Changes in Bone Mineral Density of the Proximal Tibia and Migration of the Tibial component after rTKA with or without the Use of Trabecular Metal Cone.

A randomized study.

PhD-thesis
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From

Department of Orthopaedic Surgery
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Contents

List of papers

This thesis is based on the following papers:

I. Revision Total Knee Arthroplasty with the use of Porous Tantalum Tibial Cones. A Randomized RSA Study with 1 Year of Follow-up.
Claus L Jensen, Michael M Petersen, Henrik M Schrøder, Gunnar Flivik, Bjarne Lund
Submitted for publication.

II. Changes in Bone Mineral Density of the Proximal Tibia after Revision Total Knee Arthroplasty in Patients with Severe Bone Loss. A Randomized Study with the use of Porous Tantalum Metaphyseal Cones.
Claus L Jensen, Michael M Petersen, Henrik M Schrøder, Bjarne Lund
Submitted for publication.

III. Changes in Bone Mineral Density of the Distal Femur after Revision Total Knee Arthroplasty.
Claus L Jensen, Michael M Petersen, Henrik M Schrøder, Bjarne Lund
Submitted for publication.

The papers will be referred in the text by their Roman numerals (I-III).

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Preface

This Ph.D. thesis is the result of scientific work conducted at the Department of Orthopaedic surgery U Rigshospitalet from January 2005 until November 2009. During this period of time, I was subscribed as a PhD- student at the Faculty of Health Science, University of Copenhagen and a part of the time employed as a research fellow at the Bone Mineral Research Laboratory. The Roentgen stereometric analysis was carried out at Bio labbet, Lund University Hospital, Sweden. I would like to thank my Swedish college Gunnar Flivik, Dr. Med. Sci. for making this collaboration possible and Håkan Leijon for helping me with the analysis. They have always been generous helping me and sharing their rich experience with RSA.
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Summary

Total Knee Arthroplasty (TKA) is considered a good well established treatment for patients with painful gonarthroisis. The number of TKA performed in Denmark has been increasing during the recent years, and now more than 7500 are performed each year. The survival probability of a TKA is far above 90 % after 10-years. The most common reasons for a TKA to fail are aseptic loosening, infection, wear-particle disease and pain without loosening..

Revision Total Knee Arthroplasty (rTKA) is sometimes difficult and especially if reconstruction of major bone loss is needed to secure a stable platform for fixation of the new implants. Conventional surgical options for reconstruction of the bone loss are cement filling or the use of bone grafting. A new porous Tantalum biomaterial shaped as a cone is commercially available under the trademark "Trabecular Metal Cone" (TM Cone, Zimmer, Warsaw, IN). It is designed and developed for reconstruction of bone loss in the proximal tibia during rTKA. Tantalum is well documented as a highly biocompatible material with the appearance similar to cancellous bone. Porous tantalum has the advantage to allow osseointegration, while filling out bone defects and tolerate physiological loads. At the department of Orthopaedic U, Rigshospitalet patients are admitted from large parts of Denmark to received rTKA due to failed TKA combined with severe bone loss. The use of TM Cone in rTKA in patients with considerable bone loss of the proximal tibia is evaluated in a randomized study where 40 patients were allocated to receive rTKA with or without TM Cone.

In a study using Roentgenstereometric Analysis (RSA) micromotion of the tibial implants in the two randomized groups were evaluated. In two studies using Dual Energy X-ray Absorptiometry (DEXA) changes in Bone Mineral Density (BMD) of the tibia and distal femur were measured. Due to the potential of osseointegration of the TM Cone implants our hypothesis was that less migration of the tibial implants and an increase (or less decrease) in BMD of the tibia was expected in the group of patients that received rTKA with TM Cone.

In the first study we found a tendency of less migration in the TM Cone group, but this was not a significant finding, and all implants seemed to stabilize between 6 months and 1 year of follow-up. In this study we also evaluated the knee - and function scores and both showed a significant increase, but no difference between the two study groups was found.

