Author's response to reviews

Title: Impaction grafting in the femur in cementless modular revision total hip arthroplasty: A descriptive outcome analysis of 243 Cases with the MRP-TITAN Revision Implant

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Author's response to reviews: see over
to:

Dr. Poolman

Editor

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Revisions for the manuscript:

Impaction grafting in the femur in cementless modular revision total hip arthroplasty: A descriptive outcome analysis of 243 Cases with the MRP-TITAN Revision Implant

Matthias D Wimmer, Thomas M Randau, Moritz C Deml, Rudolf Ascherl, Ulrich Noeth, Raimund Forst, Nadine Gravius, Dieter C Wirtz and Sascha Gravius

Dear Dr. Poolman, Dr. Glehr and Dr. Zhen An Zhu

Thank you very much for reviewing our manuscript and for your helpful comments.

We tried the best to answer all questions sufficiently and we will try to provide any extra information or clarify any further questions if needed.

Yours sincerely

Matthias Wimmer
Reviewer 1

Prof. Dr. med. Mathias Glehr

Level of interest:
An article whose findings are important to those with closely related research interests

Reviewer's report:

General impression and comments
The authors present a descriptive analysis within a prospective controlled trial of revision hip arthroplasty using the MRP-TITAN stem with distal diaphyseal fixation and metaphyseal defect augmentation. Postoperative clinical function was evaluated using the Harris Hip Score in a maximal follow up time of ten years. Postoperative radiologic examination evaluated implant stability, axial implant migration, signs of implant loosening, periprosthetic radiolucencies, as well as bone regeneration and resorption.

The topic seems of interest for surgeons in the field of orthopaedic revisions. But the study offers many weak points which require major revisions. Especially parts of the methods seem not appropriate and are not well described. At the moment it is not possible for me to decide on acceptance or rejection until the authors have responded to the major compulsory revisions.

1) Major Compulsory Revisions
1.1) Background, chapter six

Please state the exact aim and question of this prospective study. Please describe, how the study was initially planned (was it “prospective” planned to perform a descriptive analyses?)

The initial prospective trial mentioned was a multicentre patient registry. It was set up to evaluate the long-term outcome of the MRP stem. But the evaluation of the Impaction Bone Grafting Technique as presented in this manuscript was not part of the initial protocol. Our hypothesis that Impaction Grafting improves the outcome came up later. Thus, the analysis presented herein is retrospective and descriptive only. Subsequently, the data was analyzed retrospectively, as anonymized and aggregated data only.

As suggested and to avoid that the study presented in this manuscript might be misunderstood as prospective we changed the text in the following sections:

Abstract

Methods

We retrospectively analyzed the aggregated and anonymized data of 243 femoral stem revisions. 68 patients with 70 implants (28.8%) received an allograft augmentation for metaphyseal defects; 165 patients with 173 implants (71.2%) did not, and served as controls. The mean follow-up was 4.4 ± 1.8 years (range, 2.1–9.6 years).

(lines 38-41)

Main document

Patients
The results of 265 femoral revisions performed in 255 patients were followed in a multicenter patient registry. Patients were treated in four centers focusing on primary and revision THA in Germany. All patients received the MRP-TITAN stem. Inclusion criteria were revision THA with bony defects of the proximal femur graded as Paprosky I-III. Exclusion criteria included all kinds of tumors or secondary neoplasia diseases, NYHA III-IV and ASA IV. A total of 8 surgeons performed the operations. All surgeons were experienced attendings and board certified orthopedic-surgeons doing more than 100 primary or revision THAs a year. 22 patients were lost to follow up, thus clinical and radiographic findings were evaluated in 233 patients with 243 implants with a follow-up period of at least 2 years. 68 out of these patients with 70 implants (28.8%) received an allograft augmentation of metaphyseal defects using the implant-specific Impaction Bone Grafting System (Peter Brehm, Chirurgie-Mechanik, Weisendorf, Germany). 165 patients with 173 implants (71.2%) did not receive metaphyseal defect augmentation and served as controls.

Our hypothesis was that Impaction Bone Grafting improves stem survival. The endpoint of our study was revision surgery of the stem. Patients were retrospectively and descriptively analysed using aggregated and anonymized data.

1.2) Methods, chapter one, line one

'Within the scope of a prospective multicenter study...'. What were the initial parameters of the clinical trial. What were the exact inclusion and exclusion criteria of the study protocol?

Please see 1.1)
As mentioned in comment to question 1.1, the data presented in this manuscript was descriptively and retrospectively analyzed as aggregated and anonymized data only. Even though the manuscript presented here profits from the inclusion and exclusion criteria as the patients analyzed had to fulfill the criteria to be part of the patient registry.

The text was changed as suggested

Exclusion criteria included all kinds of tumors or secondary neoplasia diseases, NYHA IV and ASA IV. A total of 8 surgeons performed the operations. All surgeons were experienced attendings and board certified orthopedic-surgeons doing more than 100 primary or revision THAs a year.

