a paper reporting osteolysis following hip arthroplasty with an unusually high number of macrophages

E.C. Pegg • S.J. Mellon
Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford, UK

H.S. Gill (✉)
Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford, UK

Department of Mechanical Engineering, University of Bath, Bath, UK
e-mail: richie.gill@ndorms.ox.ac.uk

T. Karachalios (ed.), *Bone-Implant Interface in Orthopedic Surgery*,
DOI 10.1007/978-1-4471-5409-9_2, © Springer-Verlag London 2014

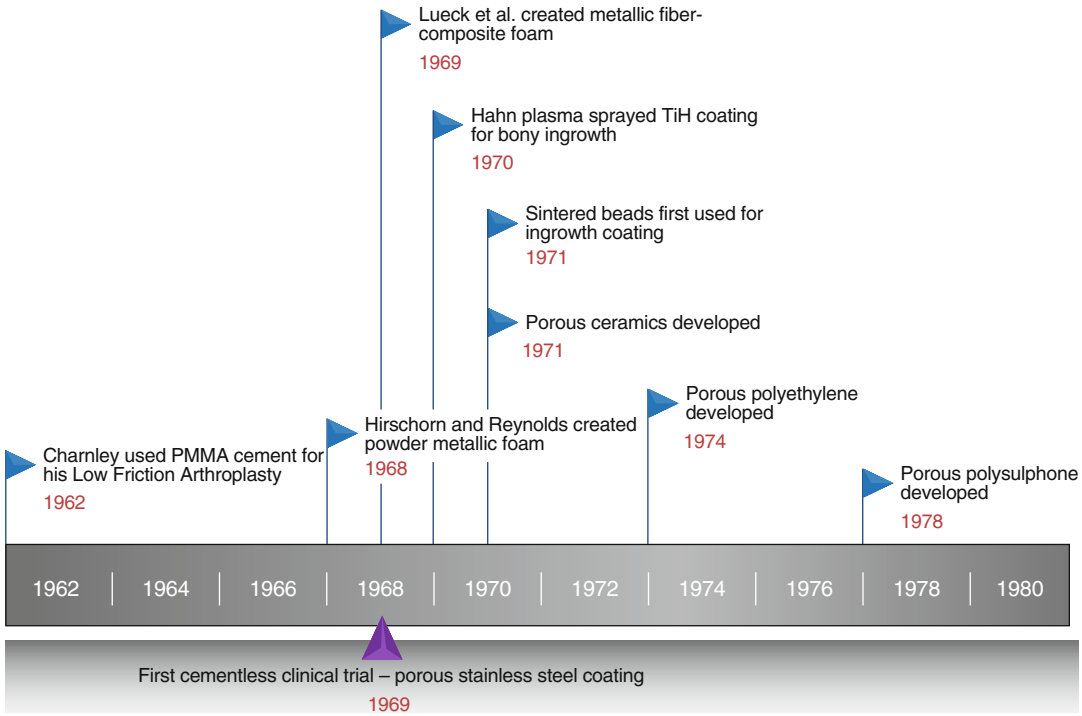

Fig. 2.1 Timeline of significant events in cementless fixation research

and voids in the surrounding tissue [5]. The tissue response was deemed to be an adverse reaction to the PMMA cement and the term "cement disease" was coined to describe this phenomenon. However, it was found later that UHWMPE wear debris was the culprit [6].

Nevertheless, as a result of these findings, attempts to produce coatings for orthopedic implants that remove the requirement of PMMA cements began in 1968 [7]. Hirschorn and Reynolds developed a porous cobalt-chrome alloy material [7]; the foam was produced using powder metallurgy techniques and demonstrated good tissue ingrowth into the open pores after 28 days of implantation in dogs. Despite these promising fixation characteristics, the authors expressed a concern regarding the mechanical strength of the material [8]. In 1969, Lueck et al. suggested that fiber-metal composites could provide a metallic foam which had both the strength and porosity adequate for orthopedic applications [9]. The materials developed by both Hirschorn [10] and Lueck [11] were not used commercially as solid implants, but did become used as coatings on metallic components. Throughout the 1970s, a variety of porous materials and coatings were produced and investigated for cementless applications. These included sintered beads [12], plasma-sprayed coatings of different metallic alloys [13, 14], porous ceramic materials [15], porous polyethylene [16], and porous polysulfone [17], to name but a few (Fig. 2.1). The cementless coatings used today are largely based upon this body of work, and it has also aided our current understanding of the mechanisms behind implant fixation.

For an orthopedic component to become well fixed within the bone, it is necessary for there to be no barrier between the implant and the bone; this barrier may take the form of fibrous tissue. Whether or not fibrous tissue or a fibrocartilage layer develops depends upon the conditions at the bone-implant interface [18]. If lamellar bone is successfully attached to implants without intervening fibrous tissue, this is often termed osseointegration [19]. The mechanism by which osseointegration occurs is generally split into two

Table 2.1 Techniques for measuring micromotion at the bone/stem interface for femoral stems implanted in cadaveric femora [48]

Authors	Year	Method	Precision
Whiteside and Easley [26]	1989	Dial gauges touching implant through holes in femur	5 μm
Walker et al. [27]	1987	Noncontact eddy current displacement transducers measured steel rod touching implant	
Nunn et al. [28]	1989	Cantilever attached to bone with pointer on implant surface	
Schneider et al. [29]	1989	5 transducers on an x-y table measuring both rotation and micromotion	
Burke et al. [30]	1991	Extensometer attached to a pin within a metal cylinder. The pin was attached to the bone. Measured variation in the position of the pin within the cylinder	1 μm
Callaghan et al. [31]	1992		
Engh et al. [32]	1992		
McKellop et al. [33]	1991	Rigid frame attached to bone. Strain gauges measured frame movement	2 μm
Gilbert et al. [34]	1992	LVDTs attached to aluminum cubes on implant	
Berzins et al. [35]	1993	LVDTs attached to three steel spheres in contact with implant	
Hua and Walker [36]	1994	LVDTs attached to plastic targets inserted into femoral component	
Harman et al. [37]	1995	Linear extensometer measured rotational displacement	
Monti et al. [38]	1999	Method used by Harman et al. plus four LVDTs measuring shear micromotion at various locations	2.3–5 μm
Baleani et al. [39]	2000		
Viceconti et al. [40]	2001		
Cristofolini et al. [41]	2003		

stages: primary stability and secondary stability. Primary stability can be achieved without secondary stability; however, secondary stability cannot be achieved without primary stability. Both primary stability and secondary stability are necessary for complete osseointegration of an implant.

Primary Stability

In this section we will examine the following questions:

- How can the primary stability of a component be experimentally assessed?
- How unstable can an implant be without it affecting the function?
- What might a patient do to reduce the stability of their joint replacement?