In the next study, we found that the bone remodelling pattern was the same in the two groups, with a significant decrease in BMD found along the stemmed tibial implant in both groups. There was no significant difference in BMD changes between the two groups after 1 year of follow-up. The second DEXA study only evaluated BMD changes at the distal femur after rTKA with the use of a 100 mm stemmed implant and a potential difference between rTKA with or without TM Cone was not evaluated. We found a significant increase in BMD in one ROI (Region of interest) after 1 year of follow-up.

Our preliminary results have shown that the use of TM Cone in rTKA in patients with severe bone loss of the proximal tibia gives the same early clinical outcome as conventional surgical management. The adaptive bone remodelling of the tibia and migration of the tibial component of the two study groups within the first postoperative year was not statistically different and further investigation with long term follow-up is warranted.

Background.

The numbers of Total Knee Arthroplasties (TKA) performed in Denmark has been increasing during the resent years. Data from the Danish Total Knee Arthroplasty Register shows that 7739 TKA were performed in 2008 (1). The number is expected to increase in the future. As a consequence the need for Revision Total Knee Arthroplasty (rTKA) is also expected to increase. Total Knee Arthroplasties (TKA) have an overall 10-year survival probability far above 90 %. The major causes of TKA failure is aseptic loosening, pain without loosening of components, instability, deep infection, and polyethylene-wear (2;3). Sierra et al. (4) have reported that patients having a revision total knee arthroplasty are at substantial risk of having one or more rTKA. The exchange of an infected or loose TKA is often complicated by a considerable bone loss in the proximal tibia caused by polyethylene particle disease, stress shielding or bone necrosis because of infection. During the operation a further loss of bone is inevitable when the prosthesis is removed. Surgical treatment of severe bone loss of the proximal tibia during revision TKA (rTKA) is difficult and challenging. The aim of rTKA is to achieve well-fixed components, and to restore normal joint-line level and flexion-extension stability. Reconstruction of the bone defect is essential for the durability of the fixation. There exists well established agreement as to the surgical management and treatment of smaller bone loss defects of the proximal tibia (5). Management of severe bone loss is dependent on the degree and location of the defect. Options are cement filling, use of metal augments, bone grafting or in severe cases mega prostheses (6;7).

A new porous Tantalum biomaterial shaped as a cone is now commercially available in different sizes under the trademark “Trabecular Metal Cone” (TM Cone, Zimmer, Warsaw, IN). It is designed and developed for reconstruction of bone loss of the proximal tibia during rTKA. Tantalum is well documented as a highly biocompatible material through its high resistance to corrosion (8) and little immunogenic response in host tissue (9;10). Porous Tantalum is fabricated through the creation of a low-density vitreous carbon skeleton. This scaffold of repeating dodecahedrons is then coated with pure Tantalum through a chemical vapour deposition creating a high volumetric interconnecting porousious (70-80 %) material. With the appearance of porous Tantalum similar to cancellous bone, the high coefficient of friction, low modulus of elasticity (stiffness) and high ultimate and yield strength (11;12), porous Tantalum has the advantage to allow osseointegration (9;13), while filling out bone defects and tolerate physiological loads. (Figure 1). Preliminary clinical results evaluating the use of porous Tantalum in general (11;14;15) and as TMC (16;17) have been encouraging.

Figure 1. Trabecular Metal Cone.

Marker based roentgenstereometric analysis (RSA) was developed in 1974 by Goran Selvik a Swedish anatomist (18). RSA is a highly precise method of measuring continuous micromotion between two defined segments (e.g. implants and host bone). A rigid three-dimensional coordinate system is created through a calibration cage of Plexiglas with defined markers in the walls. When performing knee RSA the calibration cage system is placed surrounding the joint of interest. During surgery markers are implanted in the knee implant and in the surrounding bone. It is then possible to calculate the host markers position in the three-dimensional coordinate system from the x-ray examination and calculations done by computer software. A consecutive number of examinations will show the magnitude of migration over time.

Because of the documented relationship between micromotion of implants, especially in primary hip and knee arthroplasty, and future risk of aseptic loosening, RSA has been suggested as the method of choice to evaluate new implant designs before widespread clinical use. Implants that show continuous migration between one and two years after operation are considered being at a high risk of future aseptic loosening (19;20). Although RSA has been used to evaluate primary implants for total knee and hip artroplasties, high tibial osteotomies, fracture stability, physiological growth and motion, no studies on rTKA have previously been published.

