Materials & Design 216 (2022) 110552

Contents lists available at ScienceDirect

Materials & Design

journal homepage: www.elsevier.com/locate/matdes

On the design evolution of hip implants: A review

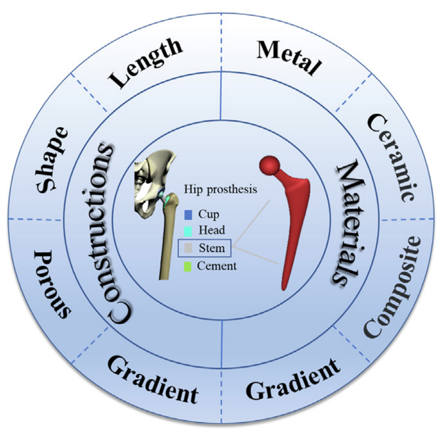
Liyao Guo [a,1], Seyed Ataollah Naghavi [b,1], Ziqiang Wang [a], Swastina Nath Varma [b], Zhiwu Han [a], Zhongwen Yao [a,*], Ling Wang [c], Liqiang Wang [d], Chaozong Liu [b,*]

[a] *Key Laboratory of Bionic Engineering, Ministry of Education, Jilin University, Changchun, China*
[b] *Institute of Orthopaedic & Musculoskeletal Science, University College London, Royal National Orthopaedic Hospital, Stanmore HA7 4LP, UK*
[c] *State Key Laboratory for Manufacturing System Engineering, School of Mechanical Engineering, Xi'an Jiaotong University, Xi'an, China*
[d] *State Key Laboratory of Metal Matrix Composites, Shanghai Jiao Tong University, Shanghai, China*

HIGHLIGHTS

- Research progress of femoral implant in the orthopaedic application is reviewed systematically.
- The design of hip implant is described.
- Materials and constructions design of the hip implants are analyzed and discussed.
- New design method by using bioinspired triply periodic minimal surface in hip implant is presented and discussed.

GRAPHICAL ABSTRACT



ARTICLE INFO

Article history:
Received 9 November 2021
Revised 2 March 2022
Accepted 13 March 2022
Available online 12 October 2021

Keywords:
Artificial hip implant
Femoral stem
Biomaterial
Structure optimization
Stress shielding

ABSTRACT

This manuscript reviews the development of femoral stem prostheses in the biomedical field. After a brief introduction on the development of these prostheses and the associated problems, we describe the standard design of these systems. We review the different materials, constructions, and surfaces used in the development of femoral stems, in order to solve and avoid various problems associated with their use. Femoral stem prostheses have undergone substantial changes and design optimizations since their introduction. Common materials include stainless steel, cobalt–chromium alloy, titanium alloy, and composites. The structural development of femoral stem prostheses, including their length, shape, porosity, and functional gradient construction, is also reviewed. The performance of these prostheses is affected not only by individual factors, but also by the synergistic combination of multiple effects; therefore, several aspects need to be optimized. The main purpose of this study is to summarize various strategies for the material and construction optimization of femoral stem prostheses, and to provide a reference for the combined optimization of their performance. Substantial research is still needed to develop prostheses emulating the behavior of a real human femoral stem.

* Corresponding authors.
E-mail addresses: zwyao@jlu.edu.cn (Z. Yao), chaozong.liu@ucl.ac.uk (C. Liu).

[1] These authors contributed equally to this work.

https://doi.org/10.1016/j.matdes.2022.110552
0264-1275/

Contents

1. Introduction

Bone consists of dense and hard connective tissue, and is considered the strongest material in the human body except for teeth, as well as one of the most dynamic and metabolically active tissues. Bones have a rich blood supply with good self-healing ability, and remain active throughout the life span of an individual. Moreover, bone tissues can adapt to changes in the external and internal environments [1]; this property is termed 'bone remodeling', reflecting the bone's ability to remodel in response to changes in the surrounding environment, which accompanies its renewal process. However, bone fractures can occur if the external loading acting on the bone exceeds its strength, or in the presence of lesions. Bone diseases such as osteoporosis and femoral head necrosis can weaken its load-bearing capacity. Despite the self-healing potential of the corresponding tissues, some bone damages are permanent and irreversible [2]. Femur is an important load-bearing bone that supports the total body's weight during activities such as standing, walking, running, and jumping. Fracture and damage to the hip can result from a variety of causes, such as traffic accidents, falls, osteoporosis, or diseases that affect joint tissues [3]. Hip injury is an extremely serious and common event that can be highly damaging, leading to permanent disability and even death. Worldwide, the number of hip fractures is expected to increase to over 6.26 million by 2050 [4].

Many patients with hip disease have difficulties carrying out daily activities; hence, hip replacement surgery has become a common procedure. Hip replacement involves replacing the diseased hip with a new artificial joint called prosthesis, which is used to transfer the load from the acetabulum to the femur by inserting a metal stem into the latter [5]. Ideally, the stem region of a hip implant should be in full contact with the surrounding femoral cortical bone to achieve stable fixation in a total joint replacement [6]. The hip implant is also responsible for receiving the physiological load from the hip and transfer some portion of it to the surrounding tissues. These are major surgical procedures, which are only undertaken when the disease has progressed to the stage where no alternative treatment is possible; their aim is to relieve pain and improve mobility. More than one million patients undergo successful total hip replacement (THR) procedures each year, and this number is expected to double in the next 20 years [7]. According to the 2013–2018 Chinese Investment Research Report on the Development of the Human Joint Industry (https://www.askci.com/), approximately 200,000 joint replacement operations are performed annually in China, and a similar figure 160,000 was also reported for the UK [8]. In other words, joint replacement is a global problem that requires timely prevention and treatment. After the introduction of artificial hip prostheses, this critical situation has dramatically changed, providing a new option to patients. Artificial hip replacement is a more mature and reliable treatment method to replace the damaged joint and recover its normal function. When an implant is placed in the body, a two-way biological interaction takes place, i.e., the body affects the implant material, and vice versa. Selecting a suitable implant (including the implant material and construction) for the patient is a key factor for the long-term success of the procedure. In addition to have no damaging effects on the host tissue (biosafety), the selected implant must also be able to elicit a beneficial host response for its optimal functioning (bifunctionality).

Artificial hip joints were initially developed in Europe and USA in early 1940 s [9]. A patient with a successful THR can recover his/her full mobility and live a hip pain-free life for approximately 15 years (https://www.nhs.uk/conditions/hip-replacement/). Although patients can return to activity (albeit at lower levels than before) after hip replacement, revision surgery may still be needed. The latter involves the replacement of a previously implanted hip joint, and is required in $\sim$ 10% of all operations [10]. This is usually due to various causes of premature failure, such as the surgical technique employed, patient-related factors, or factors associated with the implant material and design. Malchau et al. [11] reported that $\sim$ 20% of the 10,000 operations performed in Sweden (1979–1998) required revision, and 7% and 13% of the procedures were based on cemented and cementless prostheses, respectively. Revision surgery is an extremely risky procedure, especially for older patients, and complications may include heart/lung problems or death [12]. Therefore, it is important to minimize the likelihood of such complications. Kuiper et al. [10] reported that the most common reason for revision surgery in Norway was a loose stem, which accounted for nearly 64% of the cases.

Prosthetic loosening is a failure mode caused by movement of the prosthesis in bone or bone cement. The most common cause of this problem is a loss of bone mass due to stress shielding [13]. The latter process occurs in the femur, where the prosthesis bears part of the load and thus shields the bone [10,14]. Under normal circumstances, the femur itself is subjected to an external load, which is then transmitted from the femoral head through the neck of the femur to the proximal cortical bone. After implanting a hip prosthesis in a patient, the loading conditions on the cortical bone become much different. When a more rigid component is inserted into the medullary canal, it shares the load with the femur. Owing to the large mismatch between the stiffness of the prosthesis and that of cortical bone, a significant amount of the stress is absorbed by the hip implant, which only leaves a small amount of the load to be transferred to the surrounding host cortical bone [15]. The loading thus shifts from the femur alone to the prosthesis and femur together. As a result, the bone is subjected to less stress, and stress shielding occurs [16]. The upper part of the femur receives a lower load, but the femur around the distal part of the femur is overloaded. According to Wolff's law [17], the skeleton develops the structure that is best suited for its resistance function, in a self-regulation mechanism. Bone areas that are subjected to high load or stress develop an increased mass to resist the load, while those under low load or stress respond by reducing their mass, that is, by becoming less dense and weaker, owing to the absence of stimulation [18]. In other words, bone grows where it is needed and is resorbed where it is not. The growth, absorption, and remodeling of bone are all related to the stress applied on it. In the case of the stress shielding effect of hip implants, it was reported that the surrounding host cortical bone initiates the progression of osteoporosis and remodels itself to become less dense over time [19]. As the bone becomes less dense, the hip implant starts to undergo micromotion, which then increases over time and causes stem loosening. Other causes of implant loosening include osteolytic particle debris.

Two types of hip prosthesis fixation are in use: cemented and cementless (i.e., biological) fixation. The flexibility of cemented and cementless fixation is different, with the latter resulting in a higher stress shielding rate than the former. This is because cementless stems are larger in size and thus have higher stiffness than cemented ones, resulting in greater stress shielding [3].

After hip replacement, the volume of the femur is reduced. Because bones are slow to respond to environmental stimuli, it takes years for their size and mass to change [20]. In an ideal situation, stress shielding should be avoided after performing the initial hip replacement surgery. This will eventually reduce both the amount of bone resorption of the surrounding host bone and the risk of periprosthetic fracture in the revision surgery. However, after some time the prosthesis will no longer be stable in the femur, owing to the reduced support caused by stress shielding, which increases the risk of prosthetic loosening. As the latter may impair the patient's daily life, revision surgery is the only option in such cases. However, previous studies showed that the surrounding bone has a lower mass after removal of the femoral prosthesis [21]. As a result, the new prosthesis used for revision would need to be longer and thicker to fit into the medullary cavity and stabilize the femur. However, the same problem (i.e., loosening due to stress shielding) can occur again: the new prosthesis may work for a few years, until it becomes loose and is replaced, and so on. The replacement cycle varies according to the patient and the prosthesis employed. The recurrent occurrence of these problems highlights the need to eliminate stress shielding.

Swanson [22] proposed that an ideal joint prosthesis should satisfy the following criteria: ① ensure joint clearance; ② allow joint movement and stability; ③ have a simple and practical design; ④ provide long-term fixation; ⑤ be resistant to degeneration; ⑥ be compatible with the human anatomy and biomechanical mechanism, as well as biologically and mechanically acceptable to the host tissues; ⑦ have a straightforward manufacturing and sterilization process, simple manual operation tools and ensure the prosthetic stem is properly installed in place; ⑧ facilitate rehabilitation exercises. Obviously, no artificial joint can currently meet all the above requirements. Satisfying these requirements and producing a perfect artificial hip implant requires the combined effort of a multidisciplinary team consisting of clinicians, material scientists, biomechanical engineers, and experts in other related disciplines. While the era of major design innovations may be over, incremental improvements continue. Currently, in order to make an ideal joint prosthesis, in addition to the above basic requirements, research efforts are focused on three key goals: extending the implant life, improving functional outcomes, reducing complications [23].

Two major issues with current hip implants are the stress shielding effect and the integration of the prosthesis with the surrounding bone tissue. The further development of different types of materials and constructions would allow optimizing and enhancing the performance of hip implants and extend their lifetime. In this paper, we have reviewed various strategies in recent developments of femoral stem prostheses and their optimization process by considering their materials, constructions and surfaces. The reviewed materials include metals (stainless steel, cobalt chromium alloy and titanium alloy), ceramics, and composites, whereas the structural features considered include the length, shape, porosity, and functionally graded porous construction of the optimized femoral stem.

2. Methods

Inclusion criteria of data in this manuscript were: ① literature related to the materials of femoral stem prosthesis; ② literature related to the construction of femoral stem prosthesis; ③ literature on the clinical application of femoral stem prosthesis; ④ literatures related to biomaterials; ⑤ literature related to porous construction. The key words for retrieval: Hip replacement; Femoral stem prosthesis material; Femoral stem prosthesis construction; Biomaterials; Porous construction; Topology optimization; Functional gradient, Biomimetic bone structure; Optimization of femoral stem; Low modulus of elasticity. The retrieval database: Web of Science; Elsevier ScienceDirect; Springer Link; Wiley Online Library; CNKI. The search time range was 2000–2022, but some literatures were traced back to 1969–1999(a total of 19 literatures). These earlier references were obtained while reading the 2000–2022 literatures, we thought they were somehow related and necessary to add. After reading the title, abstract and full text, a total of 125 articles were selected and included for elaboration and discussion, excluding articles with repeated content.

3. Research and development of prosthetic materials

Hip replacements are one of the greatest achievements of the last century in the surgery field. Since the first operation in 1960, many design and material modifications have been explored to improve the effectiveness of the hip replacement procedure and its performance. Because hip injuries are more frequent than other joint injuries in the world, further resources are being allocated to the research and development of artificial hip implants. Continuous advances in materials science and biometrics have led to great improvements in the current generation of artificial hip stems in terms of materials, structural shape, fixed form, and optimized design. Fig. 1 shows the structure of a healthy hip joint and the main components of total hip arthroplasty [24]. The stem is a hip prosthesis attached to the femur. The stem anastomoses to the medullary canal through the epiphysis of the femur. Therefore, stem mainly replaces cancellous bone, occupies part of medullary cavity, and replaces part of femoral head tissue. Therefore, both material optimization and structural optimization should conform to the working environment and characteristics of the femoral stem prosthesis. The first materials used to produce artificial hip implants were platinum, silver, and stainless steel; then, after a long development period, they were replaced by titanium and cobalt–chromium alloys. A variety of structural shapes have gradually emerged and developed, including rectangles, columns, and

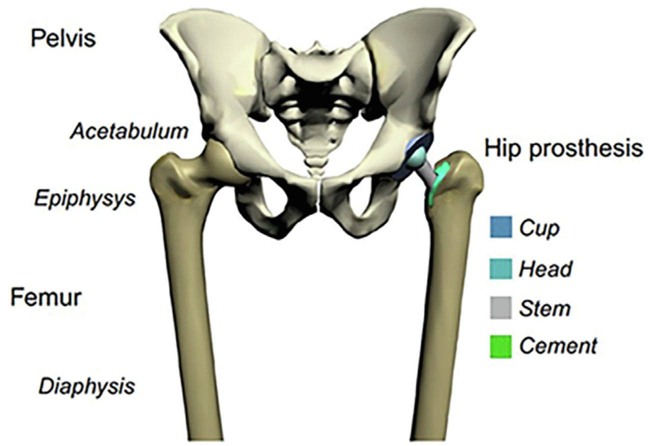


Fig. 1. Healthy hip joint and the main components of a total hip replacement [24].

porous constructions. The development of these materials and structural shapes has undoubtedly enhanced the performance of hip implants, and they can now be successfully applied to the femoral bone and work effectively within the human body. The following sections will review in detail the progress and current status of research in artificial hip implants.

