Osseointegration of hollow porous titanium prostheses loaded with cancellous bone matrix in rabbits

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This study aimed to observe the osseointegration of hollow porous titanium prostheses (HPTP) loaded with cancellous bone matrix (CBM) in rabbits using histological and biomechanical perspectives. Experimental samples were implanted into the lateral femoral condyles of 66 New Zealand rabbits, allocated into the following groups: non-porous prosthesis group (Group A, $n=22$); HPTP group (Group B, $n=22$); HPTP+CBM group (Group C, $n=22$). The rabbits were sacrificed at 3, 8 and 12 weeks, postoperatively. X-ray analyses, microscopy techniques and morphological measurement software and mechanical tests were used for evaluation. At each time point, the tissues surrounding the implants were similar in all of the groups, with bony in-growth into the 2-mm round holes observed for the defects in Groups B and C. However, the internal bone formation was significantly better in Group C than in Group B at different time points ($P<0.01$). Biomechanically, the pull-out forces were significantly greater in Groups B and C than in Group A ($P<0.01$), with no difference between Groups B and C ($P>0.05$). These results suggest that bone can grow into the cavities of HPTP to achieve more stable locking fixation, and those osteogenic materials, such as CBM, can enhance osteogenesis to achieve better osseointegration between the implant and the host bone.

joint replacement, osteogenesis, osseointegration, surface treatment, histology, mechanical test

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Aseptic loosening and the limited life spans of artificial joints still remain troublesome complications in joint replacement procedures [1–5]. Many patients with a failed primary artificial joint have to undergo additional operations that are often expensive and sometimes provide unsatisfactory results. A number of studies have been performed to explore the various potential factors that lead to these problems from both mechanical and biological perspectives [6–9]. Such studies have shown that many aspects could be to blame, with improvements in the materials, mechanical designs and surface treatments of prostheses warranting further attention [10–12].

To date, great progress has been made to improve pros-

thesis materials. Durable materials, such as new alternative metals [13], highly cross-linked polyethylenes [13,14] and bioceramics [13,15], are currently being used by prosthesis manufacturers, which may help to reduce the wear on these prostheses, and increase their current life span. Improvements have also been made in the mechanical designs and surface treatment strategies, with promising fixation deriving from more accurate anatomical and biomimetic mechanical designs minimizing contact stresses [16], and surface treatments, such as extensive or proximal hydroxyapatite (HA) coatings, titanium oxide nitride coatings [17] and application of trabecular metal (porous tantalum) [18]. Meanwhile, improved cementing techniques can extend the durability of cemented prosthesis fixation and markedly reduce the incidences of osteolysis and aseptic loosening

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[19]. Furthermore, cementless prostheses have been developed, which can decrease certain aseptic loosening and provide a better long-term survival rate than a cemented prosthesis, even if it is used with the proper indications [20]. Despite these improvements, there has not been a significant decrease in the number of patients requiring revisions in response to aseptic loosening. Some studies have shown that the bone in-growth rates at the material-host bone interface are still very limited, ranging from only 6% to 35% [21–23]. Other studies have shown that surface coating treatments are not reliable, owing to absorption and degradation of the surface materials [24–26]. Consequently, we still need to seek improved mechanical designs for successful osseointegration.

Long bones are hollow tubular structures; this structure provides the necessary biomechanical requirements for withstanding force and facilitating movement. If hollow prostheses could also provide sufficient strength required by patients in everyday life, it may be possible to adopt a partially or totally hollow porous design for better bone in-growth and osseointegration. Inspired by the successful bone regeneration applications of “interbody fusion cages” used in spinal surgeries, and “bone harvest chambers” used in animal models [27,28], we designed a device, which we have termed the “biological-compound hollow porous artificial joint prosthesis” [29–31]. In this design, some parts of the prosthesis are hollow and porous, and later loaded with osteogenic materials. We hypothesized that this would promote better bone formation and ingrowth via holes in the sides of the prosthesis to enhance locking fixation. In addition, this design would provide a reasonable elastic modulus and stress transmission to reduce stress shielding, provide a press-fit compression between the host bone and the prosthesis to block particle wear at the interface, require the use of less material, and provide the patient with a lighter weight prosthesis, among other benefits [29].