(Lines 109-112)

1.3) Methods, page two, second chapter, line six: 'The decision whether the impaction grafting technique was used or not was at surgeon’s discretion and based on his subjective evaluation of the intra-operative situation.' Please describe the parameters for this “subjective evaluation”. What was influencing the decision of the surgeons.

The decision making process to perform the Impaction Grafting Technique is one of the limitations of this manuscript. The decision whether the impaction grafting technique was used or not was made intraoperatively based on clinical criteria such as defect size, defect location and containment. Nevertheless there were no strict rules whether to use it or not, as the spectrum of potential defects is huge. This diminishes the value of our study. For future studies this aspect should be considered thoroughly. But to exclude a potential missselection by the surgeons and a selection bias, both groups, patients with and without Impaction Bone Grafting did not vary significantly according to age, sex, weight, height, body
mass index (BMI), intraoperative femoral defect size, implant stem diameter, and
preoperative function as measured by the HHS.

The text was changed as suggested:

Methods:
The decision whether the Impaction Bone Grafting technique was used or not was made
intraoperatively by the surgeon based on clinical criteria such as defect size, defect location
and containment. A relevant selection bias could be excluded because both groups, patients
with and without IBG, did not vary significantly according to age, sex, weight, height, body
mass index (BMI), intraoperative femoral defects as described by Paprosky et al. [16],
implant stem diameter, and preoperative function as measured by the HHS. (Error! Reference
source not found.)

Limitations:
Our study has potential shortcomings. The decision to use impaction grafting was made
intraoperatively based on clinical criteria such as defect size, defect location and
containment, rather than using a randomized patient allocation. However, the both groups
did not vary significantly according to age, sex, weight, body mass index (BMI), and surgical
parameters.

(lines 423-427)
1.3) Methods, radiographic evaluation, second chapter:

Was the radiographic evaluation done digital or analogue?

Radiographic evaluation was done analogue in standardized 1:1.15 plain pelvis radiographs in combination with a Lauenstein view. Digital radiographs were unfortunately not available.

The text was changed as suggested:

Analogue, standardized plain pelvis radiographs with a scale of 1:1.15 and a Lauenstein view of the symptomatic hip were routinely obtained preoperatively. The follow up radiographs were evaluated in a blinded fashion for radiologic signs of implant loosening according to the criteria published by Kavanagh and Fitzgerald [17]. Proximal femoral bone defects were evaluated according to the classification described by Paprosky et al [16].

(line 138-142)

What were the ways of standardisation, was there a millimetre standard on every x-ray?

How was it possible to evaluate the exact millimetre progression? Was the person, who did the radiographic evaluation blinded or did the person know, in which patient impact grafting was used?

All radiographs were normalized by a „millimetre standard“. The millimetre progression was measured manually. The examiners who performed the radiographic evaluation were blinded not knowing whether the patient received Impaction Bone Grafting or not. The Reviewer is right, that this might not be the most accurate way, a CT scan provided may more precise information and should be considered for future trials.

The text was changed as suggested:
All measurements were done manually by a blinded investigator, not knowing whether IBG was used or not. (lines 153-155)

1.5) Methods, Implant, second chapter, line three:

'...available as a straight-stem model in 140 mm and 200 mm length, and curved-stem version to fit the physiologic anterior bow of the femur in 200 mm length...' How many of each model were used? Did the outcome differ between the curved and the straight version?

This data is currently not available.

1.6) Methods, Surgical Technique, first chapter:

In some patients with osteopenic or osteoporotic bone structure, the femur was also stabilized with cerclage wire proximal and distal to the cortical window.' How many patients had osteopenic and osteoporotic bone structure, in how many patients you used a cerclage? Did the use of cerclages effect the outcome? Was the distribution the same in both groups (impact grafting and non impact grafting)?

This section of our manuscript was meant to illustrate the surgical procedure and potential surgical options as already published by Mumme et al. [20]. The grading as osteopenic or osteoporotic was based on the intraoperative findings described by the surgeon and we agree with the reviewer that this is a weak parameter. Unfortunately no standardized osteodensitometric scans or quantitative computed tomography (Q-CT) scans were performed to validate this. Since this section does not contribute substantially to the results presented, the section was removed.
1.7) Results, Radiographic Evaluation, second chapter:

'Evaluation of periprosthetic bone remodelling demonstrated a significant reduction in proximal stress shielding in the study group compared with the control group.' Did these patients complain about pain, was the stress shielding clinical relevant (HHS)?

Findings were added as suggested (see table 6)

Our hypothesis was that impaction bone grafting improves the survival when using the MRP-TITAN stem. Our analysis provides initial evidence of sufficient bone regeneration with graft augmentation of metaphyseal bone defects. There was a statistical significant reduction in proximal stress shielding and in periprosthetic radiolucencies in zones 1-7 according to Gruen. This corresponded to a significant improvement in clinical function, expressed as the increase in the postoperative HHS.

(lines 438-444)

1.8)

Please describe these factors which could influence the results of the study:

a.) How many surgeons take part on the study?