Changes in bone mineral density (BMD) can be measured by dual energy x-ray absorptiometry (DEXA) (21;22). No studies measuring changes in BMD of the proximal tibia after rTKA have previously been published. Studies on BMD changes in the proximal tibia after primary TKA have shown a significant decrease in BMD, sometimes reaching 20 - 36 %, independent of measuring technique (DEXA, CT bone densitometry, dual photon Absorptiometry) (23-28). However, some studies have shown an unchanged BMD (29-31) or even a small increase (32).
The effect on the postoperative adaptive bone remodeling with the use of a stemmed femoral implant in rTKA also is unknown. Several studies on BMD changes at the distal femur (in close relation to the femoral implant) after TKA exist. A common finding is a decrease in BMD from baseline up to 2 years after operation. (30;33-35). No studies on BMD changes after rTKA have previously been published, measuring the BMD changes along the stemmed femur implant.

Aim of the Ph.D. study.

The primary aim of this clinical study was to evaluate the use of TM Cone by conducting two research methods, Dual Energy X-ray Absorptiometry (DEXA) and Roentgentereofotometric Analysis (RSA). In addition a third study was performed.

Aim of study 1

To evaluate the difference in migration of the tibial component after rTKA with and without the use of TM Cone in a prospective randomized design using RSA.

Aim of study 2:

To evaluate the difference in adaptive bone remodelling of the proximal tibia and tibial shaft after rTKA with and without the use of TM Cone in a prospective randomized design using DEXA.

To evaluate the clinical outcome of rTKA with and without the use of TM Cone.

In both study 1 and 2 the clinical outcome after rTKA with and without the use of TM Cone is evaluated.

Aim of study 3

Through prospective measurements of the changes in BMD at the distal femoral shaft to evaluate the adaptive bone remodelling after rTKA using a cemented revision femoral component with a 100 mm press fit stem. The use of TM Cone in this study was not evaluated.

Hypothesis.

Given the advantageous biocompatible characteristics of porous Tantalum we expected ingrowth of new bone and vascularised fibrous tissue after implantation in patients with substantial bone loss of the proximal tibia during rTKA.

Study 1 (RSA).

We expected to find less migration of the tibial implant in the group of patients who received rTKA with TM Cone.

Study 2 (DEXA).

We expected a decrease in BMD of approximately 20 % after rTKA using conventional techniques for reconstruction and less bone loss in the TM Cone group.

Study 3 (DEXA)

We expected a decrease in BMD because of the surgical trauma and reduced mobility.

Materials

Study design

Forty consecutive patients scheduled for rTKA were randomised to receive surgical treatment reconstructing the tibial bone defects with the use of TM Cone (A) or without TM Cone using conventional technique (B). The study was approved by the local Scientific Ethical Committee of Københavns og Frederiksberg Kommuner (KF 01 276195). All patients gave their oral and written informed consent prior inclusion to the study.

Criteria of inclusion were 1. Severe bone loss of the proximal tibia where reconstruction with the use of cementation or structural grafting is optional. 2. Patients with the age of 18 to 80 years.

Criteria of exclusion were 1. patients with diseases affecting the bone metabolism (osteoporosis, Paget's disease, hyperparathyroidism ect.) 2. Patients unable to understand the informed consent and patients living in Greenland. 3. Pregnant and lactating women.

By a computer-generated block-randomisation (4 patients in each block), 40 numerated envelopes were allocated a note with A (TMC) or B (conventional = NO TMC), and sealed by an independent laboratory technician. The day before surgery, when the indication for the operation was finally set, the surgeon opened the sealed envelope to see which type of reconstruction the patient was

allocated to. The forty patients constituted the study population in study 1 and 2. In study 3, sixteen patients of the same group of 40 were selected to undergo additional DEXA examinations.
Patient characteristics are shown in Table 1.

Patient exclusion and dropout.

Study 1.