In the present study, we designed HA-coated non-porous prostheses (similar to traditional solid designs in function) and hollow porous titanium prostheses (HPTP) with 2 mm diameter holes; the terms “non-porous” and “porous” are used to refer to these two types of prostheses within this study, respectively. We implanted the non-porous and HPTP prostheses with or without loading of cancellous bone matrix (CBM) bolts into cavities created in the lateral femoral condyles of New Zealand rabbits. The rabbits were sacrificed at 3, 8 and 12 weeks, postoperatively. Results were analyzed using X-ray, light and fluorescence microscopies, scanning electron microscopy and morphological measurement software (Image-Pro Plus 6.0 System). Furthermore, biomechanical tests were performed. To explore the creation of better designs for artificial joint prostheses, we assessed the possibility of bone formation and observed the histological and biomechanical changes in rabbits implanted with HPTP loaded with CBM bolts.

1 Materials and methods

1.1 Preparation of prostheses and CBM bolts

A total of 44 HPTP and 22 non-porous prostheses were manufactured from TC4 (Ti-6Al-4V) titanium alloy rods (Tianjin Zhengtian Medical Instruments Co. Ltd.; Figure 1). All HPTP prostheses consisted of several parts. The body of the HPTP comprised a hollow cylinder of 8.5 mm in height, 7 mm in external diameter and 6 mm in internal diameter, and was implanted into bone. The side- and bottom walls of the HPTP were 0.5 mm in thickness, with 18 round holes (2 mm in diameter) evenly distributed in the sidewalls. The head part of the HPTP was 3 mm in height, 8.5 mm in external diameter and 6 mm in internal diameter, and was not implanted into bone. The head parts were carved with screw threads in the superior 2.5 mm of the internal wall, into which the supporting screw nuts and testing bar for biomechanical tests could be screwed. The non-porous prostheses were manufactured to the same size as the HPTP, but had no holes in their sidewalls (Figure 1). All body parts exposed to bone were coated with plasma-sprayed HA (Biomedical Materials Engineering Center, Sichuan University), manufactured according to a standard procedure, ISO 13779-2: (1) coated HA: $\geq 90\%$; HA crystallinity: $\geq 45\%$; (2) Ca/P atomic ratio of coated HA: 1.67–1.76; (3) amounts of impurity elements and total amount of heavy metals (as Pb) (mg/kg): arsenic (As), ≤ 3 ; cadmium (Cd), ≤ 5 ; mercury (Hg), ≤ 5 ; lead (Pb), ≤ 30 ; total amount of heavy metals, ≤ 50 ; (4) quality of surface coatings: coating thickness of 50–100 μm , gray thin layer, uniform color and tightly covering the surface of the substrate; (5) HA coating and bonding strength: tensile strength, ≥ 15 MPa. 22 round CBM bolts (5.5 mm in diameter and 7.5 mm in length) were created from fresh calf cancellous bone. All antigenic organic matter was removed by strong chemical treatment, and the remaining three-dimensional mesh-like bolts were mainly constituted of inorganic bone matrix (Tianjin Zhongjin Pharmaceutical Co. Ltd.; Figure 1). All prostheses and CBM bolts were packaged and sterilized with ethylene oxide.