Four main techniques have been used to examine the primary stability of implants: animal studies, cadaveric tests, computational modelling, and in vivo measurements. The majority of early studies were animal based. A common method employed was the "pull out" method; this is where, after a defined period of implantation time, a tensile force is applied to the implant to remove it and the resistance to that force is related to its fixation [20–22]. A different approach was necessary to examine the effect of instability on the implant region. Pilliar et al. performed a series of studies in dogs, where implants were oscillated to different distances, thus simulating varying degrees of motion [23, 24]; the implantation site was then examined histologically. Another method for assessing the primary stability of cementless components is to implant them into cadaveric bones and measure the movement of the implant within the bone (also called "micromotion") induced by physiological loading; retrieved bones with implants already in situ have also been tested [25] (Table 2.1). Experimental studies of cementless tibial components implanted into cadaveric tibiae showed micromovements in the range of 200–500 μm [42, 43]. It has also been possible to study micromotion using computational modelling. The finite element (FE) method simulates the behavior of a system based upon basic mechanical laws. Several studies have validated such models against experimental data [44]. These simulations

can provide information that is difficult to obtain experimentally. For instance, it is possible to create a complete map of the implant micromotion across the whole bone interface [45, 46], experimentally; this information is limited to where the gauges are positioned. Pancanti et al. used anatomical data from four different patients and simulated implant micromotion while performing nine different tasks; the position and force data were taken from an instrumented hip prostheses [44]. A recent statistical FE analysis demonstrated, over a simulated population of 1,000 cases, that a mismatch of up to 1 mm between the stem and the host bone at random locations of the interface is sufficient to produce a grossly loosened stem in 2 % of the patients, while for another 3–5 %, the high level of predicted micromotion is likely to prevent any substantial osseointegration [47]. These combinations of both experimental and simulation methods can be a powerful tool for examining primary stability.

In vivo assessment of implant stability is also possible through the use of radiostereometric analysis (RSA). Through taking radiographs at a variety of angles, the three-dimensional position of the implant within the bone can be determined; if this is performed over a period of time, the migration of the implant within the bone can be found [48]. According to Kärrholm et al. [49], when used in total hip arthroplasty, RSA has a precision of 0.15 mm in translation and 0.3° in rotation at the 99 % significance level. The four main methods outlined here, which examine primary stability, can help us answer many questions. One of the questions examined early on was how much stability is necessary for an implant to be successful. Several studies have clearly shown that excessive motion at the bone-implant interface has a detrimental effect on the amount of bone growth [23, 24, 50]. Pilliar et al. were the first group to suggest that there might be a micromotion threshold, whereby loosening would occur if this threshold were exceeded [23]. The authors performed a study that dynamically loaded intermedullary implants in dogs by varying degrees of oscillatory motion; when micromotion was beyond 150 μm, fibrous tissue was found surrounding the implant. This threshold value has been supported by several different studies [51–53]. Similar values have been found even on porous surfaces which (sintered beads [23] or plasma-sprayed titanium alloy [30, 51, 54, 55]) promote bone ingrowth.

The micromotion value at which bone formation changes to a combination of bone and fibrocartilage is less clear; but studies have shown it to be in the range of 20–40 μm (Fig. 2.2). In the situation where a fibrous membrane is formed, although this interface may be stable for a certain amount of time, factors such as relative motions or wear particulate can provoke inflammatory reactions causing interface bone resorption and implant loosening [56]. Patient activity shortly after surgery is thought to have a detrimental effect on primary stability of cementless components. In an animal study, dogs implanted with a smooth cementless stem that were allowed to walk early postsurgery showed a higher loosening rate than those that were protected from loading for some time [57]. Several papers have also stated the importance of rotational stability of the femoral stem for the osseointegration process of the prosthesis [58–63]. In vitro studies on cementless femoral stems have shown that the highest values of relative micromotion are recorded when the implanted femur is subjected to high torque components [59–62, 64–69] which induce shear forces at the bone-implant interface [70]. An analysis of 70 failed implants revealed that failure most commonly occurs because of high torques [71]. In vivo investigations based on instrumented hip prostheses found that stair climbing and stand to sit/sit to stand activities generated the highest torsion moments [72–74].

Secondary Stability

In this section, we will examine the following questions:

- What is osteoinduction and how does it occur?
- By what mechanism do cells attach to the implant surface?
- How is bone formed?

Once primary stability has been achieved, biological processes are stimulated which enable bone

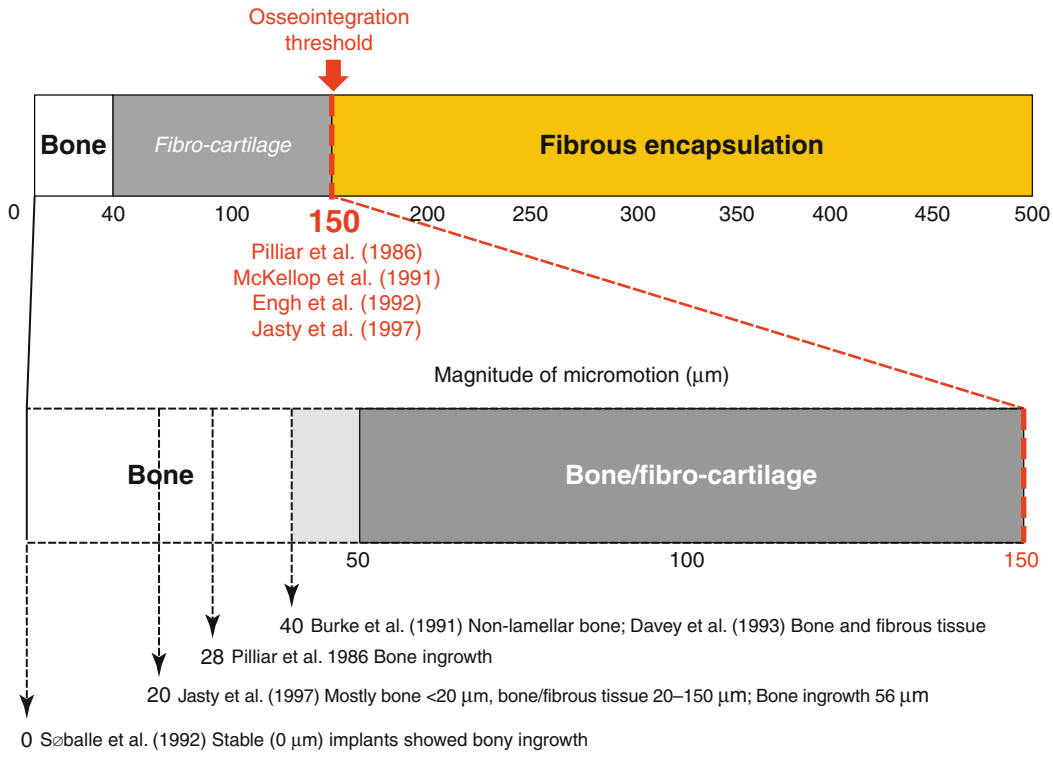

Fig. 2.2 Illustration of the tissue formation resulting from different magnitudes of micromotion