A biomaterial is defined as a natural or man-made material used to guide, complement, or replace the functions of living tissues. When a foreign material is implanted in the body, it may elicit an autoimmune response with a potentially fatal impact on the success of the implant. During the development of artificial hip joints, different manufacturing materials have been introduced and continuously improved. These include cobalt–chromium alloy, titanium alloy, stainless steel, and other materials, which are all biocompatible with the human body [25]. Regardless of the material used for the stem, it alters the biomechanical stress field of the natural femur. The basic requirement for any implant material is that it should be biocompatible and not rejected by the body's autoimmune response. Another important requirement is that it should not produce a high rate of wear debris, resulting in osteolysis and eventually aseptic loosening of the stem [26]. Since the prosthesis must ideally survive for a lifetime inside the human body, it should have no toxic or side effects and be resistant to chemical and electrochemical corrosion by body fluids. In addition, the implant material should have a low mass and an elastic modulus close to that of the host cortical bone surrounding the hip stem. Turning to the bone replacement materials, there are two major issues that need to be addressed, namely, mechanical properties and biocompatibility [27]. In the following sections we will briefly introduce the metallic, composite and functionally gradient materials used for femoral stem prostheses and ceramics materials for femoral head acetabular liner.

3.1. Metal materials

In the early 1960 s, a stainless steel stem was coupled with a polytetrafluoroethylene (PTFE) acetabular cup during total hip arthroplasty (THA). However, the wear resistance of the implant was found to be very poor; hence, stainless steel and PTFE were gradually replaced by Co–Cr–Mo alloy and ultrahigh molecular weight polyethylene (UHMWPE), respectively, and the combination of these two materials showed a good wear resistance. Sensoy et al. suggest that the optimum material option for hip prosthesis is austenitic, annealed and biodurable stainless steel (M6) [28]. Bobyn et al. [29] investigated the effect of the flexibility of the prosthetic material on stress shielding. Two kinds of porous-coated femoral prostheses with different hardness were compared, namely, cobalt–chromium and titanium alloys. The results showed that femoral bone resorption was always much lower with a flexible than a rigid femoral stem. This finding was later corroborated by the work of Sumner and Galante [30], who investigated the use of a low-stiffness, cementless, and porous-coated shank in dogs, which showed reduced loss of proximal bone in the femur. A flexible stem was found to reduce stress shielding and bone resorption compared to a rigid one, but also to increase proximal stress at the prosthesis/bone interface, which can also lead to implant failure [13]. Comparing the mechanical properties of metallic alloys, in Table 1, it is clear that titanium alloy has a lower elastic modulus (110 GPa) than Co–Cr–Mo (200–230 GPa) alloy and stainless steel (200 GPa). Since titanium alloy has a lower mismatch in the elastic modulus value between the mentioned alloys and the cortical bone (17–20 GPa) it would be a better selection between the metallic materials. However, it is worth mentioning that with the currently used titanium alloy hip stems, we still experience significant amount of stress shielding which needs to be reduced by reducing the effective stiffness of the implant as close as possible to the cortical bone elastic modulus. Eingartner et al. [31] monitored 250 cemented femoral stem prostheses based on titanium alloy implanted in 239 patients for an average of 13 years. At the follow-up time, the average Harris Hip Score was 77.3 points. This is the measure (0–100) of dysfunction of the hip implant. Patient with higher scores greater than 70 are considered to have a good result [32]. The long-term follow-up results of this prosthesis were encouraging and could be compared with those of other cemented femoral prostheses successfully used in primary total hip replace-

Table 1
Mechanical properties of bone, alloys, polymers, and ceramics for total hip arthroplasty [3,43,44].

Material	Place of use	Tensile strength (MPa)	Elastic modulus (GPa)
Alloys			
Co–Cr	Hip stem, femoral head and acetabular liner	655–1896	210–253
Co–Cr–Mo		600–1795	200–230
Titanium alloy	Hip stem, acetabular cup	960–970	110
Stainless steel 316L	Hip stem	465–950	200
Polymers			
UHMWPE	Acetabular liner/socket	21	1
PTFE		28	0.4
Ceramics			
Zirconia	Femoral head and acetabular liner	820	220
Alumina		300	380
Cortical Bone		77–98	17–20
Trabecular bone		25–55	0.2–2

ment. In addition, the combination of titanium and cement used in the femoral stem did not increase the risk of aseptic loosening. Cubillos et al. [33] evaluated and compared the chemical composition and microstructure of ISO 5832–9 austenitic stainless steel femoral stems produced by different manufacturers. The elemental compositions were determined using glow discharge emission spectroscopy. The microstructure of the stem was characterized by optical microscopy, scanning electron microscopy, X-ray diffraction, and Vickers hardness measurements. The results showed that slight differencesin chemical and microscopic differences (although within the requirements of the technical standards) led to variations in grain size, Z-phase precipitates, and hardness. The control of these characteristics has clinical significance and can directly affect the fatigue and corrosion resistance of the material.

3.2. Toxicity of metallic implants

Some widely used titanium alloy, such as Ti-6Al-4V contains almost 90% titanium, 6% aluminium and 4% vanadium. Toxicity of aluminium and vanadium have always been a serious concern for orthopaedic surgeons. It has been known that releasing of vanadium and aluminium ions during the dissolution of the alloy can promote the discoloration of the surrounding tissue and may cause inflammatory response within the body [34]. Some studies have also shown that the ionized Ti-6Al-4 V particles released from the implant can effect the deposition of a mineralized matrix via altered expression of the osteoblasts. Ion particles can also prevent the normal development of osteoblasts by disrupting the normal cell division in bone marrow [35]. It is also known that release of aluminium particles can cause Alzheimer's disease [36] and breast cancer [37]. These biological effects can lead to implant loosening due to osteolysis, cause pain inside the patient and have detrimental effects on the human body [38]. To prevent these negative health effects of Ti-6Al-4V, recent studies have focused on developing aluminium and vanadium free titanium alloy (Ti 0.4O 0.5Fe 0.08C) for medical application such as implants and osteosynthesis [39]. This alloy contains O, C, Fe, Au, Si, Nb or Mo as alloying elements and have been shown to exhibit a higher yield tensile strength and elongation at fracture when compared to the generic Ti-6Al-4V. This study also showed that Ti 0.4O 0.5Fe 0.08C alloy has a better corrosion resistance and biocompatibility than Ti-6Al-4V [39]. Similar to Titanium alloy implants, stainless steel (AISI 316L) implants have also caused concerns about the long-term biological effects of released metal ions. Nickel and chromium ions are usually produced due to corrosion and wear [40]. The main issue about the metal ions or fretting debris that can be released from a stainless steel implants is that they can cause allergic reactions and skin conditions such as swelling and reddening. Also, these elements can cause cancer and teratogenicity in humans [41]. To prevent these biological effects, some studies proposed using high-nitrogen nickel-free stainless steel (Fe–Cr–Mn–Mo–N) which also enhances the mechanical properties of this type of stainless steel [42]. Hence, we strongly recommend that these newly developed metals alloy such as titanium alloys which are free of any aluminium and vanadium and stainless steel which contain high-nitrogen and no nickel element can be promising to be replaced by the currently available orthopaedic implants.

3.3. Ceramic materials

In addition to metals, ceramics such as alumina and zirconia are also widely used in femoral head and acetabular liner prostheses. It has been reported that the wear rate of alumina on UHMWPE is 20 times lower than that of metals on the same substrate [27]. Moreover, the elastic moduli of Co-Cr-Mo alloy and alumina are approximately 10 and 19 times that of cortical bone, respectively (Table 1).

As shown in the Table 1, the elastic moduli of these materials are significantly different, and the difference between their values and that of the human cortical bone is another direct cause of stress shielding. Reducing the effective stiffness of the hip stem to cortical bone elastic moduli can significantly help reduce the amount of stress shielding effect.

3.4. Ceramic surface coating

Ceramic materials are also used to coat the surface of the cementless hip implants. This is mostly beneficial to further enhance the osseointegration of the surrounding trabecular and cortical bone to the surface of the hip stem, strengthening the bone-implant interface. Harboe et al. [45] implanted hydroxyapatite (HA) and electrochemically deposited calcium phosphate (CP) on titanium-based femoral stems with similar shapes in 35 and 12 goats, respectively. The authors measured the extraction force of the femoral stem and evaluated bone adhesion using a microscope. After applying exclusion criteria, 4 and 11 goats were selected for tests in the CP and HA group, respectively. After 6 months, the retention force of the CP coating was found to be (47 N) significantly lower than that of the HA coating (1,696 N). Bone sections showed that the CP-coated femoral stems had a lower adhesion than the HA group ones and displayed a higher amount of connective tissue at the bone/implant interface. The results showed that HA had better bone alignment in loaded implants and required a greater extraction force. The impact of different coatings on hip implants should be further evaluated. Xu et al. [46] introduced the use of a broad HA coating to fix a tapered femoral stem. This approach could achieve long-term biological fixation and maintain normal bone movement around the prosthesis. A total of 92 hip replacements with hydroxyapatite-coated (Corail) hip prostheses were monitored in 81 patients. The results showed good clinical outcomes, with an average Harris Hip Score of 92.3 ± 5.6 (72–100). A long-term analysis confirmed the reliability of the functional and radiological results.

Since the first applications of cementless hip implants, researchers have been attempting to identify the best surface coatings to enhance the osseointegration process and strengthen the bone–implant interface. Barakat et al. [47] examined the survival rate, functional, and radiological results of hydroxyapatite ceramic-coated femoral stems used in revision THA. A total of 30 hips were examined in 27 patients, and the average follow-up period was 44 months. The study found that the prosthesis stem exhibited good results in terms of functional outcome, incidence of thigh pain, radiological loosening, and survival rate of the prosthesis, with no loosening cases and 100% survival rate. The authors noted that the adopted technique is suitable for various clinical scenarios, such as adverse reactions to metal debris (ARMD), aseptic loosening, and second-stage revision of prosthetic infections. Critchley et al. [48] used radiostereometric analysis (RSA) to evaluate the long-term migration of Corail hydroxyapatite-coated cementless prostheses over a 14-year follow-up period, establishing an acceptable long-term migration pattern for cementless prostheses coated with HA. The subsidence of the femoral stem was measured and compared with previous measurements at 6 months and 1, 2, and 6 years. It was found that, during an average follow-up time of 14 years, the group of cementless prostheses had an average subsidence of 0.7 mm (range 0.06–3.61 mm). The study concluded that subsidence occurred within the first 6 months, after which the implant continued to stabilize over 14 years. This study described an acceptable long-term migration pattern that can be compared with that of new hydroxyapatite cementless prostheses.

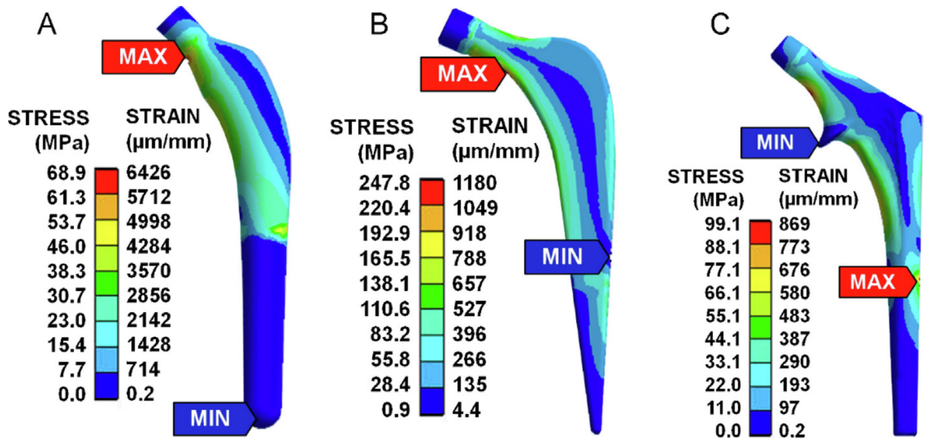


Fig. 2. FE model stress and strain distributions of hip prostheses under 3 kN axial load. (a) Composite hip stem, (b) Exeter hip stem, (c) Omnifit hip stem [49].

3.5. Composite materials

In the past, composites with low elastic modulus were used to minimize the elastic modulus mismatch between the prosthesis and the adjacent human bone [49]. However, the strength and long-term durability of these prostheses under cyclic loading are poor, leading to unsatisfactory outcomes [50]. In addition, softer materials used in hip joints in the past, such as carbon fiber, can lead to clinical complications, such as the formation and transport of macrophages to lymphatic vessels, which then circulate through the vascular system in undesirable ways [51]. Li et al. [52] used the ANSYS software to conduct a static three-dimensional finite element analysis on the prosthesis, and compared the stress distributions on the surface of titanium alloy, carbon fiber reinforced polysulfone (CFR/PSF) composite, Co–Cr–Mo alloy, and stainless steel prostheses. The stress distribution was analyzed for the influence of normal and shear stress on the prosthesis. The titanium alloy and CFR/PSF composite prostheses exhibited a better stress distribution than the Co–Cr–Mo alloy and stainless steel ones, highlighting their promising potential for clinical applications. Future research can fully harness the advantages of composite materials in terms of biocompatibility, cost, and in particular adjustable mechanical properties to design and manufacture new composite prostheses that can replace the current metal implants. The above research on composite materials thus provides a valuable theoretical basis for the clinical application of prostheses in the near future. Campbell et al. [53] studied the microstructure and biomechanical properties of a composite material based on a thermoplastic polymer matrix and continuous carbon fibers Carbon fiber/polyamide 12(CF/PA12) composite materials using static and dynamic fatigue tests. The composite showed a Young's modulus (12.2 GPa) of the same magnitude as that of cortical bone (17–20 GPa), and its fatigue performance far exceeded the requirements of femoral stems for total hip prostheses (THPs). CF/PA12 also exhibited excellent mechanical properties in bending, having a flexural modulus of 16.4 GPa which is very close to cortical bone flexural modulus of 14.3–21.1 GPa. Hence, to reduce stress shielding effect, this composite could be used to be processed into complicated shapes with customized properties, which makes it an excellent candidate material for manufacturing hip stem. Campbell et al. [54] also used the same composite to produce a femoral stem using inflatable bladder molding. The compressive stiffness of the composite structure (4.5–10.9 GPa) was close to that of cortical bone (17–20 GPa). It was also found that the compression load at failure of composites were three times higher than those of femoral bone for 10 times those for normal gait.