1.2 Grouping and operation

Sixty-six healthy New Zealand white rabbits, aged 4–6 months, weighed between 2.5–3 kg; the sex of the rabbit was ignored. The rabbits were divided into three groups depending on the prosthesis to be delivered: non-porous prosthesis group (Group A, $n=22$); HPTP group (Group B, $n=22$); and HPTP+CBM group (Group C, $n=22$, CBM bolts were placed in the HPTP cavities). Each rabbit underwent the same treatment procedure. For anesthesia, sumianxin (Beijing Chongbiwei Biological Technology Co. Ltd.) and ketamine hydrochloride (Fujian Gutian Pharmaceutical Co. Ltd.) were mixed at a ratio of 1.5 to 2.0 mL and intramuscularly injected at 0.4 mL/kg. The operative region was sterilized and draped. A lateral excision was created to ex-

pose the lateral femoral condyle of the right leg. A transverse hole in the bone (8.5 mm in depth) was drilled, and dilated with sharp and blunt broaching bits (7.2 mm in diameter; Figure 1). The implant was then placed into the hole. The incision site was closed with sutures. X-ray examinations were performed immediately after the operation, and 2×10^5 IU of penicillin was intramuscularly injected once per day until the third postoperative day.

1.3 Preparation of non-decalcified bone slices

The time points for observation were set at 3, 8 and 12 weeks, postoperatively. On days 13 and 3 prior to sacrifice, tetracycline hydrochloride (Beijing Bailingke Biological Technology Co. Ltd.) was injected at 50 mg/kg into each rabbit for fluorescence labeling, and X-ray examinations were performed prior to euthanasia using an aeroembolism method. At each time point, five rabbits from each group were sacrificed, and the femoral portions amputated at about 1 cm superior to the femoral condyles. The specimens were prepared for non-decalcified bone slices for histological observation. The specimens were dehydrated by sequential immersion in 45%, 75%, 95%, 100% and 100% alcohol (1 week for each gradient), and then soaked in dimethyl benzene for one week for transparency. The samples were then sequentially embedded in solutions I, II and III containing polymethyl methacrylate, dibutylphthalate and ben-

zoyl peroxide, respectively (1 week for each solution). Mid-level vertical slices of the embedded specimens (50 μ m thick) were sectioned using a Leica 1600 emery microtome. The slices were stained using the Giemsa method [32], and coverslipped with epoxide resin. The histological changes in the slices were observed using an Olympus BX51 biological microscope and images were acquired with an Olympus DP70 image acquisition system.

1.4 Preparation of specimens for scanning electron microscopy

A specimen from each group was used for scanning electron microscopy observation at 12 weeks, postoperatively. These specimens were pulled out from the bone of the femoral condyles, and the interface and internal tissues of the implants were acquired. The tissues were divided into several small pieces, rinsed with saline, fixed with 2.5% glutaraldehyde and refrigerated at 4°C overnight. On the next day, the samples were rinsed three times with 0.1 mol/L phosphate-buffered saline (PBS) for 30 min each, and fixed with 1% osmium tetroxide solution for 2 h. After three rinses with 0.1 mol/L PBS for 30 min each, the samples were immersed in 2% tannic acid solution twice for 30 min each. The specimens were dehydrated by a conventional graded alcohol treatment, and placed in isoamyl acetate for 40 min for transition. After vacuum critical point drying

Figure 1 Prostheses and Biomechanical testing set-up. a, HPTP (left) and non-porous (right) prostheses coated with HA; b, three-dimensional mesh-like CBM; c, image to demonstrate the exposure of the lateral femoral condyle and location of the drilled hole; d, the prosthesis inserted along the axis of the hole; e, the specimen fixed in a biomechanical testing machine; f, a biomechanical pull-out test performed; g, a load-displacement curve in Group A; h, a load-displacement curve in Group B; i, a load-displacement curve in Group C.

with a Hitachi HCP-2 critical point drying instrument and gold spray coating with a Hitachi E-102 ion sputtering instrument, the specimens were examined by scanning electron microscopy (Hitachi S-4800). The porous structure of the CBM was also viewed after drying and gold spray coating.