One patient randomised to receive rTKA with TM Cone was excluded, because of a small fracture in the proximal tibia which caused the surgeon not to use TM Cone. One patient was excluded because of reinfection (rerevision) after 3 months of follow-up. One patient died of unrelated reasons 2 months after inclusion. All remaining participating patients attended the programme with x-rays for RSA at 3, 6, and 12 months of follow-up. During final analysis 14 patients had their x-rays discarded because of difficulties with marker recognition, thus leaving 23 patients for the study (Table 1a and Tabel 1b). The markers were hidden in at least one of the x-rays behind the implant or TM Cone, resulting in lack of markers to complete the analysis (less than 3 markers present in one segment). Analysis´ with a Condition number over 50 (CN > 150) had the data describing the rotation excluded, but the translation data and MTPM was used for further statistical analysis

Study 2.

Four patients were excluded after inclusion. One patient was excluded because it was decided peroperatively to change the surgical procedure because of a small fracture of the proximal tibia. Two patients were excluded after 3 months of follow-up because of respectively death and recurrent infection requiring additional revision surgery. Finally, one patient was excluded because of poor quality of DEXA scans. Thus, 36 patients were left for the study.
Patient characteristics are shown in Table 1a and 1c.

Study 3.

No patients were excluded.

	ALL	Study 1	Study 2	Study 3
N	40	23	36	16
Age [years]	66 (40-85)	64 (40-80)	66 (40-85)	64 (40-85)
Sex (M/F)	18/22	7/16	19/17	9/7
Body Mass Index	29 (21-46)	28 (22-40)	29 (21-46)	28 (21-39)
Primary disease				
Primary arthrosis	31	18	27	11
Secondary arthrosis	5	3	5	3
Rheumatoid arthritis	1	1	1	
Sequelae after fracture	1		1	
Haemophilia	2	1	2	2
Cause of revision				
Aseptic loosening	16	13	14	8
Pain	4	3	4	0
Instability	6	4	6	4
PE-wear	2	0	2	1
Deep infection	12	3	10	3
Prosthesis type				
Rotating hinge	6	3	5	12
Constrained condylar	28	15	25	3
Posterior stabilized	6	5	6	
TM Cone	19		17	

Tabel 1a. Patients characteristics. Age, BMI are presented as mean values with range in brackets.

	TM Cone	NO TM Cone	Total
N	12	11	23
Age [years]	63	65	64
Range	*46-78*	*40-80*	*40-80*
Gender (F/M)	2/10	5/6	7/16
BMI	27	29	28
Range	*22-34*	*25-40*	*22-40*
Primary disease			
Primary arthrosis	10	8	18
Secondary arthrosis	1	2	3
Rheumatoid arthritis		1	1
Sequelae after fracture			
Haemophilia	1		1
Prostheses type			
Rotating Hinge	3	0	3
Constrained condylar	6	9	15
Posterior stabilized	3	2	5
Cause of revision			
Aseptic loosening	6	7	13
Pain	1	2	3
Instability	2	2	4
PE-Wear	0	0	0
Deep infection	3	0	3
Bone defects Tibia (AORI)			
T2b	8	10	18
T3	4	1	5

Tabel 1b. Demografic data study 1 (RSA study).

	TM Cone	NO TM Cone	Total
N	17	19	36
Age [years]	65	66	66
Range	*(46-78)*	*(40-85)*	*(40-85)*
Gender (F/M)	5/12	12/7	17/19
BMI	27	30	29
Range	*(21-36)*	*(25-46)*	*(21-46)*
Primary disease			
Primary arthrosis	14	13	27
Secondary arthrosis	1	4	5
Rheumatoid arthritis	0	1	1
Sequelae after fracture	0	1	1
Haemophilia	2	0	2
Prosthesis type			
Rotating hinge	4	1	5
Constrained condylar	10	15	25
Posterior stabilized	2	4	6
Cause of revision			
Aseptic loosening	7	7	14
Pain	1	3	4
Instability	3	3	6
PE-Wear	0	2	2
Deep infection	6	4	10
Bone defects Tibia (AORI)			
T2	12	17	29
T3	5	2	7

Tabel 1c. Demografic data study 2 (DEXA-study).

Methods.