Bougherara et al. [49] compared the mechanical behavior of a new type of carbon fiber-based composite hip joint with that of two commercially available metal hip implants, namely, the Exeter and Omnifit stems (Stryker, Mahwah, NJ, USA). The mechanical properties of the two hip implants were compared through a finite element model, using a series of experiments to measure the axial stiffness as well as the strain and stress distributions. FE model stress and strain distributions of hip prostheses under 3 kN axial load of the three hip joint femoral stems is shown in Fig. 2. Finite element models can be used to investigate biomechanical behavior of tissues and implants [55,56,57]. The strength of the carbon fiber composite materials was found to be 45%–200% lower than that of commercially available metal pieces, which indicates that carbon fiber composites may be a better choice for minimizing bone stress shielding, bone loss, and implant loosening. This was the first study where the stress distribution of the composite hip stem was evaluated and compared it directly with that of a standard metal hip joint.

Reinhardt et al. [58] also made use of thermosetting polymer-based composite material made out of resin transfer molding process. They managed to produce a hip stem prototype which consists of braided carbon fiber socks that are wrapped around a wood insert. The two-way fiber arrangement allowed for a high volume fraction of approximately 38% and had a great mechanical performance and property in fatigue and stiffness respectively, which was similar to that of the local cortical bone. However, due to excessive residual monomers within the final product made this composite unsuitable for hip implant application.

Hedia et al. [59] attempted to reduce stress shielding by designing prosthetic handles with three different components, hydroxyapatite, bioglass, and collagen. However, due to the brittleness and insufficient strength of these materials, their clinical applications are very limited.

3.6. Functionally gradient materials

According to Wolff's Law, the structure of bone is closely related to its mechanical environment [17]. Different bone components thus have a different structure, owing to the different mechanical environment in which they are located. The technological and material science advances made in the recent years have resulted in the emergence of a new class of materials, functionally gradient materials (FGMs), which exhibit a gradient pattern of material composition and/or microstructure. The FGM prostheses are reviewed below, whereas their gradient construction is described later in the manuscript.

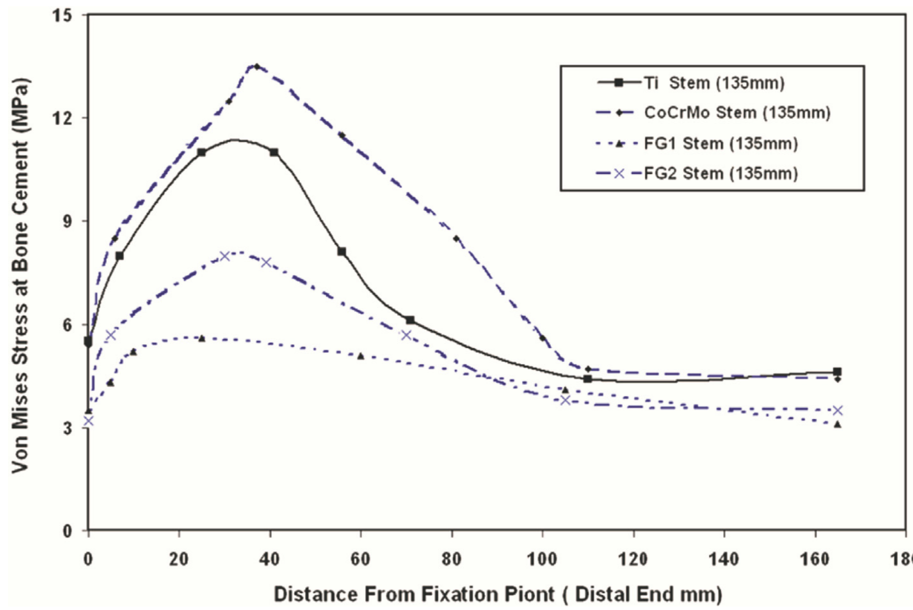


Fig. 3. Distribution of maximum von Mises stresses at bone cement along the cement length for 135 mm FG1, FG2, Ti alloy and CoCrMo stems [62].

Nemat-Alla [60] introduced the concept of two-dimensional (2D) functionally gradient materials. Subsequently, Hedia et al. [59] improved the design of cementless stems using the 2D FGMs concept; this new design reduced the maximum lateral and medial shear stresses on the femur by approximately 50% compared to those observed with a titanium stem. Gong et al. [61] found that, compared with rigid prosthetic stems, 2D FGM stems could generate stronger mechanical stimuli and produce a more uniform interfacial shear stress, with a maximum value lower than that of homogeneous flexible stems. Therefore, from a biomechanical perspective, 2D FGM stems appeared suitable as femoral implants. However, this study had some limitations: the adopted femur model was very simple, did not include cancellous bone, and did not consider patient'own load or the load and its associated changes of direction during walking. Therefore, the reliability of these results needs to be further evaluated. Al-Jassir et al. [62] found that the use of a FGM prosthetic stem with low and high stiffness at its distal and proximal ends, respectively, significantly reduced the shear stress at the cement/handle interface. When Co–Cr–Mo and Ti alloys were replaced by a FGM, the von Mises stress of bone cement and stem was significantly reduced, and the stress distribution along the bone cement length was more uniform (Fig. 3), which helped to reduce the loosening rate and improve the short- and long-term performance of the artificial hip joint. The authors analyzed the effect of using different FGM stem lengths on the total stress acting on the artificial hip joint. The results showed that the use of a functionally gradient material with low and high stiffness at its distal and proximal regions, respectively, can significantly reduce the shear stress at the bone/cement interface. Therefore, the authors suggested that an FGM-based femoral stem prosthesis could be more effective at reducing the artificial joint stress and stress shielding effect, thereby decreasing bone loss and increasing the life span of the patient. Bennett et al. [63] designed an uncemented implant (SR71) composed of a carbon fiber composite in the distal part and a porous-coated titanium alloy in the proximal part, with the aim to improve the proximal load transfer and provide good fixation. Sixty patients were enrolled and randomly received SR71 or all-metal stems. Ten years after the procedure, the study concluded that the SR71 implant provided increased proximal bone density and decreased distal bone density. The implant showed promising results during early follow-up, and the clinical results at the 10-year follow-up were similar to those of the all-metal stems.

In summary, previous studies have described many possible combinations of biomaterials for artificial hip joint femoral stems. With the continuous development of artificial hip joints, the manufacturing materials are constantly being updated. Traditionally, metals such as Co–Cr–Mo or titanium alloys and stainless steel have been used for manufacturing femoral stems. Subsequently, reinforced polymers and composite materials have played an increasingly important role in the design of femoral stems, because they can be more accurately engineered to produce more effective prostheses. Fiber-reinforced composite materials can provide a strength comparable to that of metals and have a greater flexibility [52]. The advantages of composite materials in terms of biocompatibility, cost, and adjustable mechanical properties can enable the design and manufacturing of new composite material prostheses that can replace current metal hip implants. Despite their advantages, composites still need to be optimized so that they can be fully available for clinical applications. At the same time, FGMs are gradually becoming more popular in the field. These materials can achieve a more uniform stress distribution along the bone cement length, help preserving the host bone, and improve the short- and long-term performance of the femoral stem. In recent years, coating materials have also been widely used in artificial hip joints and femoral stems. They can achieve long-lasting biological fixation and good clinical results, and can be applied in various clinical scenarios. Due to cyclic loading, implants can develop progressive and localized structural damage. Hence the fatigue resistance of materials used for hip implant has to be higher than that of femoral bone. According to ISO 7206–4:2010 [64] (Determination of endurance properties and performance of stemmed femoral components), hip implants should survive 5,000,000 cycles without failure at specific cyclic load of either 1,200 N (for short stem, <102 mm) or 2,300 N (for long stem, 120 mm < Length < 250 mm). For composites, fatigue damage would be expected at a very low endurance limit due to buckling of fibers in compression loading. Considering single-phase materials, only metals satisfy this requirement and can survive this cyclic loading. As a summary of this section, tissue/organ regeneration is the most suitable direction for advances in hip replacement surgery: this method enables the production a customized femoral stem made of biodegradable composite materials. Understanding the advantages and drawbacks of different materials can thus facilitate the identification of their most suitable combination for artificial hip prostheses.

4. Research and development of prosthesis constructions

The structural design of artificial hip joint prostheses has been the focus of many studies presented in the review article by Munting and Verhelpen [65]. In order to reduce the stress shielding phenomenon, several investigations have focused on the design of the femoral stem, especially on its stiffness, construction, and geometry. Studying the construction and geometry of the prosthesis can facilitate its selection before replacement surgery, as well as providing an important reference for its design optimization. Continuous research on the prosthesis construction now provides surgeons with more options than in the past, particularly in terms of structural reliability and biocompatibility. Reducing the stiffness of the femoral stem will increase the transfer of load to its proximal end, thereby reducing stress shielding.

The stiffness of the stem is affected by many factors, including material, construction, and cross section. The elastic modulus of the prosthetic material is the critical factor for the adequate transfer of stress to the surrounding bone. The elastic modulus of the stem (e.g., 200 GPa for cobalt–chromium) is usually much higher than that of the cortical bone it replaces (20.3 GPa) [66]. The higher the elastic modulus of the stem, the lower the load transferred to the extremity of the femur, resulting in a greater stress shielding. On the other hand, reducing the elastic modulus of the prosthesis can increase the load transmitted to the femur, minimizing bone atrophy due to stress shielding. In the following sections we review the structural development of femoral stems, mainly focusing on their length, shape, porous construction, and functional gradient construction.

4.1. Selection of femoral stem length

The final length of the stem should be determined according to the characteristics of the patient (including gender, weight, and height) and the type of disease. The length of the stem varies in different applications. There are no specific guidelines on the most suitable length for implantation. The length of the femoral stem is a practical consideration in the prevention of gait injury during total hip replacement (THA) [67].

As early as 1995, a different concept of femoral prosthesis was proposed. The femoral prosthesis has no intramedullary stem and fits into an angular resection of the femoral neck [65]. They designed a stemless prosthesis that departed from the traditional design. The implant was embedded in the neck of the femur and reinforced with some transtrochanteric screws. *In vitro* experiments on the prosthesis showed minimal fretting, while short-term clinical trials revealed a low initial failure rate. And compared with the cemented prosthesis with a stem, significant stress shielding was observed with the cemented prosthesis with a stem. This work was extended by Joshi et al. [68], who designed a prosthesis with a new geometry: they proposed that shortening the prosthetic stem could reduce stress shielding and shear stress at the interface. Instead of using the previous sessile prosthesis, they shortened the length of the femoral stem on top of the traditional femoral stem. Of course, it is our understanding that shortening the length of the femoral stem may adversely affect the stability of the implant interface. But the focus of this study was to reduce stress differences within the bone. A rectangular plate was used to achieve an even stress distribution between the femur and the prosthesis, with some cables to support the prosthesis (as shown in Fig. 4). The authors then used finite element models to compare this design with both Munting's and conventional prostheses, and found that their design resulted in less stress shielding in all parts of the femur except for the region under the greater trochanter. In other words, their proposed design will produce less stress shielding than traditional intramedullary designs and previous sessile prostheses.

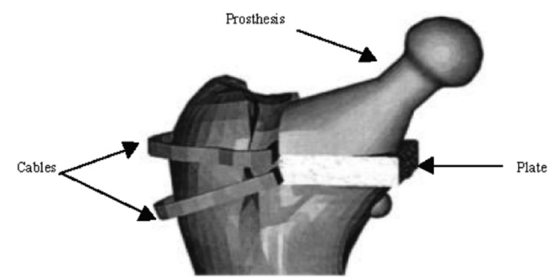


Fig. 4. Schematic diagram of shortening stem design [68].

Al-Jassir et al. [62] assessed the effect of using different stem lengths on the total stress acting on an artificial hip joint. The results of finite element analysis suggested that, for all types of prosthetic materials, the length of the prosthesis had a significant effect on the shear and von Mises stresses on the bone, prosthesis, and bone cement. The maximum von Mises stress at the bone cement increased significantly with the length of the femoral stem, while the shear stress decreased. Zou et al. [69] analyzed the stress levels on femur and prosthesis after the implantation of four kinds of prostheses with different stem lengths. The results showed that the stress on the femoral bone did not change significantly with increasing stem length. Some studies [70] suggested that increasing the length of the prosthetic stem only led to a slight improvement in the stress distribution of bone endothelium at the lower end of the prosthetic stem. Therefore, from the perspective of stress analysis, increasing the length of the prosthetic stem has no practical significance. Moreover, owing to the radian of the femur itself, increasing the length of the prosthetic stem in clinical practice will require the removal of more bone tissue during the operation, increasing the difficulty of the procedure and the associated complications [71]. Radiographic images obtained by Jergesen and Karlen [72] showed a more severe stress shielding in patients with a larger femur stem, compared with those with middle-size and small stems. Gong [73] fabricated four prostheses with femoral stem lengths of 137, 140, 143, and 146 mm to study the effect of the prosthesis length on the femoral stress after replacement. The four prostheses only differed in the stem length, but the other design parameters were the same, including the material employed for the stem (titanium alloy). The results showed that after implantation the stress on the femur increased slightly with increasing stem length, but the other stress conditions did not change; this indicated that the effect of stress on the prosthesis was not significantly influenced by the length of the femoral stem. Therefore, implants with long stems should be avoided in order to preserve the bone stock.

In addition, fretting in excess of 40 μm at the bone–implant interface resulted in partial bone ingrowth, while fretting exceeding 150 μm completely inhibited bone ingrowth [74]. Reimeringer et al. [75] conducted a static analysis of a model of rapid walking and stair climbing after total hip arthroplasty using finite element methods, and studied the effect of the reduction of the femoral stem length on the initial stability and long-term survival of the prosthesis. They implanted straight and curved prosthesis stems of five and four different lengths. The study found that reducing

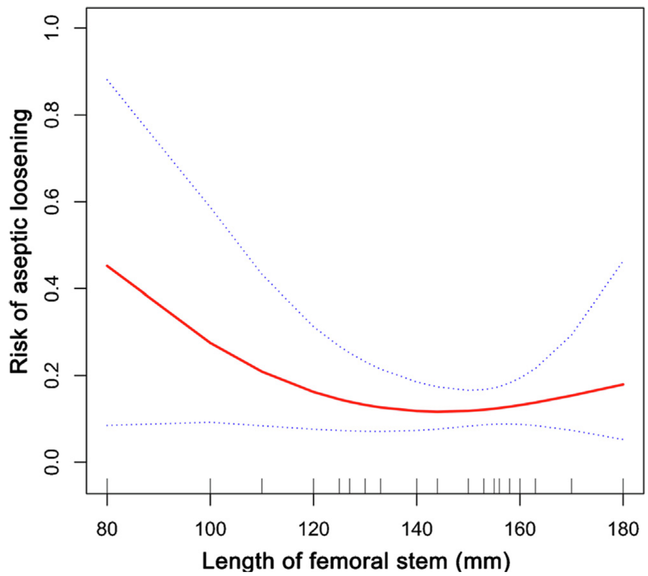


Fig. 5. The relationship between the length of femoral stem and the risk of aseptic loosening following cemented distal femoral end-of-prosthetic replacement [80].

the length of the straight stem from 146 to 54 mm increased the average micromotion between prosthesis stem and bone during rapid walking from 17 to 52 µm, while the peak value increased from 42 to 104 µm. For the curved prosthesis stem, upon reducing the length from 105 to 54 mm, the average micromotion between stem and bone increased from 10 to 29 µm, and the peak value increased from 37 to 101 µm. Similar results were obtained for the stair climbing model. Although current research shows that the length of the femoral stem affects its stability, reducing the length of the femur can facilitate surgery without compromising its stability. The potential advantages of a short femoral stem could be confirmed by a long-term clinical trial showing that the survival rate of short and standard-length femoral stems is comparable.