growth to fill the gap between the bone and the implant surface to achieve secondary stability. This process can be split into three parts; osteoinduction, osteoconduction, and osteointegration [75]. Within bone there are four fully differentiated cell types: osteoblasts (bone forming), osteoclasts (bone resorbing), bone-lining cells, and osteocytes (can form or resorb bone) (Fig. 2.3). Osteoclasts are produced from the fusion of mononuclear precursors from the blood, whereas all other cells are differentiated from the local mesenchymal cells (osteoprogenitor cells) [76]. Osteoinduction is the process whereby the osteoprogenitor cells within the bone are stimulated to differentiate into osteoblasts. This process occurs naturally in situations where bone healing is required; injury to the bone causes the release of mediators such as growth factors which simulate osteoinduction [77]. However, in the case of cementless implants coated in hydroxyapatite, which does not release growth factors or other known osteoinductive agents, the mechanism is less clear.

Osteoinduction: stimulation of osteoprogenitor cells to differentiate

Osteoinduction resulting from biomaterials has primarily been reported on calcium phosphate-based material. For this reason it has been hypothesized that the induction results from the dissolution of calcium and phosphate ions [78, 79]. However, there have been some reports of osteoinduction occurring on surfaces which do not contain calcium and phosphate; one theory is that the surface chemistry promotes the calcium and phosphate in solution surrounding the material to precipitate onto the surface [80, 81]. Another possibility is that the injury to the surrounding tissue as a result of the surgery stimulates osteoinduction [75]. Once osteoinduction has occurred and the population of osteoblast cells at the implantation site have increased sufficiently, it is likely that one or more of the cells will make direct contact with

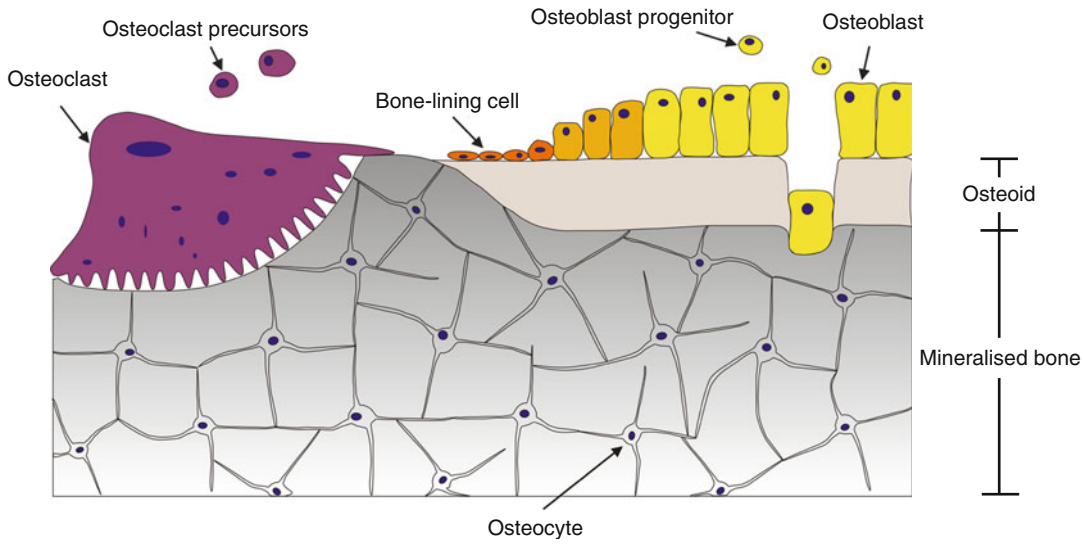

Fig. 2.3 Schematic illustration of the cells within bone [57]

the implant. The osteoconductivity of the surface is a measure of how quickly these cells attach and proliferate across the surface. The interaction of the cells with the surface occurs through transmembrane proteins called "integrins."

Osteoconduction: the attachment and proliferation of cells on the implant

Integrins are situated within the cell membrane and consist of two units (Fig. 2.4). A variety of integrins can be found within the membrane, and they have many different roles in cellular functions, one of which is adhesion. During cell adhesion, the integrins bind to a specific motif found on most extracellular matrix (ECM) proteins. This is the sequence arginine-glycine-aspartic acid (also called RGD) [82]. The bound integrins then cluster together into focal contacts triggering a flow of signalling molecules to and from the cell which cause, amongst other responses, cell adhesion. In the case of a cementless implant, the surface normally does not contain the RGD motif, unless it is artificially added [83], but integrin binding can still occur. This is because after implantation of any material into the body, proteins will quickly be absorbed onto the surface of

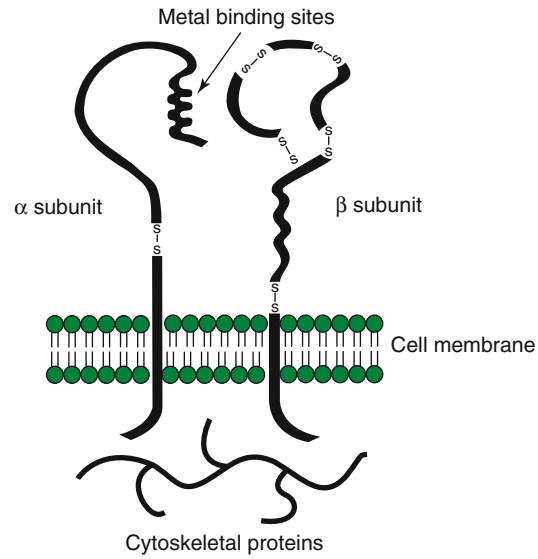

Fig. 2.4 Illustration of the structure of an integrin [118]

the implant; the integrins can therefore bind to these absorbed proteins. It has been shown that the content of the protein layer varies over time; very mobile proteins are observed to adhere early on, and these are later replaced by proteins with a greater affinity to the surface. This is referred to as the "Vroman effect" [84]. The proteins which will adhere to the surface and their final orientation are largely dependent on the surface chemistry,

roughness, and surface energy [85]. The nature of the resultant layer of proteins is thought to affect the response of the osteoblasts to the surface [86].