1.5 Bone histomorphometry analysis

Five non-decalcified bone slices from five separate specimens in Groups B and C at each time point were observed using an Olympus BX51 biological microscope, and total fluorescent images of all the slices were acquired with an Olympus DP70 image acquisition system. The images were then analyzed using an image analysis system (Image-Pro Plus 6.0 System; provided by Media Cybernetics Co.) to determine and calculate the areas of internal newly formed bone, which appeared yellow in the images of the hollow prostheses. From these measurements, we then calculated the internal relative bone formation (relative bone formation = area of newly formed bone / total internal area of the prosthesis cavity $\times$ 100%). The result for each specimen at different time points was recorded in the form of mean $\pm$ SD.

1.6 Biomechanical tests

The remaining 18 rabbits (6 per group) were sacrificed for biomechanical tests at 12 weeks, postoperatively, and their femurs were truncated inferior to the level of the greater trochanter. Eighteen aluminum boxes (2 cm $\times$ 2 cm $\times$ 5 cm) were created, and self-curing denture acrylic and liquid denture acrylic were sequentially placed into the boxes. After stirring and complete mixing, the specimens were uniformly embedded into the agglomerating mixture. Care was taken to protect the head parts of the prostheses, with plasticine used to prohibit sticking to the denture acrylic mixtures. In addition, it was ensured that a vertical axis of the prostheses was maintained to the superior aspects of the mixtures. When the mixtures had set, the aluminum boxes were removed. After burnishing the superior aspects of the finished specimens with a steel file, the screw nuts were removed from the head parts of the prostheses, and the testing bar was screwed into each specimen in turn for biomechanical testing. The specimens were individually fixed in an MTS 858 mini Bionix II instrument and subjected to pull-out biomechanical tests. The speed was set at 0.1 mm/s, and the computer operating system recorded the real-time stress changes (Figure 1). We successfully obtained all the maximum forces required to pull out the prostheses from the bone.

1.7 Statistical analysis

Inter-group *t*-tests were performed to analyze the relative

bone formation in Groups B and C, and the biomechanical differences among all three groups, using the SPSS 13.0 software (SPSS Inc. Chicago, IL, USA). Values of $P < 0.05$ were considered to indicate significant differences, while values of $P < 0.01$ were considered to indicate very significant differences.

2 Results

2.1 General observations and X-ray analysis

All rabbits were healthy, and no significant inflammatory responses were observed around any of the joints. Most of the prostheses were surrounded by dense fibrous and cartilaginous tissues which were easy to separate (Figure 2). After removal of these tissues, we observed that all of the implants were closely integrated with the surrounding bone. X-ray analyses at different time points postoperatively indicated that all the prostheses were *in situ*, and that no fractures had occurred (Figure 2). After removing the screw nuts of the specimens in Groups B and C, we observed the following phenomena at 3, 8 and 12 weeks, postoperatively. At week 3 postoperatively, hematomas and new granulation tissue were seen in the specimens from Group B; these specimens were very soft. Meanwhile, bone-like tissue was observed in the specimens from Group C, which appeared more solid than the tissues in Group B and the original CBM. Further, hematoma and granulation tissue formation was also observed. By week 8, more fibrous granulation tissues were seen in the specimens from Group B, which were still very soft; whereas, the bone-like tissues in the specimen from Group C had increased further and become much harder. At 12 weeks, a thin layer of bone-like tissue was observed at the top of the cavity in the specimens from Group B, and most of the space below this layer was still filled with an abundance of fibrous granulation tissue. By comparison, more mature bone-like tissues were observed in the specimens from Group C, which were much harder and closely integrated with the internal wall of the prosthesis (Figure 2).