Kim et al. [76] also compared ultrashort and conventional anatomical cementless stems. The clinical, radiological, and bone density results were separately compared. Follow-up results showed no difference in the efficacy score or fixation of the ultra-short and traditional cementless stems. Yu et al. [77] compared the clinical and radiological results obtained using short and conventional femoral stems in total hip arthroplasty conducted on patients aged 70 years and older. The results showed no differences in the average operation time, estimated blood loss, and hemoglobin levels at discharge of the short and conventional stems. No intraoperative fractures occurred using the short stem, but five cases were observed with the conventional stem. At the final follow-up, no statistically significant differences in Harris hip score and radiographic levels were observed between the two types of prostheses. Short-stem hip joints did not result in thigh pain, whereas six conventional-stem hip joints were associated with pain. The authors concluded that both short and conventional stems can provide stable fixation, with satisfactory results achieved in patients aged 70 years and over; however, the short stem femoral prosthesis showed a lower incidence of pain and intraoperative fractures. Similarly, Kim et al. [78] conducted a comparative study of femoral stems of short and standard length. The results revealed one proximal femoral fracture in the short stem group and one distal fracture in the standard length group, along with one dislocation in each group. In the short stem group, the stress shielding effect was significantly reduced, but no differences were found in vertical and parallel offsets. The intraoperative, imaging, and clinical evaluations of the two groups showed good results, and the authors concluded that there were no significant differences between the two groups.

Similar results were obtained in a comparative study conducted on elderly patients with femoral stem fractures treated with short and standard stems [79]. The clinical outcomes and radiological stabilities of the two groups of patients were similar. In addition, after at least 2 years of follow-up, the density of the short femoral stem around the prosthesis showed good preservation of bone in this region. Zhang et al. [80] analyzed data of patients who underwent distal femoral prosthesis replacement at their affiliated institutions from 2001 to 2017. Cox and two-stage regression models were used to analyze the relationship between the length of the stem and aseptic loosening. The study found a significant nonlinear relationship between the length of the femoral stem and aseptic loosening (Fig. 5), and the inflection point was estimated to be 143 mm. On the left side of the inflection point, for every 1 mm increase in the length of the prosthesis stem, the risk of aseptic loosening could be reduced by 6%. These findings are expected to provide reference parameters on prosthetic stems for orthopedics experts and guide clinical decision-making. Niinimâki et al. [81] used dual-energy X-ray absorptiometry (DEXA) to measure the bone mineral density in 24 patients who underwent total hip arthroplasty with a short anatomical femoral stem. The results showed that a proximal porous-coated short stem seemed to preserve bone mass better than cemented and long-stem prostheses. However, Rietbergen and Huiskes [70] investigated the effect of reducing the stem length on the load transfer of Anatomique Benoist Girard (ABG) prostheses and found that shorter stems did not substantially increase the probability of interface failure.

However, the design of short stems also has some limitations. Typical disadvantages are a poor initial stability and the difficulty in preventing the motion of the prosthetic stem during operation.

The length of the stem is a fairly controversial parameter. Purely technical factors must be considered first, such as ease of insertion into the medullary cavity and difficulty in removal. Mathematical modeling studies have shown that too short or too long a femoral stem will produce stress concentration at certain points. For example, if the stem is too long, it will increase the stress of the stem itself and create a stress shield at the proximal end of the femur. If the stem is too short, it will create a high stress at the proximal end, which may exceed the limit strength of bone and bone cement. For most patients undergoing primary replacement, a stem length between 100 mm and 130 mm is optimal. Other factors, such as cortical bone defects during revision, also have a significant impact on the outcome of prosthesis implantation.

In summary, previous studies showed that increasing the length of the prosthetic stem may help reducing stress shielding and the risk of aseptic loosening, whereas a shorter stem length enhances its stability. After implantation of short femoral stems in elderly patients, the density around the prosthesis showed good bone preservation in this region [79]. However, these benefits are not very significant. In clinical practice, it is necessary to take into account the specific conditions of the patient's bones and select the prosthesis stem that is most suitable for the physiological structure of the target femur. As for the prosthetic stem length, it is more important that the selection is made according to the physiological conditions of the patient (including height, weight, and shape). Therefore, increasing or decreasing the stem length of the prosthesis is only recommended if the objective conditions of the bone tissue allow it.

4.2. Effect of the shape of the prosthesis stem

Early prosthesis stems were generally curved, but this curved design has long been phased out. For cement-fixed femoral stems, insertion into the relatively straight medullary cavity (especially on the coronal plane) through the bend stem makes it difficult to form a complete cement sheath. With this kind of bend stem, the cement sheath is weak in the medial and lateral proximal end and the medial and distal end, which is easy to cause fatigue fracture of the cement sheath in this part and eventually lead to loosening of the prosthesis. The straight stem, with a small taper, can apply pressure to the cement during insertion and keep the cement sheath intact. The shape design of the prosthesis stem not only includes the shape characteristics of the prosthesis itself, but also includes the cross-section of the femoral stem. The cross-section of the stem of the femur describes the volume of the stem and the distribution of material along the stem axis.

Various stem geometry designs can be used to create a load transfer system through the proximal femur that closely mimics the natural process. According to some studies, a femoral stem with rectangular cross section, sharp corners, and curved design may provide better stability [74]. The stiffness of the stem can be adjusted by modifying its section, with a thicker stem bearing a higher load than a thinner one. Laine et al. [82] found that an anatomical design could improve the fitting and filling of a metaphyseal femoral stem; the shaft could be tightly fitted with a straight stem for good stability. However, good bone growth and remodeling around the distal stem indicated that stress was transferred through this region and increased the stress shielding of the proximal metaphyseal femur. Wang et al. [83] used finite element analysis and reverse engineering to simulate the static stress on the femur using an ANSYS model. The radius of the femoral stem was varied in a certain range; upon increasing it by 1.2 times, then the maximum stress on the femur was close to the upper limit; when the radius was increased by 1.5 times, the maximum stress exceeded the stress limit. Therefore, the authors concluded that the size of the prosthesis should be<20% of the diameter of the medullary cavity; values exceeding 20% will greatly increase the probability of femoral fractures. Chang et al. [84] designed a prosthetic stem with a small middle diameter to maintain a satisfactory stability. The two parameters shown in Fig. 6 were selected to improve the load transfer and stability of the prosthetic stem by reducing its cross-sectional area.

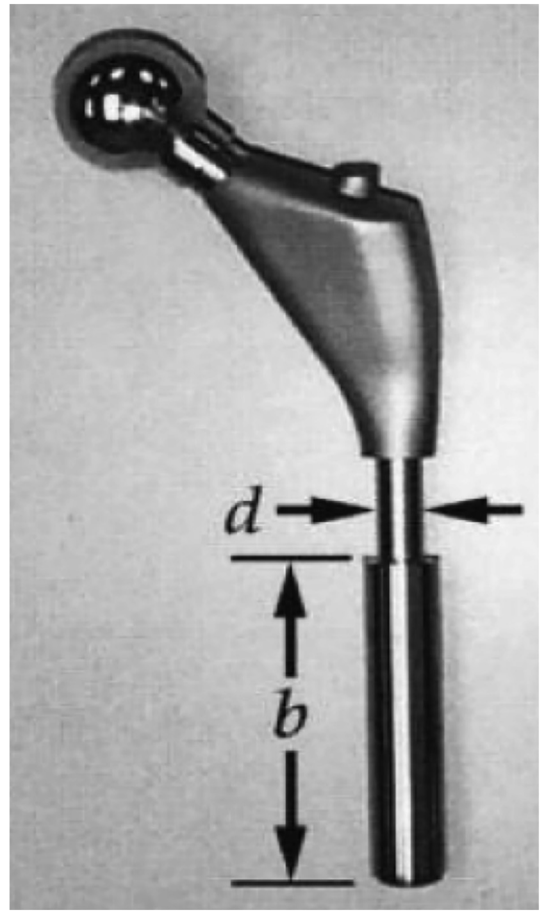


Fig. 6. Implant designed [84]. b and d represent the distance from the distal end and the reduced stem diameter, respectively.

Zheng et al. [85] designed cemented artificial femoral stems of different shapes, namely, hollow cylindrical, inverted cone, forward cone, and solid. Using finite element analysis, they found that the three hollow shapes resulted in a more reasonable distribution of von Mises stress compared to the solid shape, and the maximum von Mises stress of the inverted conical stem was smaller. Therefore, the use of an inverted cone-shaped artificial femoral stem helps to reduce the effect of stress shielding in the area where the human proximal femur contacts the prosthesis. Mattheck et al. [86] used finite element modeling to analyze a prosthetic stem with hollow construction and found that this geometry helped to reduce the peak stress at the lower end of the prosthetic tip, while increasing the stress on the proximal cortical bone by 20%. The increased load on the cortical bone resulted in a decrease in stress shielding in this area. Gross and Abel [87] optimized the design of a hollow stem. Using the internal diameter of the prosthesis as the design variable and the stress on the bone cement as the design constraint, the stress distribution of the optimized hollow stem was compared with that of a reference solid stem. However, this study adopted an oversimplified analytical method, involving only a cylindrical prosthesis handle with simple point load and boundary conditions, so that the load and constraint conditions were not very accurate.

Sabatini et al. [88] conducted a finite element analysis of femoral stems with different cross-sections (circular, elliptical, and trapezoidal). They compared the von Mises stress for each femoral stem at a specific location and recorded the displacement. The study found that a trapezoidal cross-section design worked best on the internal side of the implant, but resulted in an uneven stress distribution from the internal to the external region. While this design successfully shifted the stress away from the internal side, the authors concluded that other designs need to be considered when creating implants that minimize stress shielding. Although in most cases the circular and elliptical cross-section femoral stems did not show the lowest stress values, they minimized changes in stress at different locations, indicating that the stress distribution achieved with these two shapes was more even. Therefore, further combinations of designs need to be explored to identify an optimal design. Ellison et al. [89] studied the long-term effect of a porous plasma conical titanium stem on femoral reconstruction following total hip arthroplasty. They randomly selected 97 patients who were implanted with a Mallory–Head porous femoral stem prosthesis during primary total hip replacement, and determined the average changes in the near, middle and backbone areas. The authors concluded that, in a well-fixed and well-functioning total hip arthroplasty, stress shielding could be minimized using a Mallory–Head tapered titanium femoral stem combined with annular proximal plasma spray coating. In addition, most femurs showed increased or unchanged cortical thickness in all areas around the prosthesis. Hu et al. [90] employed finite element simulations to analyze the micromotion and stress distribution at the bone–implant interface of four common femoral stems, namely, Alloclassic, Ribbed Anatomic, VerSys, and Secur-Fit. The authors calculated the micromotions and stress distribution at the proximal interface of the four types of femoral stems under stair climbing loading conditions, selecting the inner, front, side, and back points of each section for the calculation. The four stems showed good initial stability, and significant stresses were detected at the sharp corners and ribs of the Alloclassic and Ribbed Anatomic models, respectively. The study concluded that significant stress levels were associated with sharp-edged femoral stems.

Based on computer tomography (CT) data on the human femur and the anatomical morphology of the hip joint, Tan et al. [91] established a model of an alveolar artificial hip joint. They modeled the surface of the triangular area of the artificial hip prosthesis through finite element analysis and studied the effect of a different alveolar construction and distribution on the surrounding bone stress. The results showed that the alveolar construction changes the mechanical transmission mechanism of the physiological load onto the interface between artificial stem and femur. The authors concluded that the distribution of bone stress can be controlled by optimizing the alveolar construction and its morphology. The triangular alveolar construction of the prosthetic stem could reduce the stress shielding effect on the surrounding regions of the implant. Under the same alveolar morphology conditions, a convex tooth construction was found to be superior to a concave tooth one, and a proximal 1/3 convex tooth distribution had the best effect on reducing stress shielding on the bone. Therefore, in the long-term period following of hip replacement surgery, an alveolar construction is expected to be more effective in reducing osteoporosis caused by stress shielding and can effectively extend the service life of hip prosthesis stems. Noyama et al. [92] proposed a new type of hip joint prosthesis aimed to achieve an appropriate bone function and microstructure, using the relative arrangement of biological apatite (BAp) and collagen (Col) as a representative parameter. They introduced directional grooves in the proximal end of the femoral stem to control the main stress acting on the bone within the grooves, which is the main factor affecting the Col/BAp arrangement. Using finite element analysis, the groove angle was optimized according to the stress within the grooves. The study found that only the proximal grooves oriented at 60° from the normal direction of the femoral stem surface could produce a healthy distribution of maximum principal stress. The maximum principal stress inside the groove decreased with increasing Young's modulus of the stem, but the direction of the stress did not change significantly. *In vivo* implantation experiments showed that the groove could effectively induce the formation of new bone with preferential Col/BAp arrangement along the depth of the groove. Therefore, the authors concluded that the introduction of directional grooves is an effective strategy to optimize the long-term fixation of an implant. Li [93] used the UG secondary development technology to optimize the parameters of the prosthesis, and designed three types of stems with different internal constructions, namely solid, cylindrical through-hole, and rectangular cavity stems. These parameters were adjusted to optimize the external dimensions of the stem, and rapidly establish the prosthesis model as needed. The study showed that the solid shield construction resulted in the highest stress shielding, followed by the cylindrical through-hole stem, whereas the rectangular cavity stem led to the lowest stress shielding on the femur, with a minimum value of 58.42%. The authors further adjusted the structural size of the rectangular cavity stems, and optimized them to achieve an even lower stress shielding rate, down to 54.86%. Yoshitani et al. [94] used three-dimensional (3D) CT to evaluate the relationship of the sagittal arrangement of a tapered-wedge stem with clinical and radiological results. The sagittal position of the stem was measured by CT, and the patients were divided into flexion and neutral groups. The authors compared clinical and imaging results of the two groups and evaluated the pre-femoral offset and the initial contact state. The clinical and radiographic results of the two groups of patients during an average 4.7 years of follow-up were not significantly different. The authors concluded that the increase in the anterior femoral offset and distal contact area during flexion will affect the flexion-free impact range and the probability of intraoperative fracture.