Osteointegration is the long-term attachment of the bone to the implant; this is the aim of the coating on a cementless implant. After the osteoblast progenitor cells have differentiated into osteoblast cells, and these have adhered to the surface of the implant, bone growth can begin. The osteoblasts proliferate on the surface of the material and the surface of the bone, while proliferating they also secrete a mixture of bone matrix proteins, known as osteoid. Ninety percent of osteoid is Type I collagen, and this provides the structure on which bone mineral is deposited; also released are proteoglycans, glycoproteins, and γ-carboxylated proteins, which regulate cell adhesion, migration, proliferation, and mineralization [87].

Osseointegration: bone formation between the bone and the implant surface

The events leading up to full osseointegration of an implant can take in some cases up to 3 years and often do not begin until 4–12 weeks after implantation [88, 89]. The processes outlined in this section involve many stages, and each stage is very sensitive to the environment surrounding the implant-bone interface. An understanding of these processes and the factors that influence them is vital for ensuring complete fixation of a cementless component.

Design Factors

Research into optimizing the design of cementless components has focussed on two main factors: the morphology of the implant and the surface properties of the implant. These properties affect both primary stability and secondary stability of the implant.

Implant Morphology

The geometrical shape of a cementless hip can vary widely, and there is much dispute as to the optimal design. Khanuja et al. categorized current cementless hips into six different types based upon their design [90]; examination of the outcome of the different designs demonstrated that there was little difference between the survival rates of the different stems (Table 2.2). Nevertheless, there is a clear philosophy behind each design, and the stem type can be tailored for a specific scenario.

Early designs of cementless hip aimed to fix the stem strongly in the distal region of the femur; this meant that many designs had increased stem lengths and large diameters distally. It soon became apparent that this resulted in distal loosening due to stress shielding [91] and designs were modified accordingly. Later designs promoted proximal fixation, and consequently, many cementless hip designs apply coating to just the proximal region [91].

Table 2.2 Summary of clinical studies examining the survivorship of different cementless hip stem designs

Stem type	Description	Total no. of hips	Mean duration of follow-up (range) (year)	Mean stem survivorship (%)	References
1	Single wedge	737	14.1 (6–22.6)	95.1	[1–9]
2	Double wedge	872	11.3 (5–20)	98.7	[10–13]
3A	Tapered, round	1,942	10.1 (2–23)	97.1	[14, 15]
3B	Tapered, spline/curve	94	11.5 (10–14)	91.5	[16]
3C	Tapered, rectangle	196	13.4 (10–17.25)	100.0	[17, 18]
4	Cylindrical fully coated	2,557	12.2 (0–29)	97.8	[19–24]
5	Modular	1,065	9.6 (2–17)	99.5	[25–44]
6	Anatomic	714	12.9 (8–17.2)	97.0	[29–51]

Results from each study have been summed together

The design of a hip stem is often based upon the desired loading region [90]. For instance, tapering of the proximal region can be used to ensure proximal loading (Types 1–3 in Table 2.2). Type 4 hip stems aim for even loading throughout the length of the stem, and thus the entire stem is coated. Type 6 anatomic stems aim to match the endosteal geometry, and thus careful preparation of the bone is required to ensure the patient bone shape matches that of the stem [92]. Reaming of the bone in preparation for implantation is an important factor in both the primary stability of the implant and the resultant stem design. In order to achieve good primary stability, it is necessary to have a close fit between the bone and the implant surface. This is often achieved by rasping a hole in the bone which is slightly smaller than the implant enabling press-fit fixation. Often the distal region of the femur is not reamed; this minimizes the risk of damage to the endosteal blood supply. The shape of the hip stem is also limited to shapes that can be reamed out from above.

One feature of hip stem design for which there has been much debate is the function of a collar and whether the presence of a collar affects the outcome and stability of a cementless hip (Fig. 2.5). Collars were introduced to ensure the stem does not subside into the femur and to distribute load more evenly onto the medial cortex to prevent stress shielding [93]. Broadly speaking, collar designs were split into two categories: large and small. In 1990 Kwong et al. reported bone resorption at the collar-calcar interface [94]; a later clinical study also indicated calcar resorption after 5 years of implantation of large collared stems [95]. The proposed causes for bone resorption primarily relate to the quality of contact between the collar and the calcar [96]; it was suggested that uneven loading could result from poorly cut bone which does not match the collar angle or poor cementing. The small collared stems, however, demonstrated good clinical results, and several studies showed little difference between small collared and collarless stems [97, 98]. Both designs are still used in current practice.

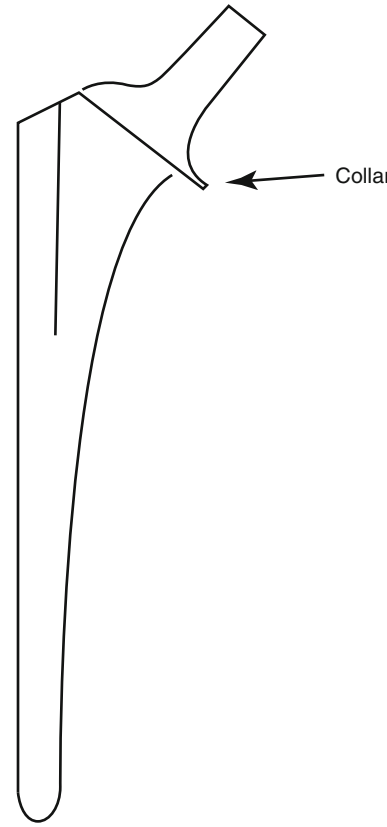

Fig. 2.5 Illustration of a collared hip stem

Coating Design

Cementless implants are designed to promote osteointegration; commercially the surfaces are normally roughened and coated with hydroxyapatite (Table 2.3). Surfaces can be roughened chemically [99] or mechanically [100]; another approach is to apply a rough coating to the implant either by plasma-spraying metallic particles [101] (Fig. 2.6) or bonding metallic "beads" to the surface [100]; alternatively ,the whole implant might be a porous metallic mesh manufactured from tantalum or titanium alloys [102]. These surface coatings are both rough and porous. The pore size of surfaces has been shown to affect osteointegration. Studies have shown that if the pore size is too small, the quality of bone ingrowth is poor [103, 104], whereas very large pores can cause fibrous tissue formation [105]. Good osteointegration is observed with pore sizes of 100–400 μm [106].

