Histological ex vivo analysis of retrieved human tantalum augmentations

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Abstract

Purpose The characteristics of tantalum augment osseointegration in human ex vivo specimens from re-revision procedures are unknown and limited data in this regard is available. The purpose of this study was to investigate the osseointegration pattern into porous tantalum augmentations harvested during re-revision procedures.

Methods Between 2007 and 2010 a total of 324 hip and knee revisions with a tantalum augmentation were performed in our institution. Out of this cohort, seven patients (2.2 %) had to be re-revised. To analyse the status of trabecular ingrowth in the retrieved cases (four hips, three knees), all specimens were analysed by contact radiography, subjected to undecalcified processing, histology, thin-section analysis and backscattered electron imaging.

Results Trabecular and vascular ingrowth could be found along the bone-augment-interface in two of seven revised specimens, respectively. The depth of bone ingrowth reached up to 2.6 mm. However, the analysis of the remaining cases revealed no bony ingrowth into trabecular metal. Rather, large parts of the implants were embedded in cement or pores were filled with autologous bone.

Conclusions Although the cause for the missing bony ingrowth seems to be multifactorial, some fundamental

conditions, such as the provision of the greatest possible interface between the tantalum implant and the host bone, should be met and thus, bone cement and autologous bone grafts should be used with caution.

Introduction

Revisions of total hip and knee arthroplasties are demanding procedures. One of the most challenging aspects of these operations is related to the management of extensive bone loss of the acetabulum in hip revision and the distal femur and the proximal tibia in revision of total knee arthroplasty [1, 2]. In acetabular revisions the presence of cavitary and segmental deficiencies (Paprosky Type IIIA and IIIB defects) often necessitates more complex reconstruction techniques with impaction bone grafting, structural allografting or reinforcement rings [1, 3–8]. Treatment options for the management of severe bone deficiencies during total knee revision also include the use of impacted bone grafting, structural allografts and prosthetic augmentation [9, 10].

Over the past ten years porous tantalum (trabecular metal) constructions, which are designed to maximise the degree of biological fixation, have emerged as an alternative treatment option for the management of severe bony deficiencies [2, 6, 11–17]. Animal studies [18] and in vitro studies [19–21] have confirmed significant bone ingrowth into porous tantalum components leading to stable bone–implant interfaces. In vivo studies have shown promising clinical and radiographic short and midterm results for porous tantalum implants (trabecular metal) in complex hip and knee revisions [2, 6, 12–14, 16, 17]. In order to determine the extent of bony ingrowth into the porous tantalum, a number of studies tried to analyse the osteoconductive effects of trabecular metal constructions from postoperative serial radiographs [2, 6, 12–14, 16, 17]. However, studies

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characterising possible host bone ingrowth into trabecular metal augments in vivo are rare and to the best of our knowledge, few histological studies on porous tantalum osteonecrosis implants are available [22, 23].

Thus, the purpose of this study was to investigate the in vivo osseointegration pattern into porous tantalum augmentations harvested during re-revision procedures.

Patients and Methods

Between November 2007 and March 2010 a total of 324 hip and knee revisions with a tantalum augmentation and a mean follow-up of 9.6 ± 6.2 months were performed in our institution. Out of this cohort, seven patients (2.2 %) needed revision at a mean time in situ of 11 months (range, 1–24 months) (Table 1). The reasons for re-revision were periprosthetic acetabular fractures in two, loosening of a tibial component in one, loosening of a femoral component in one, and periprosthetic infections in three cases (two hips, one knee). Following revision surgery, all specimens were immediately fixed in 4 % buffered formalin solution and transferred to our laboratory. The retrieved porous tantalum implants were three acetabular wedges, two tibial cones, one femoral cone and one trabecular metal revision cup (Table 1). Clinical information including patient demographics, pre- and postoperative X-ray (Fig. 1), medical history as well as cementation technique used was recorded. All retrieved implants including adherent cement and bone tissue were photographed (Fig. 2a). Using a diamond coated band saw a slice from an area with apparent host bone was dissected out for further preparation. The specimens were contact radiographed and once again photographically documented (Fig. 2b, c). For further preparation the specimens were subjected to an

undecalcified infiltration process as described previously [24, 25]. Following dehydration and degreasing in an ascending ethanol series the undecalcified samples were plastic embedded. Preliminary tests showed that light-polymerising resin Technovit 7200 VLC (Heraeus Kulzer, Werheim Ts, Germany), which is regularly used, was not suitable for the dark and large-pored modular tantalum augmentations due to insufficient hardening of the plastic material. Therefore temperature-dependent polymethyl methacrylate (PMMA) was used to achieve optimal embedding results. Obviously, the PMMA could only infiltrate pores with an intact connection to the implant surface, as could the host bone. Pores that were embedded in bone cement had no connection to the interface and thus were not infiltrated. After completion of the polymerisation procedure the specimens were ready to be ground by an automatic grinding device (EXACT, Norderstedt, Germany). To avoid possible misinterpretation due to projections, all specimens were ground to a thickness of 30 μm , stained by toluidine blue (Fig. 3a).