For the optimization of prosthesis stem shape, in addition to its own shape design, there is also the optimization of its cross section design. Most of the early prosthesis stems were curved stems, which were difficult to fit closely with the distal end of the prosthesis due to its poor torsional stability and difficulty in inserting the curved stems into the medullary cavity. Straight femoral stem is the best choice for both cemented and non-cemented femoral stem. For cement-based femoral stem, the straight stem shape is more likely to form a complete cement-based sheath. For the cementless femoral stem, it is easier, more accurate, and simpler to use the straight stem for the femoral marrow cavity. The distal end of the bend stem is difficult to fit closely with the bone marrow cavity, and it is not easy to add anti-rotation grooves to the distal end of the bend stem. The whole stem body has a porous covering and a bend stem with bone growth, which is extremely difficult to take out during revision. As a result, the bend stem was constantly optimized and eventually retired.

Some optimization of cross section design and detailed design on the surface of the stem body gradually came into view. The cross section of the stem, combined with the physical properties of the material, can at least partially represent the structural characteristics of the stem, such as the strength and hardness of the stem. The cross-sectional morphology of some prostheses produces a better mechanical environment than others. The stem of the femur should be avoided with sharp angles, which can cause significant stress concentration and fracture of the cement and bone. For cement-fixed femoral stems, some stems with thicker lateral surfaces have better flexural resistance, resulting in less tensile stress on cement. However, some femoral stems with thicker inner sides have less compressive stress on the cement sheath, because the compressive strength of cement is three times higher than the tensile strength, so when designing cement-type femoral stems, the tensile stress of the stem to the cement should be reduced as far as possible, so that the use of such stems is relatively safe. The shape of the cross section of the stem partly represents the macro stability of the stem. In order to reduce the hardness of the stem, grooves and pits are needed to reduce the volume of the stem and reduce the influence of stress shielding after meeting the macroscopic locking mechanism. The goal of our efforts is to develop a common geometry of the femoral stem that restores as much as possible the natural load transfer mechanism in the proximal femur.

4.3. Porous and functionally gradient constructions

Porous constructions are usually divided into homogeneous and gradient constructions; the latter are often designed to mimic the microstructure of natural bones. Porous materials are widely used in prostheses, and their main purpose is to promote bone tissue growth and the long-term fixation of the implant [95].

Metal foam denotes a special metallic material with a porous construction. It can be regarded as a metal–air composite material, which is a feasible solution to reduce the elastic modulus of an implant. The increased porosity is accompanied by a decrease of the Young's modulus of the implant. Rahman and Mahamid [96] explored the use of a cellular metal alloy implant, which exhibited a very good adaptability, almost matching that of a normal femur. Compared to other implants, cellular implants have a sponge-like topology, which increases the load transferred to the bone, thus reducing stress shielding. Cellular constructions constitute a promising feature for bone growth because it confirms their firm fixation in the implantation [97]. However, with the increase in porosity, the strength of the metal foams is significantly reduced.

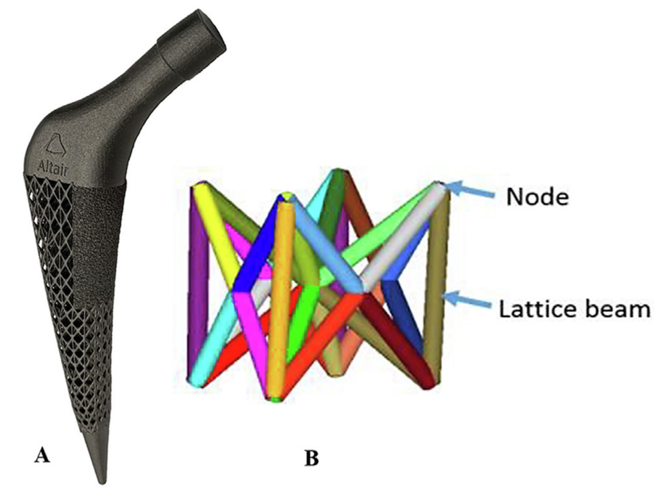


Fig. 7. (A) EOS Printed Titanium Solid-Lattice Hip Implant, **(B)** Face and Body Centered Cubic with Vertical Struts Unit Cell (FBCCZ) [103].

Yan et al. [98] studied the effect of a porous titanium femoral prosthesis on bone reconstruction by using the finite element method to calculate the stress and strain field of the femur after hip arthroplasty. According to the bone reconstruction theory based on the strain value, the impact of the implant material on bone reconstruction was evaluated by analyzing the loss of bone density. The study considered different implant materials, including Co–Cr alloy, titanium alloy, and porous titanium with different porosities, and explored a wide range of porosities to assess their impact on bone reconstruction. The study concluded that the use of porous titanium instead of cobalt–chromium solid implants would result in a sharp drop in bone volume, accompanied by bone density loss. Bone loss around the implant was found to be related to the elastic modulus of the implant, with a higher elastic modulus resulting in a greater loss of bone density. A large-scale porosity study (20%–60% porosity) showed that the loss of bone density decreased almost linearly with increasing porosity, but an increase in porosity would reduce the strength of porous titanium. The authors concluded that stress analysis is required to meet the relevant strength requirements for the design of femoral stem prostheses based on porous titanium. The study showed that porous titanium is a suitable implant material, which can reduce stress shielding after total hip replacement. However, further research is needed on the fracture and fatigue properties of this material to enable its effective use as a femoral stem replacement. The mechanical properties of porous structures change with the porosity, which affects their overall fatigue properties [99]. It was also mentioned in another article, flexural testing of the stems was carried out according to the ISO 7206–4 standard, and a flexural stiffness reduction of 47% was obtained when comparing the porous stem to its dense counterpart [100]. He et al. [101] recently aimed to develop an optimized porous hip stem that could reduce both stress shielding and implant loosening over time. A major concern about fully porous hip implants is that they must also meet fatigue requirements. In Gilbert et al.'s study, a finite element model was used to understand the stress shielding effect in three different models including an intact femur, an implanted femur with a generic solid implant, and an implanted femur with an optimized porous implant. Two standard loading conditions (ISO 7206–4 and ISO 7206–6) were considered. These standards ensure that the porous

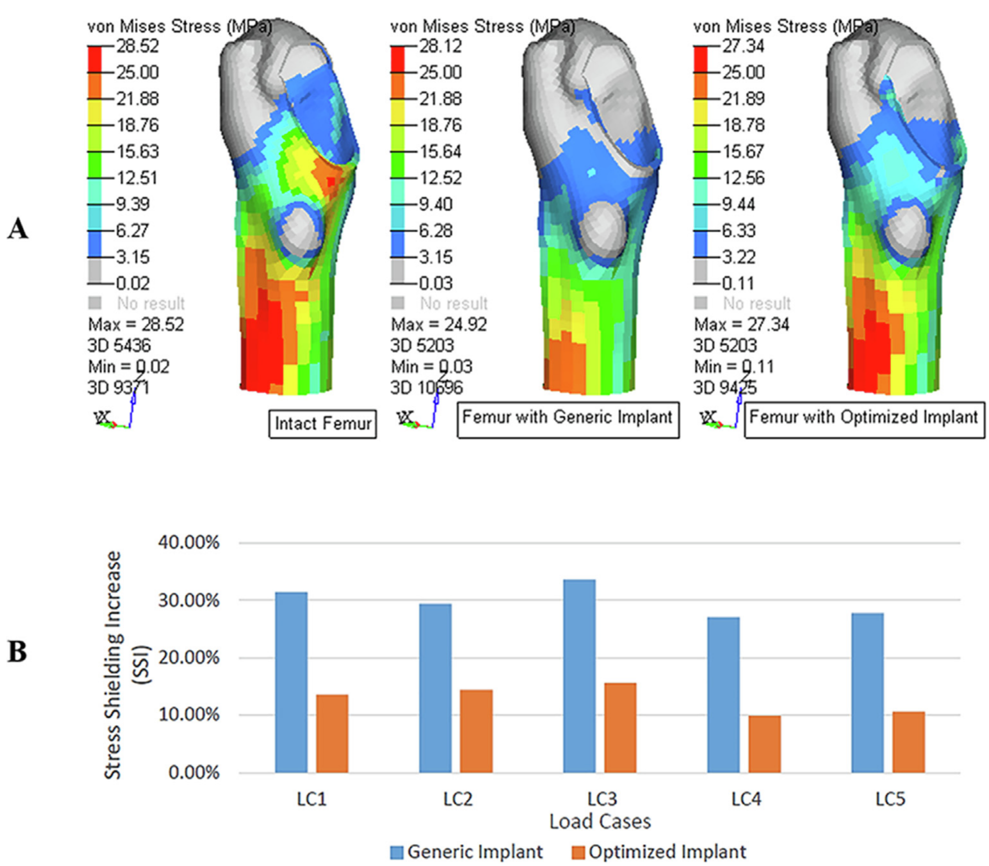


Fig. 8. (A) Stress shielding reduction with optimised implant under stairs up load case scenario, **(B)** Upper cortical bone stress shield increase with generic implant and optimised implant [101].

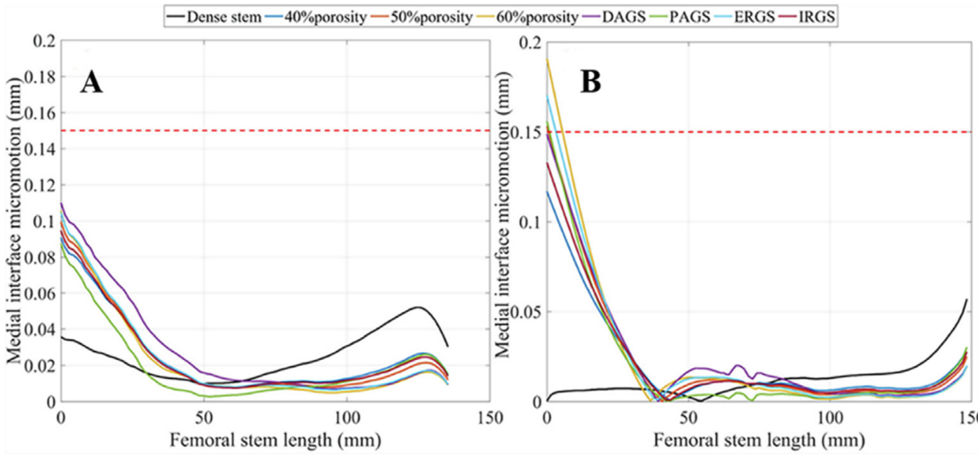


Fig. 9. Relative micromotion between the implant and host bone. **(A)** Medial bone-implant interface, **(B)** Lateral bone-implant interface [104].

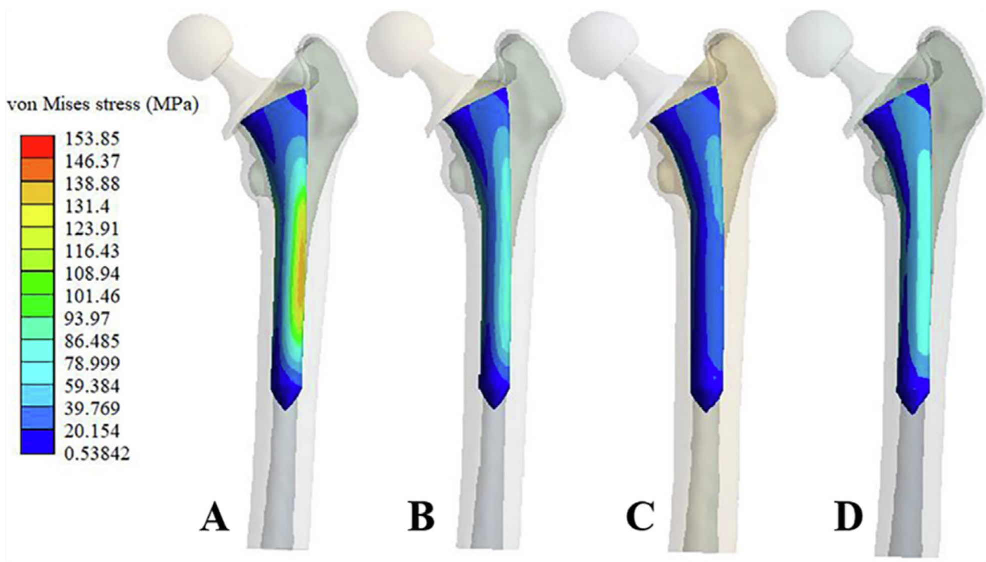


Fig. 10. Stress distributions of femoral stems.**(A)** Fully dense stem, **(B)** Homogenous porous stem with 40% porosity, **(C)** DAGS, **(D)** IRGS [104].

hip stem has good fatigue strength (surviving for 10^7 cycles) while in use by the patient. It has been previously shown that Ti–6Al–4 V can last 10^7 cycles under a 680 MPa stress [102]; therefore, the authors used this stress value as their design criterion for stem design optimization. The lattice construction of the porous hip implant involved a face and body-centered cubic with vertical struts (FBCCZ) unit cell (Fig. 7), which is one of the strongest printable cells [103]. Finite element analysis (FEA) was performed on all three models; Fig. 8 shows that the surface stress of cortical bone and stress shielding increased. The stress shielding was evaluated from the change in strain energy after introducing the implant. For the optimized implant under stairs-up load [Fig. 8 **(A)**], the upper section of the cortical bone showed a very similar stress distribution to the intact femur, suggesting a reduction in stress shielding. Fig. 8 **(B)** shows that the optimized implant led on average to a 57.3% lower stress shielding increase (SSI) value over the five load cases [combined loading (LC1), standing up (LC2), standing (LC3), stairs-up (LC4), and jogging (LC5)] considered in the study. The optimized implant was validated with both ISO standards noted above, and the maximum stress experienced by the optimized porous stem was 575 MPa; this value was lower than the endurance limit stress, indicating that the optimized implant met standard fatigue requirements [101]. Wang et al. [104] used finite element analysis to explore the application of different porous femoral stems to ease bone resorption and promote osseointegration. They proposed an intuitive visualization method based on a diamond grid construction to understand the relationship between pore size, porosity, bone ingrowth criteria, and additional manufacturing constraints. The authors examined porous femoral stems along four different gradient directions, including axial gradient femoral stems with distally and proximally increased porosity (DAGS and PAGS, respectively) as well as radial gradient femoral stems with inward and outward increased porosity (IRGS and ERGS, respectively). The obtained micromotions and von Mises stress distribution in the femoral stem implants are shown in Figs. 9 and 10**,** respectively. The results showed that DAGS and IRGS could maintain the relative micromotions at the bone/implant interface within the safe range for bone growth, while PAGS and ERGS cannot meet the osseointegration requirements in terms of relative micromotion, which would impair the long-term stability of the femoral stem. The volumes of bone with density loss for DAGS and IRGS were 3.6% and 3.3%, respectively, which were almost 74% lower than that of the fully dense femoral stem. Therefore, DAGS and IRGS showed obvious advantages in promoting osseointegration and reducing bone resorption, highlighting the promising application potential of gradient femoral stems. Zoubi et al. [105] established three-dimensional finite element model of cubic porous cellular constructions with porosity of 30–70%. Different volumetric porosity arrangements were used within the stems' layer, representing 15 different designs. Stems with 70% average porosity were found to have the best match with the intact bone mechanical properties for the stem inside the epoxy model. And functionally graded porous stems tend to transfer higher stress values to the bone compared to the bulk stem.