Implants

The NexGen® (Zimmer Warsaw, USA) revision system was used in all cases, and the following types of revision prostheses were used: Rotating Hinge Knee (n=6), Legacy®Knee-constrained condylar (n=28) and Legacy® Knee-Posterior stabilized (n=6) (Table 1). Press fit stems with or without off-set tibia and femur implants were used in all patients. The mean tibia stem diameter was 14 mm (10 mm-18 mm) and mean stem length was 110 mm (100 mm-155 mm). The mean femur stem diameter was 18 mm (14 mm -24 mm) and the mean stem length was 110 mm (100 mm -155 mm). Nineteen patients had femoral augments, 8 patients had both tibial and femoral augments, and 2 patient had only a tibial augment, whereas 11 patients did not receive any augments. Five All Poly Patella (NexGen® Zimmer) implants were used. Nineteen TM Cone were used.

Surgical Technique and procedure.

The same surgeon performed all operations. The surgical procedure of rTKA using TM Cone is identical with the conventional rTKA procedure, except for the implantation of TM Cone (reconstructing the bone loss of the proximal tibia). Failed implants are removed, all surfaces are carefully debrided, and the bone loss of the proximal tibia is assessed and classified. Then the intramedullary canals are reamed and the joint is prepared for a prosthesis of relevant size and constraint.

TM Cone has only been used for management of type T2 and T3 bone loss defects. A provisional cone of relevant size is placed in the defect cavity to make sure it fits. A high-speed burr is often used to shape the cavity of the often sclerotic bone to obtain optimal adaptation. By press-fit, the TM Cone is implanted in the bone defect. The cranial surfaces of the TM Cone and proximal tibia are intended to flush. Morselized bone graft is used to fill out gaps between the TM Cone and proximal tibia in order to prevent cement between host bone and TM Cone. Once the TM Cone is implanted (Figure 2), cementation of the tibial component is the next step. Bone cement with gentamicin (Refobacin Bone Cement R, Biomet®) was used in all procedures and was generally applied between the tray and the stem connection. Straight or offset press-fit stems were chosen for proper alignment and optimal coverage of the bony surface.

During surgery, all patients were prepared for RSA examinations by the insertion of 6 tantalum markers (0.8 mm) in the polyethylene insert and at least 8 tantalum markers in the proximal tibia. Peroperative tissue cultures were taken in all patients and intravenous cefuroxim (Zinacef) was given three times daily, starting preoperatively and continuing until negative tissue cultures were confirmed, usually 5 days postoperatively. All patients had low molecular heparin as thrombosis prophylaxis for 7 days. Patients were generally allowed to mobilise with full weight bearing helped by a physiotherapist from the first postoperative day. In a few cases mobilisation was not allowed before the postoperative x-ray control had been seen.