The 30- μm thin-ground specimens were further analysed by contact radiography (Fig. 3b) and histology (Fig. 4a–c) regarding host bone and vascular ingrowth as well as appearance of bone tissue within the porous tantalum. At first, they were analysed qualitatively to describe possible tissue reactions to the implant material. Afterwards, the bone ingrowth into the implant was quantitatively analysed directly from the ground specimens using a measuring eyepiece (Carl Zeiss AG, Germany, accuracy of 0.1 mm) [26]. These measurements were compared to the results obtained using backscattered electron imaging. For this, the ground specimens were carbon-coated and measured with a scanning electron microscope

Table 1 Patients and specimens characteristics of the revised cases / retrieved specimens

Case	Age at revision (years)	Sex	Primary diagnosis	Localisation	Paprosky type	Preceding operations	Failure mode	Time in situ (months)	TM-type
I	53	Female	Tibial aseptic loosening	Right knee	–	6	Aseptic loosening	12	Tibial TM-cone
II	69	Female	Tibial aseptic loosening	Right knee	–	4	Periprosthetic infection (Str. spec), SIRS	12	Tibial TM-cone
III	70	Male	Acetabular aseptic loosening	Right hip	3 A	3	Periprosthetic fracture	6	Acetabular TM-wedge
IV	76	Female	Acetabular aseptic loosening	Right hip	3 A	6	Periprosthetic infection (Staph. spec)	1	Acetabular TM-wedge
V	77	Female	Femoral aseptic loosening	Right knee	–	5	Aseptic loosening	24	Femoral TM-cone
VI	72	Female	Acetabular aseptic loosening	Right hip	2 B	6	Periprosthetic infection (Staph. epi)	20	Acetabular TM-wedge
VII	72	Female	Periprosthetic infection (Staph. epi)	Right hip	3 A	7	Periprosthetic fracture	1	Acetabular TM-wedge

Fig. 1 Aseptic cup loosening with Type IIIA defect. Preoperative radiograph (07/2009). One-month postoperative radiograph (08/2009). Six-month postoperative radiograph demonstrating the failure

of the reconstruction. The TM-wedge was subjected to histological analysis (02/2010). One-month postoperative radiograph (03/2010)

(LEO 435 VP, Leo Electron Microscopy Ltd., Cambridge, UK) at 20 kV and a constant working distance of 20 mm (BSE Detector, Type 202, K.E. Developments Ltd., Cambridge, UK). The maximum ingrowth was determined as the maximum distance between the implant surface surrounded by host bone and the most distant pore of the implant containing bone tissue.

Results

We detected fibrous tissue within the tantalum implant in all seven cases analysed. In two of seven cases, we could determine ingrowth of vital bone (cases I and IV)

and vascular ingrowth (cases I and II) into the porous tantalum. Focal new bone formation could be found directly within the pores at the implant surface to the host bone (Fig. 4). In as little as one month after implantation first signs of woven bone formation could be seen within the pores at the tantalum implant surface in one case (case IV). Partially long-distance direct bone-to-implant contacts were found (Figs. 3 and 4). The maximum depth of bone ingrowth into the porous tantalum was 2.6 mm after 12 months (Fig. 5a). Furthermore, the ground specimens as well as backscattered electron imaging showed new bone formation directly from the implant/porous surface, often in small cavities within the porous tantalum implant (Fig. 5b).

Fig. 2 **a** After retrieval of trabecular metal construction. **b** For further analysis all specimens were dissected by means of a diamond coated saw and subjected to contact radiography **c**

Fig. 3 All retrievals were processed to 30- μ m thin-ground specimens and stained by toluidine blue (*left*) and again subjected to contact radiography (*right*)

However, the remaining cases (cases III, V, VI, VII) showed no signs of bony ingrowth. Rather, the analysis revealed that large parts of the implants were completely embedded in cement. In some interface regions bone cement could even be found within the porous structure of the implant. Further sections right at the host bone–implant interface but without bony ingrowth were filled with autologous bone. No histological signs of necrosis or tumours in the analysed cases were found.

Discussion

Porous tantalum is attractive to applications in orthopaedic surgery, due to its structure that allows ingrowth of bone, and its physical properties of strength, low stiffness, and high

coefficient of friction [19, 20, 27]. Results from both preclinical [18–21, 28] and clinical investigations [2, 6, 12–14, 16, 17] indicate that porous tantalum opens new perspectives in reconstructive orthopaedic surgery. In this study, our objective was to characterise the *in vivo* response to tantalum augmentations that had been harvested at the time of re-revision.

An analysis of various biomaterials including tantalum by Findlay et al. showed its suitability for human osteoblast growth and differentiation [21]. The findings were supported by an initial cell attachment to tantalum, an osteoblast-like cell morphology on tantalum, a similar growth rate of cells on tantalum as on the other biomaterials tested, and a similar expression of a number of genes (OCN, OPG, BSP-1, COL-1, RANKL, CBFA1) associated with osteoblastic function.