In order to reduce the stress shielding problem, Ridzwan [106] focused on the potential application of topology optimization methods. The aim of topology optimization is to obtain the best distribution of materials in a fixed region under the applied boundary conditions. The optimized prosthesis showed an increased load transfer in both the medial and lateral femur compared to the non-optimized prosthesis. In other words, the optimized prosthesis was more effective of the conventional prosthesis in reducing stress shielding. Currently emerging additive manufacturing (AM) technologies, such as selective laser melting (SLM), electron beam melting (EBM), and selective laser sintering (SLS), which can provide customized complex geometries at the microscopic scale, provide more freedom for prosthesis design. Selective laser sintering (SLS) is an additive manufacturing (AM) method widely used in hip implant [107,108,109]. These technologies use distinct materials, such as ceramics, metals, liquids and so on [110]. For example, Pattanayak et al. [111] used SLM to produce a pure porous titanium prosthesis, whose microstructure was similar to that of human cancellous bone, with a porosity of 55–75% and a compressive strength of 35–120 MPa. SLM is capable of repeatedly manufacturing a functionally graded CoCrMo femoral stem that is 48% lighter and 60% more flexible than a traditional fully dense stem [112]. SLM is an auspicious process for the direct manufacture of hip implants with expectable mechanical performance [113]. Li et al. [114] prepared a Ti–6Al–4 V porous microstructure by EBM. The uniform porosity of Ti–6Al–4 V was approximately 66% and its elastic modulus was only 2.5 GPa, which was close to that of human trabecular bone. Bandyopadhyay et al. [115] used laser engineered net shaping (LENS^{TM}) to fabricate a porous Ti–6Al–4 V construction with a porosity of 18–32% and an elastic modulus of 7–60 GPa. Khanoki et al. [116] proposed a method for the design of prosthetic stems with a gradient porous construction. They proposed a combination of multiscale analyses and structural optimizations to optimize the density distribution of the prosthesis, with the aim of reducing bone resorption and stress at the bone/prosthesis interface, while limiting micromotions of the prosthesis to allowed values. Wang et al. [117] customized a microstructured hip implant consisting of a 3D lattice and a tetrahedral topological construction, and applied various constraints on the pore size, porosity, and thickness of the lattice construction. The bone loss of the optimized structure was only 41.9% of that of a solid titanium implant, highlighting its potential advantages in reducing the risk of periprosthetic fracture and the probability of revision surgery.

A recent study by Kladovasilakis et al. [118] compared the topology optimization of three well known bioinspired lattice constructions namely Voronoi, Gyroid and Schwarz Diamond. Gyroid and diamond construction are known to have great osseointegration and enhanced mechanical strength amongst other triply periodic minimal surfaces (TPMS) construction. These constructions were investigated through finite element analysis (FEA) under in vivo loading and construction optimization was done through functional gradation of the cellular material. Construction optimization is done via altering the strut thickness and relative density (50–65%) according to the initial stress distribution on the struts with uniform distribution (Fig. 11). A load of 5,300 N was applied to different micro-structured hip implants and was shown that Scharwarz Diamond construction had the lowest peak compressive stress (529 MPa) when compared to Gyroid (615 MPa) and Voronoi (1088 MPa) constructions. Factor of safety of Scharwarz Diamond, Gyroid and Voronoi were also calculated to be 2.08, 1.79 and 1.01 respectively. Based on these results, it is shown that the functionally graded TPMS Scharwarz Diamond could withstand almost twice the maximum static load that the hip implant receives.

Various types of femoral stems for artificial hip joints with different shapes and constructions are emerging. Both the external shape and internal construction of the femoral stem have been optimized. Various shapes of femoral stem cross sections have gradually developed, including trapezoidal, circular, and elliptic sections [88]. The external shape of the femoral stem can also be very different, ranging from cylindrical to inverted- and right-cone shapes. Internal construction optimizations found that solid femoral stems have the greatest stress shielding effect, followed by cylindrical through-hole stems, while rectangular cavity stems result in the lowest stress shielding on the femur [93]. The long-term fixation of the implant can be optimized by introducing directional grooves to control the distribution of bone stress. The increased porosity will reduce the strength of materials such as porous titanium, making them suitable for implantation. Porous and functionally graded constructions are increasingly used in femoral stem prostheses, and their material and construction optimization is the key to achieve prosthetic stems with superior properties. Femoral stem with gradient porous construction also has promising application prospects. However, as discussed above, the performance of a femoral prosthesis stem cannot be optimized by focusing on only one aspect, and the combined optimization of multiple factors is needed to achieve the best performance. Despite the availability of many design optimization schemes, further combination designs may be required for this purpose.

5. Discussion and future perspectives

In this paper, we reviewed the status of femoral stem prostheses in the biomedical field, with particular emphasis on their structural optimization process, and suggested some possible directions for future research. As the development of femoral stems was described in higher detail, we summarized its main aspects here.

The hip joint plays an important role in our daily activities, such as walking, cycling, driving, and playing. Unfortunately, there is no guarantee that this articulation will always be in good conditions: damage to it can occur in many unexpected ways, such as accidents or osteoporosis-like diseases. The damaged femur needs to be replaced by total or hemi hip arthroplasty. The insertion of a prosthesis into the femur can lead to effects such as stress shielding and rejection. Therefore, the design of the prosthetic stem must be optimized to minimize these effects; many solutions have been proposed and applied over a long period of time.

In the past few decades, many studies have aimed at identifying the issues controlling the performance of hip stems over time. Understanding bone at the structural and material level, which occurs during a person's lifetime or evolution, has many applications in translational and clinical research to understand and treat bone disorders [119]. This article aimed to review the evolution of hip implants in terms of materials and constructions, discuss the issues that affect their in vivo performance, and provide insights into their design and development, in order to achieve a stable mechanical and biological fixation of the implant and improve its clinical performance. A variety of material optimization methods are currently available, and excellent results have already been achieved. In addition to traditional Co–Cr alloy, titanium alloy, and stainless steel, reinforced polymers as well as composite, func-

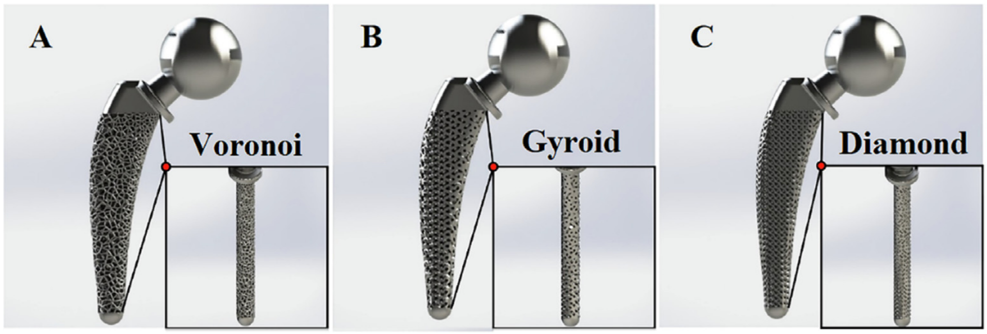


Fig. 11. Functionally graded hip stem for lattice constructions: **(A)** Voronoi; **(B)** Gyroid; **(C)** Schwarz Diamond [1 1 8].

tionally gradient, and coating materials have emerged and showed great advantages in terms of performance, cost, and adjustability. The construction of femoral stems for artificial hip joints is no longer restricted to traditional designs, but has been optimized in different aspects, including the length, cross-sectional shape, and internal construction of the femoral stem. Of course, tissue and/ or organ regeneration is the ideal direction for hip replacement. The analysis of real-life examples reveals that the different characteristics of patients can affect the design of the prosthesis to varying degrees. Therefore, the characteristics of the patient must be fully taken into account in the design of the femoral stem. Despite the availability of many material and construction optimization approaches, the replacement of artificial hip stems is still affected by various problems. The selection of the most suitable design can be facilitated a better understanding of the various materials and constructions involved. As discussed in the previous sections, the performance of a femoral stem prosthesis is not determined by a single factor, but is the result of a combination of factors. The choice of the optimal combination is the most important problem that needs to be solved at present.

Owing to their rapid development in the recent years, 3D printing technologies have received widespread attention, especially in the field of biomedicine [120]. Although, 3D printing technology is still not extensively used in mass production owing to low speed [121,122,123]. This emerging technology allows the use of specific biocompatible materials such as different types of metals, alloys, ceramics, plastics, and composites [124]. The method allows printing complex geometric shapes, including biological ones, which are difficult or sometimes impossible to manufacture by traditional techniques (casting, plastic deformation, or machining). The recent advances in the 3D printing technology now enable significant improvements in implant design [125]. In the long term, the advanced features and convenience of 3D printing can be combined with the optimization of materials and constructions of prosthetic stems to produce personalized hip implants based on the femur geometry and bone properties of the patient, as captured by quantitative computed tomography (QCT). Various parameters such as porosity, interconnectivity, and pore size of the hip stem can influence bone ingrowth into the implant. Therefore, future studies should consider different types of lattice construction, porosity, interconnectivity, and pore size to produce optimal hip implants with reduced stress shielding, along with enhanced osseointegration and bone ingrowth into the implant.

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

CRediT authorship contribution statement

Liyao Guo: Writing – original draft, Conceptualization, Investigation, Writing – review & editing. **Seyed Ataollah Naghavi:** Writing – original draft, Conceptualization, Investigation, Writing – review & editing. **Ziqiang Wang:** Writing – review & editing. **Swastina Nath Varma:** Writing – review & editing. **Zhiwu Han:** Supervision. **Zhongwen Yao:** Supervision. **Ling Wang:** Supervision. **Liqiang Wang:** Supervision. **Chaozong Liu:** Supervision.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

The authors would like to thank the financial support from Program for JLU Science and Technology Innovative Research Team (No. 2020TD-03) and European Union via H2020-MSCA-RISE program (BAMOS project, grant no: 734156); Engineering and Physical Science Research Council (EPSRC) via DTP CASE programme (Grant No. EP/T517793/1). Royal Society via International Exchange Programme (grant no: IEC\NSFC\191253) and Ministry of Science and Technology of China via National Key R&D Program (2018YFE0207900).

References

[1] H.M. Frost, Skeletal Structural Adaptations to Mechanical Usage (SATMU): 2. Redefining Wolff's Law: The Remodeling Probiem, The Anatomical Record 226 (1990) 414–422.
[2] G.L. Koons, M. Diba, A.G. Mikos, Materials design for bone-tissue engineering, In. Nat. Rev. Mater. 5 (8) (2020) 584–603, https://doi.org/10.1038/s41578-020-0204-2.
[3] M.I.Z. Ridzwan, S. Shuib, A.Y. Hassan, A.A. Shokri, M.N. Mohamad Ib, Problem of Stress Shielding and Improvement to the Hip Implant Designs: A Review, In. J. Medical Sciences 7 (3) (2007) 460–467, https://doi.org/10.3923/jms.2007.460.467.
[4] C. Cooper, G. Campion, L.J. Melton, Hip fractures in the elderly: a world-wide projection, Osteopor. Int. 2 (6) (1992) 285–289.
[5] A. Terrier, Adaptation of bone to mechanical stress: Theoretical model, experimental identification and orthopedic applications, Swiss Federal Institute of Technology, 1999. Ph.D. Thesis.
[6] M. Reimeringer, N. Nuño, The influence of contact ratio and its location on the primary stability of cementless total hip arthroplasty: A finite element analysis, J. Biomech. 49 (7) (2016) 1064–1070.
[7] R. Pivec, A.J. Johnson, S.C. Mears, M.A. Mont, Hip Arthroplasty, Lancet 380 (9855) (2012) 1768–1777.
[8] ASKCI Consulting Co., Ltd. China's artificial joint industry development analysis and investment research report in 2013-2018, http://www.askci.com/.
[9] P.F. Gomez, A. Jose, M.D. Morcuende, Early attempts at hip arthroplasty-1700s to 1950s, Lowa. Orthop. J. 25 (2005) 25–29.
[10] J.H. Kuiper, Numerical optimization of artificial hip joint designs, Katholieke Universiteit Nijmegen, 1993. Ph.D. Thesis.
[11] H. Malchau, P. Herberts, P. Soderman, A. Odén, Prognosis of total hip replacement, update and validation of results from the Swedish Natiorial hip arthroplasty registry 1979–1998, Proceedirigs Scientific Exhibition Presented at the 67th Arinual Meetirig of the American Academy of Orthopaedic Surgeoris (2000).