Table 2.3 Summary of the different commercial cementless fixation products currently available

Manufacturer	Product	Roughening technique	HA coating method
Smith & Nephew	StikTite	Sintered pure titanium powder	
	RoughCoat	Sintered pure titanium beads	
	Porous Plus	Sintered pure titanium beads	Plasma sprayed
DePuy	Porocoat	Sintered pure titanium beads	
	Duofix	Sintered pure titanium beads	Plasma sprayed
Biomet	Regenerex	Porous titanium alloy foam	
	PPS+OsteoCoat	Plasma-sprayed titanium alloy	Plasma sprayed
	PPS+BoneMaster	Plasma-sprayed titanium alloy	Electrochemical deposition
Zimmer	Trabecular metal	Porous tantalum alloy foam	
	CSTi	Sintered pure titanium powder	Plasma sprayed
	Fiber metal	Titanium fiber mesh	Plasma sprayed
Stryker	Tritanium	Arc-deposited pure titanium onto polyurethane foam	
	PS	Plasma-sprayed pure titanium	
	PureFix	Chemically roughened	Plasma sprayed
	Secur-Fit HA	Arc-deposited pure titanium	Plasma sprayed
	Peri-Apatite	Plasma-sprayed pure titanium	Solution precipitated

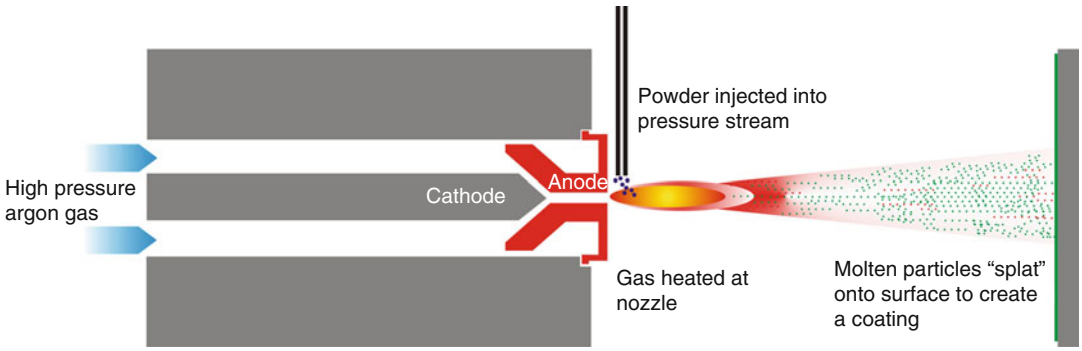

Fig. 2.6 Schematic of the plasma-spraying process used to create porous coatings

Plasma spraying: thermal spraying technique where the coating material is passed into a plasma jet at 10,000 K where it partially melts and is then projected at 300 m/s onto the surface

The adherence of the coating to the substrate is crucial; factors affecting the strength of the coating are the coating thickness, the content and crystallinity of the coating, and parameters involved in the plasma-spraying process such as the heat and the pressure of the jet. All commercial coatings have to be regularly tested, in accordance with international standards [107] to minimize the risk of coating delamination. Hydroxyapatite (HA) has approximately the same chemical composition as the mineral phase of bone and can be synthetically produced or harvested from natural sources (Fig. 2.7). For commercial orthopedic components, HA tends to be plasma sprayed onto implants as a coating to promote osteointegration [108]; however, it can also be deposited electrochemically onto surfaces [109] or by solution precipitated onto a surface [110]. In some cases the entire component can be made from HA where biodegradation is desired [111].

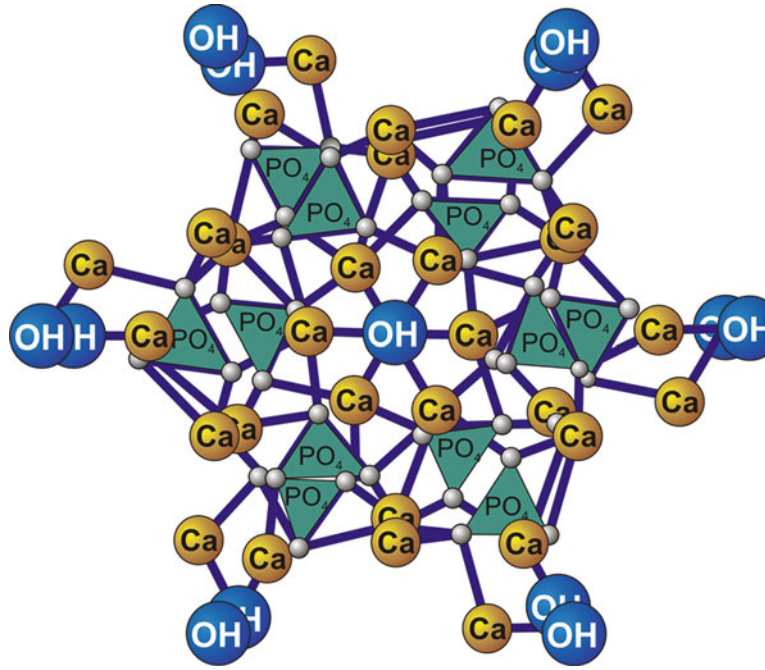

Fig. 2.7 Structure of hydroxyapatite

With the aim of further improving the bioactivity of HA coatings, some researchers have included silicon into the composition [112]. Silicon is known to play a role in the formation of bone [113], and in vitro results have shown increased osteoblastic growth on silicon-doped HA coatings [114, 115]; some in vivo testing has been performed on animals [116, 117]. However, further work is required before the coatings may be used commercially.

Summary

Successful cementless implant fixation is essential for the survivorship and good function of a joint replacement. Fixation is often split into two events: stability of the joint in the initial stages (primary stability) and biological growth towards the surface of the implant resulting in full fixation (secondary stability). Good primary stability of the joint can be achieved by ensuring a press fit between the bone and the implant surface. For this to be possible, it is important that there is a good match between the shape of the implant and the reamed bone. The roughness of the implant surface can also aid primary stability by causing a "scratch fit" into the bone. Many authors support the theory that a certain amount of micromotion of the implant within the bone is acceptable but that if this exceeds the threshold of 150 μm, then fibrous tissue will surround the implant and primary stability will not be possible. The patient activity immediately after surgery is also of great importance and should be minimized to ensure the implant remains fixed. As has been outlined, achieving primary stability is only part of the story. For full fixation of an implant within the bone, bone growth needs to occur to fill the gap between the bone and the implant surface. This secondary fixation relies upon the correct biological signals to be produced to stimulate the osteoblasts to produce mineralized bone. These signals can be influenced by many factors including surface chemistry and roughness. Most commercially available coatings incorporate a rough metallic coating underlayer and a hydroxyapatite top coating; these are applied to the surfaces of implants in the region where bone fixation is desired. More recently, metallic foams manufactured from titanium and tantalum alloys have been introduced which provide a highly porous surface for bone ingrowth

and can be applied as coatings or used as solid materials. These innovations in cementless component design have enabled current cementless components to be a viable alternative to cemented components, with comparable survivorship and outcome. New designs are constantly helping to increase our understanding of what causes an implant to become well fixed and how we can improve the function of these components further.