2.2 Light microscopy observations

Light and fluorescent microscopic images of the specimens in all three groups were compared at different time points. At week 3 postoperatively, the regions around the prostheses in all three groups were filled with large numbers of osteoblastic cells, with minor fibrous tissue and blood vessels. There was still evidence of hematoma formation, although the presence of new bone-like tissues was also observed (Figure 3). Similar tissue formation was seen in the holes of the prostheses in Groups B and C. In Group B, the internal cavity of the prosthesis was filled with an abundance of soft fibrous granular tissue, with quite a few osteoblasts. In Group C, the original structure of the CBM was

Figure 2 Images depicting the removal of specimens from the rabbits. a, General view of the implant within the femoral condyle; b–d, X-rays of implants after 12 weeks, postoperatively, from Groups A, B and C, respectively; e, f, representative specimens from Group B and C, respectively, at 12 weeks, post-operatively; g, view of a non-porous prosthesis after pull-out from a representative specimen from Group A; h, view of an HPTP after pull-out from a representative specimen from Group C; i, views of a non-porous prosthesis from Group A and an HPTP from Group C.

still clearly visible, with no obvious absorption; however, abundant bone-like tissues had formed near and inside the CBM, filled with numerous osteoblasts.

The degree of fibrous tissue around the prostheses in all three groups had decreased greatly by week 8, with an increase in the proportion of newly formed bone (Figure 3). In Group B, more bone-like tissues were observed in the holes of the prosthesis, although no significant increase in the amount of fibrous granular tissue was observed in the prosthesis cavity, as compared with the 3 week time point. In Group C, there was clear formation of bone-like tissue in the holes of the prosthesis, and part of the original CBM in the cavity had been absorbed and replaced by new bone-like tissue.

At week 12 postoperatively, a large amount of mature bone had formed in the periphery of the prostheses in all three groups. We observed many complete bony trabeculae and haversian systems, as well as compact integration be-

tween the bone and the prostheses. In Group B, the mature bone in the holes of the HPTP was combined with the host bone surrounding the HPTP and had filled the cavity. There was also an abundance of organized fibrous tissue and very few sparse trabecular structures within the hollow cavity (Figure 3). In Group C, there was a further increase in the degree of mature bone trabeculae formation within the holes and cavity of the HPTP, with limited fibrous tissue and replacement of most of the original CBM by bone.

2.3 Scanning electron microscopy observations

The microstructures of the three-dimensional mesh-like CBM and the newly formed bone around HA-coated prostheses are shown in Figure 4. The results revealed an increase in the density of newly formed trabeculae as they grew closer to the coated HA, with the presence of scattered osteocyte-like cells in the spaces between the trabeculae.

Figure 3 Histochemical results at (a–c) 3 weeks, (d–f) 8 weeks, and (g–i) 12 weeks, postoperatively. a, Interface between bone and a prosthesis in Group B at 3 weeks (bar = 31.25 μ m); b, fluorescent microscopic view of hybrid bone-like tissues in the HPTP cavity in Group C at 3 weeks (bar = 125 μ m); c, light microscopic view of hybrid bone-like tissues in the HPTP cavity in Group C at 3 weeks (bar = 125 μ m); d, interface between bone and prosthesis in Group B at 8 weeks (bar = 31.25 μ m); e, bone tissues in the holes of an HPTP in Group B at 8 weeks (bar = 125 μ m); f, light microscopic view of mixed bone-like tissues in the HPTP cavity in Group C at 8 weeks (bar = 125 μ m); g, fluorescent view of a specimen in Group B at 12 weeks (bar = 1 mm); h, hybrid bone-like tissues in the HPTP cavity in Group C at 12 weeks (bar = 125 μ m); i, overall light microscopic view of a specimen in Group C at 12 weeks (bar = 1 mm).

These observations were similar among the different groups. Bone tissues were observed growing into the holes of the prosthesis (Figure 4), and trabecular structures covered with some fibers and matrix were also identified. In the HPTP cavity loaded with the CBM, bone-like tissue, mixed with some fibrous tissue, was observed at week 12, postoperatively (Figure 4).

2.4 Bone histomorphometry analyses in the cavities of the HPTP

Statistical analyses using *t*-tests revealed that the relative bone formation in Groups B and C differed significantly at the different time points ($P<0.01$ for all), and that the relative bone formation was significantly better in Group C than in Group B (Table 1).