[12] M.W. Pagnano, L.A. McLamb, R.T. Trousdale, Primary and revision total hip arthroplasty for patients 90 years of age and older, Mayo Clin. Proc. 78 (3) (2003) 285–288.
[13] H.W.J. Huiskes, H. Weinans, B. van Rietbergen, The relationship between stress shielding and bone resorption arOUFtd total hip stems and the effects of flexible materials, Clin. Orthopaedics 2° 4 (1992) 124–134.
[14] J.P. Paul, Strength requirements for internal and external prostheses, J. Biomechanics 32 (4) (1999) 381–393.
[15] G. Cortis, I. Mileti, F. Nalli, E. Palermo, L. Cortese, Additive manufacturing structural redesign of hip prostheses for stress-shielding reduction and improved functionality and safety, Mech. Mater. 165 (2022) 104173, https://doi.org/10.1016/j.mechmat.2021.104173.
[16] G. Yu, Z. Li, S. Li, Q. Zhang, Y. Hua, H. Liu, X. Zhao, D.T. Dhaidhai, W. Li, X. Wang, The select of internal architecture for porous Ti alloy scaffold: a compromise between mechanical properties and permeability, Mater. Des. 192 (2020) 108754, https://doi.org/10.1016/j.matdes.2020.108754.
[17] J.L. Wolff, The Law of Bone Remodeling, translated by Marquet P, Furlong R, Springer, Berlin, Germany, 1986.
[18] W.D. Bugbee, C.J. Sychterz, C.A. Engh, Bone remodeling around cementless hip implants, Southern Med. J. 89 (11) (1996) 1036–1040.
[19] Office of the Surgeon General (US). Bone Health and Osteoporosis: A Report of the Surgeon General. Rockville (MD): Office of the Surgeon General (US); 2004. 2, The Basics of Bone in Health and Disease. Available from: https://www.ncbi.nlm.nih.gov/books/NBK45504/.
[20] M. Bagge, A model of bone adaptation as an optimization 33 (2000) 1349–2135.
[21] C.A. Engh, T.J. Ellis, L.M. Koralewicz, J.P. McAuley, C.A. Engh, Extensively Porous-Coated Femoral Revision for Severe Femoral Bone Loss, The Journal of Arthroplasty 17 (8) (2002) 955–960.
[22] A.B. Swanson, Finger Joint Replacement by Silicone Rubber Implants and the Concept of Implant Fixation by Encapsulation, Ann. Rheum. Dis. 28 (Suppl 5) (1969) 47–55. PMID: 5379851.
[23] R.J. Ferguson, A.JR. Palmer, A. Taylor, M.L. Porter, H. Malchau, S. Glyn-Jones, Ferguson; Antony Jr Palmer; Adrian Taylor; Martyn L Porter; Henrik Malchau, Sion Glyn-Jones. Hip replacement. Lancet 392 (10158) (2018) 1662–1671.
[24] R. De Santis, A. Gloria, L. Ambrosio, Composite materials for hip joint prostheses, in: Biomedical Composites, Elsevier, 2017, pp. 237–259.
[25] S.M. Darwish, A.M. Al-Samhan, Optimization of Artificial Hip Joint Parameters, Materials Sci. Engineering Technology 40 (3) (2009) 218–223, https://doi.org/10.1002/mave.20090430.
[26] M. Zhang, Biocompatibility of materials, Biomaterials Tissue Engineering (2004) 83–143.
[27] Katti, K.S., 2004. Biomaterials in total joint relpacement. Colloids and Surfaces B: Biointerfaces, 39: I 33-142.
[28] A.T. Şensoy, M. Çolak, I. Kaymaz, F. Findik, Optimal Material Selection for Total Hip Implant: A Finite Element Case Study, Arabian J. Sci. Eng. 44 (12) (2019) 10293–10301, https://doi.org/10.1007/s13369-019-04088-y.
[29] J.D. Bobyn, A.H. Glassman, H. Goto, J.J. Krygier, J.E. Miller, C.E. Brooks, The effect of stem Stiffness on femoral bone resorption after canine porous-coated total hip arthroplasty, Clin. Orthopaedics 261 (&NA;) (1990) 196???213, https://doi.org/10.1097/00003086-199012000-00022.
[30] D.R. Sumner, J.O. Galante, Determinants of stress shielding: Design versus materials versus interface, Clin. Orthopaed. Related Res. 274 (1992) 202–221.
[31] C. Eingartner, S. Piel, K. Weise, Results of a cemented straight titanium alloy femoral stem after mean follow-up of 13 years, Eur. J. Orthop. Surg. Traumatol. 17 (2007) 587–593, https://doi.org/10.1007/s00590-007-0232-2.
[32] W.H. Harris, Traumatic arthritis of the hip after dislocation and acetabular fractures: treatment by mold arthroplasty. An end-result study using a new method of result evaluation, J. Bone Joint Surg. Am. 51 (4) (1969) 737–755.
[33] Patrícia Ortega Cubillos, Claudio Teodoro dos Santos, Ieda Maria Vieira Caminha, Maurício de Jesus Monteiro, Vinícius Oliveira dos Santos, et al, Robson de Oliveira Centeno, 2017.
[34] A. Choubey, R. Balasubramaniam, B. Basu, Effect of replacement of V by Nb and Fe on the electrochemical and corrosion behavior of Ti–6Al–4V in simulated physiological environment, J. Alloy. Compd. 381 (1-2) (2004) 288–294.
[35] G.J. Thompson, D.A. Puleo, Ti-6Al-4V ion solution inhibition of osteogenic cell phenotype as a function of differentiation timecourse in vitro, Biomaterials 17 (20) (1996) 1949–1954.
[36] M. Geetha, A.K. Singh, R. Asokamani, A.K. Gogia, Ti based biomaterials, the ultimate choice for orthopaedicimplants – A review, Prog. Mater Sci. 54 (3) (2009) 397–425.
[37] S.J. Mandriota, M. Tenan, P. Ferrari, A. Sappino, Aluminium chloride promotes tumorigenesis and metastasis innormal murine mammary gland epithelial cells, Int. J. Cancer 139 (12) (2016) 2781–2790.
[38] G. Khadija, A. Saleem, Z. Akhtar, Z. Naqvi, M. Gull, M. Masood, S. Mukhtar, M. Batool, N. Saleem, T. Rasheed, N. Nizam, A. Ibrahim, F. Iqbal, Short term exposure to titanium, aluminum and vanadium (Ti 6Al 4V) alloy powder drastically affects behavior and antioxidant metabolites in vital organs of male albino mice, Toxicol. Rep. 5 (2018) 765–770.
[39] F. Haase, C. Siemers, L. Klinge, C. Lu, P. Lang, S. Lederer, T. König, J. Rösler, P. Villechaise, B. Appolaire, P. Castany, M. Dehmas, C. Delaunay, J. Delfosse, A. Denquin, E. Gautier, L. Germain, N. Gey, T. Gloriant, J.-Y. Hascoët, S. Hémery, Y. Millet, D. Monceau, F. Pettinari-Sturmel, M. Piellard, F. Prima, B. Viguier, Aluminum- and Vanadium-free Titanium Alloys for Medical Applications, MATEC Web Conf. 321 (2020) 05008, https://doi.org/10.1051/matecconf/202032105008.
[40] M. Pulido, A. Parrish, Metal-induced apoptosis: mechanisms, Mutation Research/Fundamental and Molecular Mechanisms of Mutagenesis 10 (2003) 533 227.
[41] K.e. Yang, Y. Ren, Nickel-free austenitic stainless steels for medical applications, Sci. Technol. Adv. Mater. 11 (1) (2010) 014105, https://doi.org/10.1088/1468-6996/11/1/014105.
[42] J. Menzel, W. Kirschner, High Nitrogen Containing Ni-free Austenitic Steels for Medical Applications, ISIJ Int. 36 (1996) 893–900.
[43] E. Szabo, C. Rimnac, Biomechanics of immature human cortical bone: A systematic review, J. Mech. Behav. Biomed. Mater. 125 (2022) 104889, https://doi.org/10.1016/j.jmbbm.2021.104889.
[44] X. Wang, S. Xu, S. Zhou, W. Xu, M. Leary, P. Choong, M. Qian, M. Brandt, Y.M. Xie, Topological design and additive manufacturing of porous metals for bone scaffolds and orthopaedic implants: A review, Biomaterials 83 (2016) 127–141.
[45] K. Harboe, N.R. Gjerdet, E. Sudmann, K. Indrekvam, K. Soreide, Assessment of retention force and bone apposition in two differently coated femoral stems after 6 months of loading in a goat model, Journal of Orthopaedic Surgery and Research 69 (2014) 1–8, https://doi.org/10.1186/s13018-014-0069-4.
[46] X.u. Jianda, Z. Xie, J. Zhao, Y.i. Gao, H. Zhao, L. Peng, et al., Results of a hydroxyapatite-coated femoral stem (Corail) in Chinese: a minimum 10-year follow-up, SpringerPlus 5 (2016) 1–5, https://doi.org/10.1186/s40064-016-3656-5.
[47] A. Barakat, J. Quayle, P. Stott, J. Gibbs, M. Edmondson, Results of hydroxyapatite ceramic coated primary femoral stem in revision total hip replacement, Int. Orthop. 44 (9) (2020) 1655–1660, https://doi.org/10.1007/s00264-020-04579-w.
[48] O. Critchley, S. Callary, G. Mercer, D. Campbell, C. Wilson, Long-term migration characteristics of the Corail hydroxyapatite-coated femoral stem: a 14-year radiostereometric analysis follow-up study, Arch. Orthop. Trauma Surg. 140 (1) (2020) 121–127, https://doi.org/10.1007/s00402-019-03291-8.
[49] H. Bougherara, R. Zdero, A. Dubov, S. Shah, S. Khurshid, E.H. Schemitsch, A preliminary biomechanical study of a novel carbon-fibre hip implant versus standard metallic hip implants, Med. Eng. Phys. 33 (1) (2011) 121–128, https://doi.org/10.1016/j.medengphy.2010.09.011.
[50] S.L. Evans, P.J. Gregson, Composite Technology in Load-Bearing Orthopaedic Implants, Biomaterials 19 (15) (1998) 1329–1342.
[51] A. Brandwood, K.R. Noble, K. Schindhelm, Phagocytosis of Carbon Particles by Macrophages In Vitro, Biomaterials 13 (9) (1992) 646–648.
[52] W. Li, L. Hao, K. Sun, X. Qiao, Three-dimensional finite element analysis of stress distribution of composite and metal hip joint prosthesis, Orthopaedic Biomechanics Materials and Clinical Study. 2 (3) (2005) 1–4.
[53] Melissa Campbell, Martin N. Bureau, L' Hocine Yahia (2008). Performance of CF/PA12 composite femoral stems. Journal of Materials Science: Materials in Medicine, 19: 683-693. doi: 10.1007/s10856-007-3073-y.
[54] M. Campbell, J. Denault, L' Hocine Yahia, Martin N. Bureau, (2008). CF/PA12 camcomposite femoral stems: Manufacturing and properties. Composites Part A: Applied Science and Manufacturing, 9 (2008) 796–804. doi: 10.1016/j.compositesa.2008.01.016.
[55] H. Mehboob, F. Ahmad, F. Tarlochan, A. Mehboob, S.H. Chang, A comprehensive analysis of bio-inspired design of femoral stem on primary and secondary stabilities using mechanoregulatory algorithm, Biomech. Model. Mechanobiol. 19 (6) (2020) 2213–2226, https://doi.org/10.1007/s10237-020-01334-3.
[56] S.E. Alkhatib, H. Mehboob, F. Tarlochan, Finite element analysis of porous titanium alloy hip stem to evaluate the biomechanical performance during walking and stair climbing, J. Bionic Eng. 16 (6) (2019) 1103–1115.
[57] S.E. Alkhatib, F. Tarlochan, H. Mehboob, R. Singh, K. Kadirgama, W.S.B.W. Harun, Finite element study of functionally graded porous femoral stems incorporating body-centered cubic structure, Artif. Organs 43 (2019) E152–E164.
[58] A. Reinhardt, S.G. Advani, M.H. Santare, F. Miller, Preliminary study on composite hip prostheses made by resin transfer molding, J. Compos. Mater. 33 (9) (1999) 852–870.
[59] H.S. Hedia, M.A.N. Shabara, T.T. El-Midany, N. Fouda, Improved Design of Cementless Hip Stems Using Two-Dimensional Functionally Graded Materials, J. Biomed. Mater. Res. B. 79B (1) (2006) 42–49.
[60] M. Nemat-Alla, Reduction of thermal stresses by developing two-dimensional functionally graded materials, Int. J. Solids Struct. 40 (26) (2003) 7339–7356.
[61] H.e. Gong, W. Wu, J. Fang, X. Dong, M. Zhao, T. Guo, Effects of Materials of Cementless Femoral Stem on the Functional Adaptation of Bone, J. Bionic Eng. 9 (1) (2012) 66–74, https://doi.org/10.1016/S1672-6529(11)60098-X.
[62] F.F. Al-Jassir, H. Fouad, O.Y. Alothman, In vitro assessment of Function Graded (FG) artifical Hip joint stem in terms of bone/cement stresses: 3D Finite Element (FE) study, Biomed. Eng. Online 12 (5) (2013) 1–17, https://doi.org/10.1186/1475-925X-12-5.
[63] D. B. Bennett, J. C. Hill, J. Dennison, S. O' Brien, D. E. Beverland (2014). Metal-Carbon Fiber Composite Femoral Stems in Hip Replacements. Journal of Bone and Joint Surgery, 2062-2069. doi: 10.1016/S0021-9355(14)74482-0.
[64] ISO 7206-4:2010, Implants for surgery - Partial and total hip joint prostheses Part 4: Determination of endurance properties and performance of stemmed femoral components, Standard, International Organization for Standardization, Geneva, CH (Sep. 2020).