References

1. Ring P. Complete replacement arthroplasty of the hip by the Ring prosthesis. J Bone Joint Surg Br. 1968; 50B(4):720.
2. Alsen S, Olsson O. Loosening and fracture of Judet's hip prosthesis. Acta Chir Scand. 1956;111(2):158–64.
3. Charnley J. The bonding of prostheses to bone by cement. J Bone Joint Surg Br. 1964;46B:518–29.
4. DePisa J, Sih G, Berman A. The temperature problem at the bone-acrylic cement interface of the total hip replacement. Clin Orthop. 1976;121:95–8.
5. Harris WH, et al. Extensive localized bone resorption in the femur following total hip replacement. J Bone Joint Surg Am. 1976;58A:612–8.
6. Kadoya Y, Kobayashi A, Ohashi A. Wear and osteolysis in total joint replacements. Acta Orthop Scand. 1998;278(S):1–16.
7. Hirschhorn J, Reynolds J. Powder metallurgy fabrication of surgical implant materials. J Metal. 1968;20(8):A36–7.
8. Hirschhorn JS, McBeath AA, Dustoor MR. Porous titanium surgical implant materials. J Biomed Mater Res. 1971;5(6):49–67.
9. Lueck RA, et al. Development of an open pore metallic implant to permit attachment to bone. Surg Forum. 1969;20:456–7.
10. Young FA, Spector M, Kresch CH. Porous titanium endosseous dental implants in rhesus monkeys: microradiography and histological evaluation. J Biomed Mater Res. 1979;13(6):843–56.
11. Turner TM, et al. Bone ingrowth into the tibial component of a canine total condylar knee replacement prosthesis. J Orthop Res. 1989;7(6):893–901.
12. Welsh RP. Surgical implants: the role of surface porosity in fixation to bone and acrylic. J Bone Joint Surg Am. 1971;53A(5):963.
13. Bortz SA, Onesto EJ. Flame and plasma sprayed ceramics for uses in biomedical applications. Composites. 1974;5(4):151–6.
14. Hahn H, Palich W. Preliminary evaluation of porous metal surfaced titanium for orthopedic implants. J Biomed Mater Res. 1970;4(4):571–7.
15. Klawitter JJ, Hulbert SF. Application of porous ceramics for the attachment of load bearing internal orthopedic applications. J Biomed Mater Res. 1971; 5(6):161–229.
16. Sauer BW, et al. The role of porous polymeric materials in prosthesis attachment. J Biomed Mater Res. 1974;8(3):145–53.
17. Spector M, et al. A high-modulus polymer for porous orthopedic implants: biomechanical compatibility of porous implants. J Biomed Mater Res. 1978;12(5): 665–77.
18. Prendergast PJ, Huiskes R, Soballe K. Biophysical stimuli on cells during tissue differentiation at implant interfaces. J Biomech. 1997;30(6):539–48.
19. Albrektsson T, Albrektsson B. Osseointegration of bone implants – a review of an alternative mode of fixation. Acta Orthop Scand. 1987;58(5):567–77.
20. D'Lima DD, et al. Bone response to implant surface morphology. J Arthroplasty. 1998;13(8):928–34.
21. Basarir K, et al. Osseointegration in arthroplasty: can simvastatin promote bone response to implants? Int Orthop. 2009;33(3):855–9.
22. Bereiter H, Burgi M, Rahn BA. Behaviour of the anchorage of a cement-free cup component of a hip-prosthesis over time in animal-experiments. Orthopade. 1992;21(1):63–70.
23. Pilliar RM, Lee JM, Maniatopoulos C. Observations on the effect of movement on bone ingrowth into porous-surfaced implants. Clin Orthop. 1986;208: 108–13.
24. Cameron HU, Pilliar RM, Macnab I. Effect of movement on bonding of porous metal to bone. J Biomed Mater Res. 1973;7(4):301–11.
25. Monti L, Cristofolini L, Viceconti M. Methods for quantitative analysis of the primary stability in uncemented hip prostheses. Artif Organs. 1999;23(9): 851–9.
26. Whiteside LA, Easley JC. The effect of collar and distal stem fixation on micromotion of the femoral stem in uncemented total hip arthroplasty. Clin Orthop Relat Res. 1989;239:145–53.
27. Walker PS, Schneeweis D, Murphy S, Nelson P. Strains and micromotions of press-fit femoral stem prostheses. J Biomech. 1987;20(7):693–702.
28. Nunn D, Freeman MA, Tanner KE, Bonfield W. Torsional stability of the femoral component of hip arthroplasty. Response to an anteriorly applied load. J Bone Joint Surg Br. 1989;71B:452–5.
29. Schneider E, Eulenberger J, Steiner W, Wyder D, Friedman RJ, Perren SM. Experimental method for the in vitro testing of the initial stability of cementless hip prostheses. J Biomech. 1989;22(6–7):735–44.
30. Burke DW, O'Connor DO, Zalenski EB, Jasty M, Harris WH. Micromotion of cemented and uncemented femoral components. J Bone Joint Surg Br. 1991;73B:33–7.
31. Callaghan JJ, Fulghum CS, Glisson RR, Stranne SK. The effect of femoral stem geometry on interface motion in uncemented porous-coated total hip prostheses. Comparison of straight-stem and curved-stem designs. J Bone Joint Surg Am. 1992;74A: 839–48.
32. Engh CA, O'Connor D, Jasty M, McGovern TF, Bobyn JD, Harris WH. Quantification of implant