In vitro studies and animal models have confirmed bone ingrowth within porous tantalum structures. Using a

Fig. 4 **a** An undecalcified ground specimen stained with toluidine blue indicates bone ingrowth into the porous-coated implant. **b** At higher magnification (50 $\times$) bone trabeculae can be seen within the

pores of the trabecular metal. **c** Polarised light microscopy shows the run of lamellar fibres in the mineralised trabeculae

Fig. 5 **a** Backscattered electron imaging of case I shows new bone formation within a maximum distance (red asterisks) of 2.67 mm from the host bone. **b** Bone trabeculae in direct contact with the implant surface can be seen in higher magnification

transcortical canine model, Bobyn et al. evaluated two different pore sizes after implanting porous tantalum cylinders with subsequent histological and mechanical testing at interval follow-up. They were able to show an increase in shear strength that was attributed to the increased porosity of the tantalum cylinders, leading to a higher volume of bone occupying the pores for any given percentage filled [28]. In another study, Bobyn et al. reported on 22 cementless porous tantalum acetabular components studied *in vivo* in a canine model for a period of six months [18]. Stable bone–implant interfaces were detected on histology, radiography, and electron microscopy. The depth of ingrowth ranged from 0.2 to 2 mm and was found in all 22 cups. The mean bone ingrowth for all sections was 16.8 %, whereas the periphery averaged 25.1 %. These pre-clinical results in laboratory and animal models have led to the development of further applications for use in total joint arthroplasty, spinal fusions, and structural support of osteonecrosis related lesions.

To our knowledge few studies have investigated the histological pattern of bone–tantalum interaction in humans and this exclusively in retrieved porous tantalum osteonecrosis implants. Tanzer et al. [22] performed a histopathological retrieval analysis of 15 clinically failed specimens in 2008. Using backscattered scanning electron microscopy Tanzer et al. confirmed the presence of bone ingrowth in 13 of the 15 cases. When compared to Bobyn's canine models [18], in Tanzer's study the extent of bone ingrowth into the osteonecrosis implant was minimal. Most of the documented bone ingrowth was patchy and occurred along the edge of the implant, extending to a depth of less than two millimetres. Additional sparse and disconnected islands of bone, extending from two to five millimetres from the implant periphery, were identified in eight cases. Fernández-Fairen et al. [23] analysed five tantalum implants of the femoral head likewise used for treatment of avascular necrosis which were retrieved between six weeks and 20 months after implantation. They observed new bone around and within the analysed tantalum implants. However, the observed bone ingrowth proved to be slower and less intense compared to the results shown in animal studies.

In our study we report the results of an *ex vivo* analysis on seven human tantalum augmentations retrieved at revision procedures. However, apart from the complicated clinical course, the analysis provided a great opportunity to evaluate the histological response to porous tantalum augments *in vivo*. Our findings showed, nevertheless, that two out of seven cases showed bony and vascular ingrowth, respectively, into the pores of the tantalum implant. Findings with a maximum bony ingrowth of 2.6 mm in a retrieved case after 12 months *in situ* are in accordance with the findings of Tanzer et al. [22] and Fernández-Fairen et al. [23] for porous tantalum osteonecrosis implants. Four revised cases showed a total lack of bony or vascular ingrowth although all tantalum augmentations were explanted with caution. However, intraoperatively, a mechanically stable connection to the host-bone had been found for many regions. The reasons for these findings, however, may be multifactorial. On the one hand, one case was retrieved after one month *in vivo*, so the lack of bony ingrowth might be related to the short time *in situ*. On the other hand, specimens were retrieved for loosening or periprosthetic infections, which can affect tissue reactions to the implant. Another possible and important reason for the lack of bone tissue could be that large areas of the analysed trabecular metal cases were embedded within bone cement, which inhibited any possibility of bone ingrowth.

Our study has several limitations. First, the analysed specimens showed great differences in implant durations. Second, contact radiographies, thin-cut or thin-ground specimens show only a two-dimensional image of three-dimensional bone structure, which must be taken into

account in the interpretation. However, for obvious reasons we were not able to include and analyse the surviving tantalum augmentations and thus we can make no statements on the status of bony ingrowth in these cases. We are aware of the fact that this study only allows a preliminary assessment due to the small number of specimens and the relatively short follow-up. To investigate the full osteoconductive potential of tantalum augmentations and their potential for knee and hip revision surgery, histological post-mortem studies on unrevised tantalum implants will be required.

Conclusions

The aim of this study was to investigate osseointegration into porous tantalum augmentations harvested during revision procedures. We conclude that tantalum augmentations can provide a good substrate for attachment, formation and ingrowth of bone tissue in vivo even under difficult conditions. However, some fundamental conditions, such as the provision of the greatest possible interface between the tantalum implant and the host bone, should be met and thus, bone cement and autologous bone should be used with caution.

Conflict of interest The authors state that there is no conflict of interest.

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