[65] E.Munting, M.Verhelpen(1995). Fixation and effect on bone strain pattern of a stemless hip prosthesis. Journal of Biomechanics, 28(8): 949-961. doi: 10.1016/0021-9290(94)00146-U.
[66] C. Bitsakos, J. Kerner, I. Fisher, A.A. Amis, The effect of muscle loading on the simulation of bone remodelling in the proximal femur, J. Biomechanics 38 (1) (2005) 133–139.
[67] A.V. Wiik, A. Aqil, B. Al-Obaidi, M. Brevadt, J.P. Cobb, The impact of reducing the femoral stem length in total hip arthroplasty during gait, Arch. Orthop. Trauma Surg. 141 (11) (2021) 1993–2000, https://doi.org/10.1007/s00402-021-03852-w.
[68] M.G. Joshi, S.G. Advani, F. Miller, M.H. Santare, Analysis of a femoral hip prosthesis designed to reduce stress shielding, J. Biomechanics 33 (12) (2000) 1655–1662.
[69] Y. Zou, Bio-mechanical Study on the Artificial Hip Prosthesis System, Tianjin University, [Tianjin], 2006 [master's thesis].
[70] X.W. Zheng, H.R. Meng, Finite element analysis of femoral stem stress after artificial medullary joint replacement, J. Xidian University 24 (4) (2004) 459–462.
[71] B. van Rietbergen, R. Huiskes, Load transfer and stress shielding of the hydroxyapatite-ABG hip: a study of stem length and proximal fixation, J. Arthroplasty 16 (8) (2001) 55–63.
[72] H.E. Jergesen, J.W. Karlen, Clinical outcome in total hip arthroplasty using a cemented Titanium femoral prosthesis, J. Arthroplasty 17 (5) (2002) 592–599.
[73] H. Gong, The Three-dimensional Reconstruction of Femur and Finite-Element Analysis of Hip Joint Replacement. [master's thesis], Xiamen University, [Xiamen], 2009.
[74] R.M. Pilliar, J.M. Lee, C. Maniatopoulos, Observation of the effect of movement on bone ingrowth into porous-surfaced implants, Clin Orthop Relat Results. 208 (1986) 108–113.
[75] M. Reimeringer, N. Nuño, C. Desmarais-Trépanier, M. Lavigne, P.A. Vendittoli, The influence of uncemented femoral stem length and design on its primary stability: a finite element analysis, Comput. Methods Biomech. Biomed. Eng. 16 (11) (2013) 1221–1231, https://doi.org/10.1080/10255842.2012.662677.
[76] Y.-H. Kim, J.-W. Park, J.-S. Kim, Ultrashort versus Conventional Anatomic Cementless Femoral Stems in the Same Patients Younger Than 55 Years, Clin. Orthop. Relat. Res. 474 (2016) 2008–2017, https://doi.org/10.1007/s11999-016-4902-4.
[77] Y.u. Huachen, H. Liu, M. Jia, H.u. Yuezheng, Y.u. Zhang, A comparison of a short versus a conventional femoral cementless stem in total hip arthroplasty in patients 70 years and older, Journal of Orthopaedic Surgery and Research 1–9 (2016), https://doi.org/10.1186/s13018-016-0367-0.
[78] S.S. Kim, H.J. Kim, K.W. Kim, Y.H. Jung, S.Y. Heo, Comparative Analysis between Short Stem and Conventional Femoral Stem in Patients with Osteonecrosis of Femoral Head: Metha Stem and Excia Stem, Orthop. Surg. 12 (3) (2020) 819–826.
[79] J.-Y. Lim, H.-J. Park, Y.-K. Lee, Y.-C. Ha, K.-H. Koo, Comparison of Bone Preservation in Elderly Patients with Femoral Neck Fracture After Bipolar Hemiarthroplasty Using Shorter Femoral Stem and Standard Femoral Stem, Indian J. Orthopaedics 54 (6) (2020) 868–878, https://doi.org/10.1007/s43465-020-00115-5.
[80] Hao-ran Zhang, Jing-yu Zhang, Xiong-gang Yang, Rui-qi Qiao, Ji-kai Li, Zhi-peng Ren,et al(2020). The effects of length stem on aseptic loosening following cemented distal femoral endoprosthetic replacement in tumour surgery. International Orthopaedics, 2020. doi: 10.1007/s00264-020-04629-3.
[81] T. Niinimäki, J. Junila, P. Jalovaara, A proximal fixed anatomic femoral stem reduces stress shielding, Intl. Orthopaedics 25 (2) (2001) 85–88.
[82] H.J. Laine, T.J.S. Puolakka, T. Moilanen, K.J. Pajamäki, J. Wirta, M.U.K. Lehto, The effects of cementless femoral stem shape and proximal surface texture on "fit-and-fill" characteristic and on bone remodeling, Int. Orthop. 24 (2000) 184–190, https://doi.org/10.1007/s002640000150.
[83] J. Wang, Y. Qiu, L. Peng, Modeling and finite element analysis of femur after implantation of prosthesis, Chinese J. Appl. Mech. 23 (1) (2006) 41–43.
[84] P.B. Chang, B.J. Williams, K.S.B. Bhalla, T.W. Belknap, T.J. Santner, I.W. Notz, D. L. Bartel, Environmental variables design and analysis of robust total joint replacements: Finite element model experiments with environmental variables, J. Biomechanical Eng. 123 (2001) 239–246.
[85] X. Zheng, X. Feng, Y. Feng, Finite element analysis of the influence of artificial femoral stem shape and surface treatment on stress distribution of prosthesis and human femur after replacement, J. Medical Biomechanics. 21 (4) (2006) 322–327.
[86] C. Mattheck, U. Vorberg, C. Kranz, Effects of hollow shaft endoprosthesis on stress distribution in cortical bone, Biomed. Eng. 35 (1990) 316–319.
[87] S. Gross, E.W. Abel, A finite element analysis of hollow stemmed hip prostheses as a means of reducing stress shielding of the femur, Biomechanics 34 (8) (2001) 995–1003.
[88] A.L. Sabatini, T. Goswami, Hip implants VII: Finite element analysis and optimization of cross-sections, Mater. Des. 29 (7) (2008) 1438–1446, https://doi.org/10.1016/j.matdes.2007.09.002.
[89] B. Ellison, N.A. Cheney, K.R. Berend, A.V. Lombardi, T.H. Mallory, Minimal stress shielding with a Mallory-Head titanium femoral stem with proximal porous coating in total hip arthroplasty, J. Orthopaedic Surgery Research (2009) 1–10, https://doi.org/10.1186/1749-799X-4-42.
[90] K. Hu, X. Zhang, J. Zhu, C. Wang, W. Ji, X. Bai, Periprosthetic fractures may be more likely in cementless femoral stems with sharp edges, Ir. J. Med. Sci. 179 (3) (2010) 417–421, https://doi.org/10.1007/s11845-009-0442-1.
[91] R. Tan, H. Fan, W. Fang, J. Chen, J. Luo, X. Zhang, Three-dimensional finite element analysis of bone stress distribution in alveolar artificial hip joint, J. Biomed. Eng. 28 (4) (2011) 732–736.
[92] Y. Noyama, T. Nakano, T. Ishimoto, T. Sakai, H. Yoshikawa, Design and optimization of the oriented groove on the hip implant surface to promote bone microstructure integrity, Bone 52 (2) (2013) 659–667, https://doi.org/10.1016/j.bone.2012.11.005.
[93] L. Li, Optimization Design of Femoral Prosthesis Stem, Huaqiao University, [Fujian], 2017 [master's thesis].
[94] J. Yoshitani, T. Kabata, Y. Kajino, T. Takagi, T. Ohmori, T. Ueno, K. Ueoka, H. Tsuchiya, The effect of flexion alignment in total hip arthroplasty with a cementless tapered-wedge femoral stem, Eur. J. Orthop. Surg. Traumatol. 28 (8) (2018) 1625–1632, https://doi.org/10.1007/s00590-018-2227-6.
[95] G. Ryan, A. Pandit, D. Apatsidis, Fabrication Methods of Porous Metals for Use in Orthopaedic Applications, Biomaterials 27 (13) (2006) 2651–2670.
[96] A. Rahman, M. Mahamid, Functiorially graded cellular metal alloys for joint implants, Columbia University, New York, NY, 2002.
[97] A. Nazir, K.M. Abate, A. Kumar, J.-Y. Jeng, A state-of-the-art review on types, design, optimization, and additive manufacturing of cellular structures, Int. J. Adv. Manuf. Technol. 104 (9-12) (2019) 3489–3510, https://doi.org/10.1007/s00170-019-04085-3.
[98] W. Yan, J. Berthe, C. Wen, Numerical investigation of the effect of porous titanium femoral prosthesis on bone remodeling, Mater. Des. 32 (4) (2011) 1776–1782, https://doi.org/10.1016/j.matdes.2010.12.042.
[99] H. Mehboob, F. Tarlochan, A. Mehboob, S.-H. Chang, S. Ramesh, W.S.W. Harun, K. Kadirgama, A novel design, analysis and 3D printing of Ti-6Al-4V alloy bio-inspired porous femoral stem, J. Mater. Sci. - Mater. Med. 31 (9) (2020), https://doi.org/10.1007/s10856-020-06420-7.
[100] C. Simoneau, P. Terriault, B. Jetté, M. Dumas, V. Brailovski, Development of a porous metallic femoral stem: Design, manufacturing, simulation and mechanical testing, Mater. Des. 114 (2017) 546–556, https://doi.org/10.1016/j. matdes.2016.
[101] He, Y, Burkhalter, D, Durocher, D, & Gilbert, JM. (2018). Solid-Lattice Hip Prosthesis Design:Applying Topology and Lattice Optimization to Reduce Stress Shielding From Hip Implants. 2018 Design of Medical Devices Conference. Minneapolis, Minnesota, USA. April 9–12, 2018. V001T03A001. ASME. doi: 10.1115/DMD2018-6804.
[102] Y. Liu, Q. Ouyang, R. Tian, Q. Wang, Fatigue Properties of Ti-6Al-4V Subjected to Simulated Body Fluid, Tech Science Press 2 (3) (2009) 169–175, https://doi.org/10.1115/DMD2018-6804.
[103] M. Leary, M. Mazur, J. Elambasseril, M. McMillan, T. Chirent, Y. Sun, M. Qian, M. Easton, M. Brandt, Selective laser melting (SLM) of AlSi12Mg lattice structures, Mater. Des. 98 (2016) 344–357, https://doi.org/10.1016/J.MATDES.2016.02.127.
[104] S.u. Wang, X. Zhou, L. Liu, Z. Shi, Y. Hao, On the design and properties of porous femoral stems with adjustable stiffness gradient, Med. Eng. Phys. 81 (2020) 30–38, https://doi.org/10.1016/j.medengphy.2020.05.003.
[105] N.F. Al Zoubi, F. Tarlochan, H. Mehboob, F. Jarrar, Design of Titanium Alloy Femoral Stem Cellular Structure for Stress Shielding and Stem Stability: Computational Analysis, Appl. Sci. 12 (2022) 1548, https://doi.org/10.3390/app12031548.
[106] Ridzwan, M.I.Z., Solehuddin Shuib, A.Y. Hassan, A.A. Shokri and M.N.M. Ibrahim, 2006. Optimization in implant topology to reduce stress shielding problem. J. Applied Sci., 6: 2768-2773.
[107] R. Kumar, M. Kumar, J.S.S. Chohan, J. Manuf. Process. 64 (2021) 828–850.
[108] H.R. Syed, H.M. Syed, A.R.R. Rizwan, C. Sanjeet, Selective Laser Sintering in Biomedical Manufacturing, Amsterdam, The Netherlands, Metallic Biomaterials Processing and Medical Device Manufacturing; Elsevier, 2021.
[109] D. Stoia, E. Linul, L. Marsavina, Influence of Manufacturing Parameters on Mechanical Properties of Porous Materials by Selective Laser Sintering, Materials 12 (6) (2019) 871, https://doi.org/10.3390/ma12060871.
[110] L. Zengguang, W. Yanqing, C. Chunzhi, A critical review of fused deposition modeling 3D printing technology in manufacturing polylactic acid parts, Int. J. Adv. Manuf. Technol. 2 (2019) 1–13, https://doi.org/10.1007/s00170-019-03332.
[111] D.K. Pattanayak, A. Fukuda, T. Matsushita, M. Takemoto, S. Fujibayashi, K. Sasaki, N. Nishida, T. Nakamura, T. Kokubo, Bioactive Ti Metal Analogous to Human Cancellous Bone: Fabrication by Selective Laser Melting and Chemical Treatments, Acta Biomater. 7 (3) (2011) 1398–1406.
[112] K.B. Hazlehurst, C.J. Wang, M. Stanford, An investigation into the flexural characteristics of functionally graded cobalt chrome femoral stems manufactured using selective laser melting, Mater. Des. 60 (2014) 177–183, https://doi.org/10.1016/j. matdes.2014.03.068.
[113] K.M. Abate, A. Nazir, J.-Y. Jeng, Design, optimization, and selective laser melting of vin tiles cellular structure-based hip implant, The International Journal of Advanced Manufacturing Technology 112 (7–8) (2021) 2037–2050, https://doi.org/10.1007/s00170-020-06323-5.
[114] X. Li, C. Wang, W. Zhang, Y. Li, Fabrication and Characterization of Porous Ti6Al4V Parts for Biomedical Applications Using Electron Beam Melting Process, Mater. Lett. 63 (3-4) (2009) 403–405.
[115] A. Bandyopadhyay, F. Espana, V.K. Balla, S. Bose, Y. Ohgami, N.M. Davies, Influence of Porosity on Mechanical Properties and In Vivo Response of Ti6Al4V Implants, Acta Biomater. 6 (4) (2010) 1640–1648.
[116] S.A. Khanoki, D. Pasini, Multiscale Design and Multiobjective Optimization of Orthopedic Hip Implants With Functionally Graded Cellular Material, ASME J. Biomech. Eng. 134 (3) (2012) 031004.

[117] Wang, Y., Arabnejad, S., Tanzer, M., and Pasini, D. (2018). "Hip Implant Design With Three-Dimensional Porous Architecture of Optimized Graded Density." ASME. J. Mech. Des. November,140(11): 111406. doi: 10.1115/1.4041208.
[118] Kladovasilakis N., Tsongas K., Tzetzis D. Finite Element Analysis of Orthopedic Hip Implant with Functionally Graded Bioinspired Lattice Structures. Biomimetics. 2020; 5:44. doi: 10.3390/biomimetics5030044.
[119] B.M. Willie, E.A. Zimmermann, I. Vitienes, R.P. Main, S.V. Komarova, Bone adaptation: safety factors and load predictability in shaping skeletal form, Bone 131 (2020) 115114, https://doi.org/10.1016/j.bone.2019.115114.
[120] H.S. Sidhu, S. Kumar, R. Kumar, S. Kumar, Experimental investigation on design and analysis of prosthetic leg, Journal of Xidian University 15 (5) (2020) 4486–4501. https://doi.org/10.37896/jxu14.5/491.
[121] B. Pérez, H. Nykvist, A.F. Brøgger, M.B. Larsen, M.F. Falkeborg, Impact of macronutrients printability and 3D-printer parameters on 3D-food printing: a review, Food Chem. 287 (2019) 249–257.
[122] Z. Chen, Z. Li, J. Li, C. Liu, C. Lao, Y. Fu, C. Liu, Y. Li, P. Wang, Y.i. He, 3D printing of ceramics: a review, J. Eur. Ceram. Soc. 39 (4) (2019) 661–687.
[123] M.A. Pop, C. Croitoru, T. Bedő, V. Geamăn, I. Radomir, M. Cosniță, S.M. Zaharia, L.A. Chicos, I. Milosan, Structural changes during 3D printing of bioderived and synthetic thermoplastic materials, J Appl Polym Sci Symp 136 (17) (2019) 47382, https://doi.org/10.1002/app.v136.1710.1002/app.47382.
[124] X. Zhao, S. Li, M. Zhang, Y. Liu, T.B. Sercombe, S. Wang, Y. Hao, R. Yang, L.E. Murr, Comparison of the microstructures and mechanical properties of Ti-6Al-4V fabricated by selective laser melting and electron beam melting, Mater. Des. 95 (2016) 21–31, https://doi.org/10.1016/j.matdes.2015.12.135.
[125] H.E. Burton, N.M. Eisenstein, B.M. Lawless, P. Jamshidi, M.A. Segarra, O. Addison, D.E.T. Shepherd, M.M. Attallah, L.M. Grover, S.C. Cox, The design of additively manufactured lattices to increase the functionality of medical implants, Mater. Sci. Eng., C 94 (2019) 901–908, https://doi.org/10.1016/j.msec.2018.10.052.