micromotion, strain shielding, and bone resorption with porous-coated anatomic medullary locking femoral prostheses. Clin Orthop. 1992;285:13–29.
33. McKellop H, Ebramzadeh E, Niederer PG, Sarmiento A. Comparison of the stability of press-fit hip prosthesis femoral stems using a synthetic model femur. J Orthop Res. 1991;9(2):297–305.
34. Gilbert JL, Bloomfeld RS, Lautenschlager EP, Wixson RL. A computer-based biomechanical analysis of the three-dimensional motion of cementless hip prostheses. J Biomech. 1992;25(4):329–40.
35. Berzins A, Sumner DR, Andriacchi TP, Galante JO. Stem curvature and load angle influence the initial relative bone-implant motion of cementless femoral stems. J Orthop Res. 1993;11(5):758–69.
36. Hua J, Walker PS. Relative motion of hip stems under load. An in vitro study of symmetrical, asymmetrical, and custom asymmetrical designs. J Bone Joint Surg Am. 1994;76A:95–103.
37. Harman MK, Toni A, Cristofolini L, Viceconti M. Initial stability of uncemented hip stems: an in-vitro protocol to measure torsional interface motion. Med Eng Phys. 1995;17(3):163–71.
38. Monti L, Cristofolini L, Viceconti M. Methods for quantitative analysis of the primary stability in uncemented hip prostheses. Artif Organs. 1999; 23(9): 851–9.
39. Baleani M, Cristofolini L, Toni A. Initial stability of a new hybrid fixation hip stem: experimental measurement of implant-bone micromotion under torsional load in comparison with cemented and cementless stems. J Biomed Mater Res. 2000;50(4): 605–15.
40. Viceconti M, Cristofolini L, Baleani M, Toni A. Preclinical validation of a new partially cemented femoral prosthesis by synergetic use of numerical and experimental methods. J Biomech. 2001;34(6): 723–31.
41. Cristofolini L, Teutonico AS, Monti L, Cappello A, Toni A. Comparative in vitro study on the long term performance of cemented hip stems: validation of a protocol to discriminate between "good" and "bad" designs. J Biomech. 2003;36(11):1603–15.
42. Branson PJ, et al. Rigidity of initial fixation with uncemented tibial knee implants. J Arthroplasty. 1989; 4(1):21–6.
43. Volz RG, et al. The mechanical stability of various non-cemented tibial components. Clin Orthop. 1988;226:38–42.
44. Pancanti A, Bernakiewicz M, Viceconti M. The primary stability of a cementless stem varies between subjects as much as between activities. J Biomech. 2003;36(6):777–85.
45. Tissakht M, Eskandari H, Ahmed AM. Micromotion analysis of the fixation of total knee tibial component. Comput Struct. 1995;56:365–75.
46. Dammak M, Shirazi-Adl A, Zukor DJ. Analysis of cementless implants using interface nonlinear friction. Experimental and finite element studies. J Biomech. 1997;30(2):121–9.
47. Viceconti M, et al. Primary stability of an anatomical cementless hip stem: a statistical analysis. J Biomech. 2006;39(7):1169–79.
48. Britton C, Lyons G, Prendergast PJ. Measurement of the relative motion between an implant and bone under cyclic loading. Strain. 2004;40(4): 193–202.
49. Karrholm J, et al. Radiostereometry of hip prostheses – review of methodology and clinical results. Clin Orthop. 1997;344:94–110.
50. Cook SD, Thomas KA, Haddad RJ. Histologic analysis of retrieved human porous-coated total joint components. Clin Orthop. 1998;234:90–101.
51. Jasty M, et al. In vivo skeletal responses to porous-surfaced implants subjected to small induced motions. J Bone Joint Surg Am. 1997;79A:707–14.
52. McKellop H, et al. Comparison of the stability of press-fit hip-prosthesis femoral stems using a synthetic model femur. J Orthop Res. 1991;9(2):297–305.
53. Engh CA, et al. Quantification of implant micromotion, strain shielding, and bone-resorption with porous-coated anatomic medullary locking femoral prostheses. Clin Orthop. 1992;285:13–29.
54. Søballe K, et al. Tissue ingrowth into titanium and hydroxyapatite-coated implants during stable and unstable mechanical conditions. J Orthop Res. 1992; 10(2):285–99.
55. Davey JR, O'Connor DO, Burke DW, Harris WH. Femoral component offset. Its effect on strain in bonecement. J Arthroplasty. 1993;8(1):23–6.
56. Spector M, et al. Tissue changes around loose prostheses – a canine model to investigate the effects of an anti-inflammatory agent. Clin Orthop. 1990;261:140–52.
57. Massin P, et al. Cementless fixation of hip prostheses in dogs. Int Orthop. 1991;15(4):299–303.
58. Karrholm J, Snorrason F. Subsidence, tip, and hump micromovements of noncoated ribbed femoral prostheses. Clin Orthop. 1993;287:50–60.
59. Phillips TW, Nguyen LT, Munro SD. Loosening of cementless femoral stems – a biomechanical analysis of immediate fixation with lading vertical, femur horizontal. J Biomech. 1991;24(1):37–48.
60. Nunn D, et al. Tortional stability of the femoral component of hip arthroplasty. Responce to an anteriorly applied load. J Bone Joint Surg Br. 1989;71B:452–5.
61. Sugiyama H, Whiteside LA, Kaiser AD. Examination of rotational fixation of the femoral component in total hip-arthroplasty – a mechanical study of micromovement and acoustic-emission. Clin Orthop. 1989;249:122–8.
62. Schneider E, et al. A comparative-study of the initial stability of cementless hip prostheses. Clin Orthop. 1989;248:200–9.
63. Hua J, Walker PS. Relative motion of hip stems under load. An in vitro study of symmetrical, asymmetrical, and custom asymmetrical designs. J Bone Joint Surg Am. 1994;76A:95–103.
64. Callaghan JJ, et al. The effect of femoral stem geometry on the interface motion in uncemented porous-coated total hip prostheses – comparison of