Table 1 Relative bone formation in Groups B and C at different time points (%)

Time (weeks)	Group B	Group C	<i>P</i> value
3	5.1 $\pm$ 1.4	27.5 $\pm$ 2.7	$P<0.01$
8	6.6 $\pm$ 2.0	41.3 $\pm$ 3.2	$P<0.01$
12	7.0 $\pm$ 1.3	57.6 $\pm$ 4.1	$P<0.01$

2.5 Biomechanical tests

Inter-group *t*-tests of the pull-out strengths among all three groups at week 12 were assessed. The results revealed a significantly greater pull-out strength for the specimens in Groups B and C than in Group A ($P<0.01$), with no significant differences between Groups B and C ($P>0.05$) (Table 2). These differences were also qualitatively observed during biomechanical testing. In Group A, the interfaces between the bone and the coated HA of the non-porous prostheses were occasionally broken, and the prostheses were often pulled out with the coated HA split and chipped from the surface (Figure 2). However, for Groups B and C, less severe damages to the coated HA were seen. In both groups, bone tissue near the holes of the HPTP, as well as at the interface between the bone and the coated HA, needed to be manually broken to pull the HPTP from the rabbit bones,

Table 2 Pull-out strengths of individual specimens in the three groups (units: N)

Group	1	2	3	4	5	6	Mean $\pm$ SD
A	276	211	169	278	285	234	242 $\pm$ 46
B	420	470	325	447	550	453	447 $\pm$ 73
C	398	425	489	367	438	496	435 $\pm$ 50

Figure 4 Microstructures of the CBM and the newly formed bone around prostheses. a, Three-dimensional mesh-like structure of the CBM (bar = 500 μm); b, bone tissues outside the original HA coat of a prosthesis in Group A (bar = 120 μm). All three groups showed similar findings for these bone tissues. c, Bone tissues formed in the holes of an HPTP in Group B (bar = 30 μm). Groups B and C showed similar findings for these bone tissues. d, Bone-like tissues in the cavity of an HPTP in Group C (bar = 50 μm).

with fractures occurring at sites where there was strong fixation between the prostheses and peripheral bone (Figure 2).

3 Discussion

After decades of development, surgeries for all types of artificial joint replacements have continued to improve; however, limited life spans and aseptic loosening in the long term continue to impede success in this field [1–6]. Two questions are evident: (1) How can host bone ingrowth around the surface of prostheses be improved, and (2) how can the combined strengths and ranges between prostheses and peripheral bone be increased for better fixation and longer stability? These issues are still some of the main targets for improving biological fixed prostheses. In our study, we first conceived and manufactured a “biological-compound hollow porous artificial joint prosthesis” in an attempt to address these issues (simplified to HPTP or hollow porous titanium prostheses). The present study not only observed increased osteogenesis at the HPTP/host bone interface, but also identified positive results to enhance the osteogenic potential within the internal cavities of HPTP with or without osteogenic materials, such as cancellous bone matrix (CBM). Overall, this research provides experimental and theoretical evidence for the clinical application of this design in artificial joint replacements.

The stability of a biological fixed prosthesis depends not only on the initial stability provided by its geometric shape,

but also the long-term stability that stems from prosthesis/peripheral host bone integration; of which, the latter is more important [11]. Surface treatments play important roles in enhancing this integration, with studies employing traditional surface treatments, such as extensive or proximal HA coatings, titanium oxide nitride coatings [17] and trabecular metal (porous tantalum) [18] in the manufacturing of prostheses. However, as observed in our present experiments and confirmed by many other studies, surface coating treatments are unreliable because of the absorption and degradation of the surface materials [24–26]. Besides, although some studies have reported the osseointegration effects of macroscopic or microscopic holes in coatings, such as HA and titanium, respectively [33–36], no studies have previously considered combining macroscopic holes and HA coatings to achieve better osseointegration. In our design, a porous surface combining macroscopic holes (2 mm in diameter) and an HA coating was adopted to achieve better stability, and our results indeed indicate a better locking fixation from both histological and biomechanical aspects. The locking mechanisms of bone in the macroscopic holes of the prosthesis may take on some of the load, and thereby decrease the occurrence of splitting and chipping of the surface coatings, increasing the overall stability of the joint.