Patients were treated in four centers focusing on primary and revision THA in Germany. A total of 8 surgeons performed the operations. All surgeons were experienced attendings and board certified orthopedic-surgeons doing more than 100 primary and / or revision THAs a year.

The text was changed as suggested

A total of 8 surgeons performed the operations. All surgeons were experienced attendings and board certified orthopedic-surgeons doing more than 100 primary or revision THAs a year.

(lines 110-112)
b.) How was the distribution of the surgical technique for each surgeon? Did the outcome between the surgeons differ?

To all surgeons the Impaction Bone Grafting System was available. All surgeons used the same Surgical Technique as described in the methods section. Our sample size was not set up for stratification by surgeon. To avoid the appearance of data dredging we did not include this in the manuscript.

The following section describes the surgical technique as suggested

Commercially available allograft bone chips with an average size of 5-10 mm$^3$ were produced with Luer forceps or with a bone grinder. The technique avoided the use of a heat-producing saw. The bone grafts were introduced into the metaphysis in layers. Each layer was meticulously compressed using the impaction grafting system (IGS) with impactors in sizes of 3, 5, and 7 mm. Care was taken to obtain a uniform mixture of various particle sizes so as to optimize surface contact among the chips [21] (Figure 2).

(d.) How was the surgical experience of the different surgeons (cases of hip revision, years of surgical experience)?

All surgeons were experienced and board certified orthopedic-surgeons and attending surgeons in their clinics doing more than 100 primary and / or revision THAs a year.

Text updated as suggested:

All surgeons were experienced attendings and board certified orthopedic-surgeons doing more than 100 primary and / or revision THAs a year.
Limitations

Please state and describe the limitations of the study detailed in a chapter.

Section “Limitations” was added as suggested.

Our study has potential shortcomings. The decision to use impaction grafting was made intraoperatively based on clinical criteria such as defect size, defect location and containment, rather than using a randomized patient allocation. However, the both groups did not vary significantly according to age, sex, weight, body mass index (BMI), and surgical parameters. Another limitation is that multiple surgeons performed the operations. Even though all of them were experienced attending-surgeons and all of them used the MRP-TITAN stem and the same Impaction Grafting System this might have compromised our results. With a mean follow-up period of 4.4 ± 1.8 years, the present study does not allow a definitive assessment of the long-term results of impaction bone grafting technique. Due to the limitations of a retrospective and descriptive study the level of evidence remains low. A future prospective controlled trial seems essential.

Minor Essential Revisions

Background, 2 chapter, line three and four:

'The bone cement cannot provide an intrusive, interlocking bond in a smooth-walled osteolytic femoral canal.' Please ad citation
2.2) ‘Cemented fixation can be combination with impaction grafting.’ Please add citations

Citation added as suggested


2.3.)

Discussion

Please update literature and discussion. There some publication about impaction grafting of the femur in hip arthroplasty revisions published in the last years.

The literature was updated and the text changed as suggested.

But please note, that the citations you suggested all report on cemented implants with impaction grafting. We present the largest series of an uncemented implant with IBG an this is in our perspective novel, unique and adds to the literature.
Reviewer 2

Zhen An Zhu

Level of interest:
An article whose findings are important to those with closely related research interests

Reviewer's report:
This paper is well organized, clear and easy to read. And they present the largest analysis of the impaction grafting technique in combination with cementless distal diaphyseal stem fixation published so far.

I have only one question for this paper.

1) Minor Essential Revisions

1.1)
How did the authors describe the change of stress shielding in the proximal femur? You mentioned ‘in the form of radiologically verifiable bone resorption’ as stress shielding in the second paragraph of your discussion. But it’s somewhat confused. You should describe it more specifically in the "Radiographic Evaluation".

The text was changed as suggested.

Analogue, standardized plain pelvis radiographs with a scale of 1:1.15 and a Lauenstein view of the symptomatic hip were routinely obtained preoperatively. The follow up radiographs were evaluated in a blinded fashion for radiologic signs of implant loosening according to the
criteria published by Kavanagh and Fitzgerald [17]. Proximal femoral bone defects were evaluated according to the classification described by Paprosky et al [16].

I think you implant the graft in this area, which will definitely increase the bone mineral density in this area. Also we cannot see this change you mentioned in your example (figure 3). The A and B in fig3 have evident shadow of soft tissue which affect the bone mineral density in this area. So we cannot evaluate the bone resorption in this area. Please provide the exact example for this paper. The best way is that your example should include one case representing the study group and another case representing control group which can show the change of proximal stress shielding in your paper. So we can see “There was a significant reduction in proximal stress Shielding” in your conclusion.

The figure was changed and improved as suggested. Preoperative and two years postoperative follow-up radiographs of revisions with implantation of a MRP-TITAN stem with distal diaphyseal fixation. 3.A: preoperatively, 3.B: postoperatively with metaphyseal defect augmentation by impaction bone grafting. 3.B. shows consolidation of the metaphyseal allograft after impaction grafting. 3.C: preoperatively, 3.D: postoperatively without impaction bone grafting and stress shielding in the proximal femur.
bone regeneration with Impaction Gratfting

stress shielding without Impaction Gratfting