straight-stem and curved-stem designs. J Bone Joint Surg Am. 1992;74A:839–48.
65. Gustilo RB, et al. Rationale, experience, and results of long-stem femoral prosthesis. Clin Orthop. 1989;249:159–68.
66. Harman MK, et al. Initial stability of uncemented hip stems – an in-vitro protocol to measure torsional interface motion. Med Eng Phys. 1995;17(3):163–71.
67. Ishiguro N, et al. Macrophage activation and migration in interface tissue around loosening total hip arthroplasty components. J Biomed Mater Res. 1997;35(3):399–406.
68. Maloney WJ, et al. Biomechanical and histologic investigation of cemented total hip arthroplasties – a study of autopsy-retrieved femurs after in-vivo cycling. Clin Orthop. 1989;249:129–40.
69. Martens M, et al. The mechanical characteristics of the long bones of the lower-extremity in torsional loading. J Biomech. 1980;13(8):667–76.
70. Alfaro-Adrián J, Gill HS, Murray DW. Should total hip arthroplasty femoral components be designed to subside? A radiostereometric analysis study of the Charnley Elite and Exeter stems. J Arthroplasty. 2001;16(5):598–606.
71. Wroblewski BM. Mechanism of fracture of the femoral prosthesis in total hip-replacement. Int Orthop. 1979;3(2):137–9.
72. Bergmann G, Graichen F, Rohlmann A. Is staircase walking a risk for the fixation of hip implants. J Biomech. 1995;28(5):535–53.
73. Hodge WA, et al. Contact pressures from an instrumented hip endoprosthesis. J Bone Joint Surg Am. 1989;71A:1378–86.
74. Kotzar GM, et al. Telemeterized in-vivo hip-joint force data – a report on 2 patients after total hip-surgery. J Orthop Res. 1991;9(5):621–33.
75. Albrektsson TA, Johansson CJ. Osteoinduction, osteoconduction and osseointegration. Eur Spine J. 2001;10:S96–101.
76. Marks SC, Popoff SN. Bone cell biology: the regulation of development, structure, and function in the skeleton. Am J Anatomy. 1988;183(1):1–44.
77. Frost HM. The biology of fracture healing: an overview for clinicians. Part I. Clin Orthop. 1989;248:283–93.
78. Yuan H, et al. Bone formation induced by calcium phosphate ceramics in soft tissue of dogs: a comparative study between porous α-TCP and β-TCP. J Mater Sci Mater Med. 2001;12(1):7–13.
79. Barrère F, Blitterswijk CAV, Groot KD. Bone regeneration: molecular and cellular interactions with calcium phosphate ceramics. Int J Nanomed. 2006;1:317–32.
80. Fujibayashi S, et al. Osteoinduction of porous bioactive titanium metal. Biomaterials. 2004;25(3):443–50.
81. Takemoto M, et al. Mechanical properties and osteoconductivity of porous bioactive titanium. Biomaterials. 2005;26(30):6014–23.
82. Ruoslahti E, Pierschbacher M. New perspectives in cell adhesion: RGD and integrins. Science. 1987;238(4826):491–7.
83. Massia SP, Hubbell JA. Covalent surface immobilization of Arg-Gly-Asp- and Tyr-Ile-Gly-Ser-Arg-containing peptides to obtain well-defined cell-adhesive substrates. Anal Biochem. 1990;187(2):292–301.
84. Vroman L, et al. Interaction of high molecular weight kininogen, factor XII, and fibrinogen in plasma at interfaces. Blood. 1980;55(1):156–9.
85. Boyan BD, et al. Role of material surfaces in regulating bone and cartilage cell response. Biomaterials. 1996;17(2):137–46.
86. Anselme K. Osteoblast adhesion on biomaterials. Biomaterials. 2000;21(7):667–81.
87. Mackie EJ. Osteoblasts: novel roles in orchestration of skeletal architecture. Int J Biochem Amp Cell Biol. 2003;35(9):1301–5.
88. Galante J, et al. Sintered fiber metal composites as a basis for attachment of implants to bone. J Bone Joint Surg Am. 1971;53-A(1):101–4.
89. Zweynuller K, Lintner K, Semlitsch M. Biologic fixation of a press-fit titanium hip joint endoprosthesis. Clin Orthop. 1988;235:195–206.
90. Khanuja H, et al. Cementless femoral fixation in total hip arthroplasty. J Bone Joint Surg Am. 2011;93-A(5):500–9.
91. Engh CA, Bobyn JD, Gorski JM. Biological fixation of a modified Moore prosthesis. Orthopedics. 1984;7(2):285–98.
92. Goldberg VM. Anatomic cementless total hip replacement: design considerations and early clinical experience. Acta Orthop Belg. 1993;59(S1):183–9.
93. Fagan MJ, Lee AJC. Role of the collar on the femoral stem of cemented total hip replacements. J Biomed Eng. 1986;8(4):295–304.
94. Kwong KS. The biomechanical role of the collar of the femoral component of a hip replacement. J Bone Joint Surg Br. 1990;72B:664–5.
95. Carlsson AS, et al. A large collar increases neck resorption in total hip replacement. 204 hips evaluated for 5 years. Acta Orthop Scand. 1995;66(4):339–42.
96. Jeon I, et al. The biomechanical effect of the collar of a femoral stem on total hip arthroplasty. Comp Meth Biomech Biomed Eng. 2011;14(1):103–12.
97. Meding JB, et al. Comparison of collared and collarless femoral components in primary uncemented total hip arthroplasty. J Arthroplasty. 1997;12(3):273–80.
98. Meding JB, et al. A comparison of collared and collarless femoral components in primary cemented total hip arthroplasty: a randomized clinical trial. J Arthroplasty. 1999;14(2):123–30.
99. Azzam KA, Austin MS, Sharkey PF. Early failure of a nonmodular titanium femoral stem after primary hip arthroplasty. J Arthroplasty. 2010;25(2):333.e1–5.
100. Svehla M. Morphometric and mechanical evaluation of titanium implant integration: comparison of five surface structures. J Biomed Mater Res A. 2000;51(1):15.
101. Park MS, et al. Plasma spray-coated Ti femoral component for cementless total hip arthroplasty. J Arthroplasty. 2003;18(5):626–30.

102. Levine B. A new era in porous metals: applications in orthopaedics. Adv Eng Mater. 2008;10(9):788–92.
103. Bobyn JD, et al. The optimum pore size for the fixation of porous-surfaced metal implants by the ingrowth of bone. Clin Orthop. 1980;150:263.
104. Hulbert SF, et al. Potential of ceramic materials as permanently implantable skeletal prostheses. J Biomed Mater Res. 1970;4(3):433–56.
105. Kent JN, Homsy CA, Hinds EC. Proplast in dental facial reconstruction. Oral Surg Oral Med Oral Path. 1975;39(3):347–55.
106. Itälä AI, et al. Pore diameter of more than 100 μm is not requisite for bone ingrowth in rabbits. J Biomed Mater Res. 2001;58(6):679–83.
107. ISO 13779-1:2008 Implants for surgery – Hydroxyapatite, in part 1: ceramic hydroxyapatite.
108. de Groot K, Geesink R, Klein CP, Serekian P. Plasma sprayed coatings of hydroxylapatite. J Biomed Mater Res. 1987;21(12):1375–81.
109. Rößler S. Electrochemically assisted deposition of thin calcium phosphate coatings at near-physiological pH and temperature. J Biomed Mater Res A. 2003; 64(4):655.
110. Hansson U, Ryd L, Toksvig-Larsen S. A randomised RSA study of Peri-Apatite™ HA coating of a total knee prosthesis. Knee. 2008;15(3):211–6.
111. Veis A, et al. Osseointegration of Osseotite and machined titanium implants in autogenous bone graft. A histologic and histomorphometric study in dogs. Clin Oral Implants Res. 2004;15(1):54–61.
112. Gibson IR, Best SM, Bonfield W. Chemical characterization of silicon-substituted hydroxyapatite. J Biomed Mater Res A. 1999;44(4):422.
113. Carlisle EM. Silicon: a possible factor in bone calcification. Science. 1970;167(3916):279.
114. Thian ES, et al. The response of osteoblasts to nanocrystalline silicon-substituted hydroxyapatite thin films. Biomaterials. 2006;27(13):2692–8.
115. Thian ES, et al. Magnetron co-sputtered silicon-containing hydroxyapatite thin films. An in vitro study. Biomaterials. 2005;26(16):2947–56.
116. Porter AE, et al. Comparison of in vivo dissolution processes in hydroxyapatite and silicon-substituted hydroxyapatite bioceramics. Biomaterials. 2003;24(25): 4609–20.
117. Patel N, et al. A comparative study on the in vivo behavior of hydroxyapatite and silicon substituted hydroxyapatite granules. J Mater Sci Mater Med. 2001;13(12):1199–206.
118. Hynes RO. Integrins: versatility, modulation, and signaling in cell adhesion. Cell. 1992;69(1):11–25.