Our use of an osteogenic material was crucial for enhancing bone formation in the hollow cavity of HPTP through the sidewall holes. While the hollow design permits increased revascularization and bone in-growth in the side-

wall holes [37], bone formation within the hollow cavity of HPTP is also important for better biomechanical strength. Interestingly, in the absence of osteogenic materials, we observed a marked reduction in bone formation in the HPTP cavity; this differs from the results for traditional bone harvest chambers [27,28]. This discrepancy may arise from the different sizes of these hollow implants. For larger hollow implants, osteogenic materials should be used for better osteoinductive and osteoconductive activities, with ideal osteogenic materials promoting effective bone regeneration [38].

Osteogenic materials include many kinds of autogenic, allogeneic and heterogenic grafts [39] or substitute materials, such as HA, bioactive polymers, biphasic calcium phosphate ceramics and porous bioactive titanium [40–43]. The best osteogenic materials are generally thought to be autogenic grafts, such as bone blocks resected from joints during replacements. However, we used cancellous bone matrix in our study because of its availability and effectiveness. CBM demonstrates increased biocompatibility and biomechanical strength, as compared with other substitute materials, and is mainly composed of inorganic bovine bone matrix [44]. In our study, CBM within the hollow cavity of HPTP promoted osteogenic activity and bone formation in the HPTP cavity. It encouraged the formation of new bone in the hollow spaces of the HPTP and increased the strength of the whole structure, achieving “combining integration”; it is hypothesized that this prosthesis/host bone integration would also decrease the impact of particle wear on aseptic loosening in the long term. With the development of tissue engineering techniques, many engineered scaffolds and bioactive factors (bone morphogenetic proteins) may represent an alternative source of osteogenic material for this porous prostheses [42,45–47].

Our study demonstrated that a hollow porous prosthesis, combining macroscopic holes and surface coatings, is more advantageous and feasible than traditional solid designs with surface coatings alone. In addition, the osseointegration effects are further enhanced by filling the cavity with osteogenic materials. This design may provide a new perspective that prevents aseptic loosening and lengthens the postoperative life span of prosthesis in the long term. However, we still have many problems to solve to put this design into practice. First, reasonable sizes, shapes and densities of the holes need to be optimized to induce the best bone ingrowth into the holes. At present, this is still inconclusive. Some researchers have reported that pores of 100–500 μm in diameter are appropriate for bone ingrowth [33,48]; however, we increased the diameter of the sidewall holes to 2 mm to supply better nutrition and vascularization for the internal tissues during the early stages of healing, and achieve rigid fixation during the later stages. Second, more attention should be paid to the distribution of the hollow porous design and traditional surface coatings, as an inappropriate distribution may cause complications, such as

biomechanical failure or persistent pain in patients after total joint replacements [30,49]. Besides, while limited by the animal and prosthesis models used in this study, only “pull-out” biomechanical tests were used to test the axial shear strengths in the specimens of the three groups, and we still require more rotational and bending quantitative strengths tests in more advanced models.

4 Conclusion

Our new hollow porous design for artificial joint prostheses offers a highly advantageous and feasible solution to prevent aseptic loosening and lengthen the life span of the prosthesis. With a combination of macroscopic holes, surface coatings, and osteogenic material, this design facilitates prostheses/host bone integration to achieve a much faster locking fixation and increased bone formation within the hollow cavities. However, this research is only preliminary, and further studies are required before this design can be used in a clinical setting. Future studies should investigate the osseointegration effects of different sizes and densities of macroscopic holes, the actual strengths and durability that the design can withstand, and the most appropriate osteogenic materials for clinical practice.

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