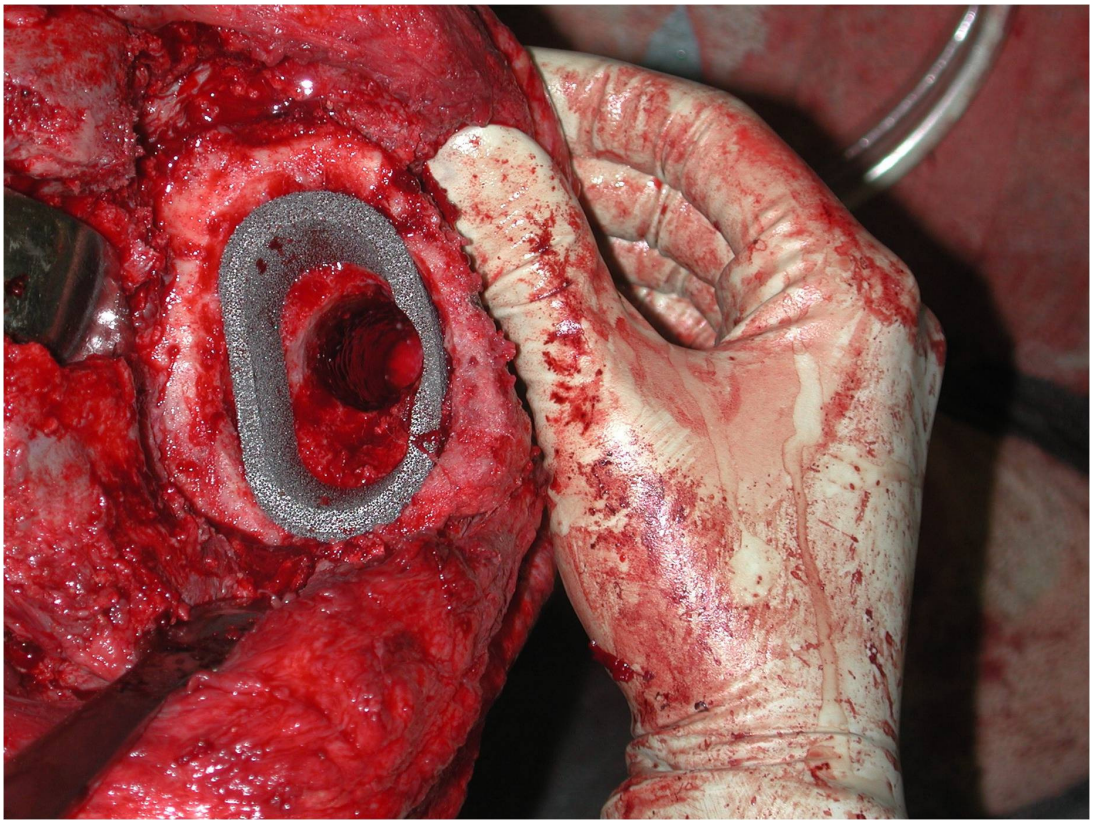

Figure. 2. Proximal tibia with exposed bone defect reconstructed with a tibial full cone.

AORI

Bone loss defects in the proximal tibia were classified according to the Anderson Orthopaedic Research Institute (AORI) bone classification (36) on conventional X-rays. Evaluation of preoperative radiographs according to the AORI classification showed 5 T3 bone loss defect and 35 T2b defects. The final classification of bone defects was not changed reviewing the postoperative radiographs.

Knee and Function scores

Clinical examination with evaluation of the knee function using the Knee Society´s Knee Scoring System (37) were performed preoperatively and with follow-up after one year.

RSA (Study 1)

During the rTKA operation patients were prepared for RSA by insertion of Tantalum markers with a diameter of 0.8 mm. 6 markers were inserted in the polyethylene insert defining the proximal segment (implant) and 8-10 markers were inserted in the proximal tibia defined the distal segment

(bone segment). All markers were spread as widely and non-linear as possible. Supine RSA examinations were performed at a mean of 6 days (range 4-12) after operation and at 3, 6 and 12 months of follow-up at the Department of Radiology X, Rigshospitalet. Patients were positioned standardized at each examination with the affected knee positioned inside a Plexiglas calibration knee cage with defined locations of Tantalum markers in the walls. (Calibration cage 21, Tilly medical products AB, Sweden). Ceiling mounted X-ray tubes were aimed at the knee in the horizontal and coronal plane in a distance of 100 cm, thus creating a bi-planar RSA arrangement with a 90-degree angle between the two tubes. The same physician positioned the patients at each examination. All radiographs were digital with high-resolution 9 pixel/mm. The radiation intensity at each RSA examination was 55 kV and 20 milliAmpere second (mAs). The digital images were burned to a CD-ROM and transported to the Department of Orthopaedics, Lund University Hospital, Sweden, where the images were imported with the use of UmRSA DICOM Link with an image resolution of 254 DPI, in DICOM 3.0 format. UmRSA V. 6.0 software was used for measuring of images and calculation. The software allows semi-automated determination of marker centers.

Condition number (CN): The distribution of Tantalum markers inserted in each segment shaping the rigid bodies are estimated by the software at each examination. If the Tantalum markers are inserted narrowly and linear, the CN is high. Conversely, a low CN indicates a rigid body with a wide spatial distribution of Tantalum markers in a non-linear configuration. In examinations with high CN, the rotation data was excluded while translation was evaluated.

Mean Error (ME): The inserted tantalum markers have to be closely attached to bone or prosthesis to prevent loosening. Markers that loosen between two examinations make the rigid body deform and unstable, resulting in a high mean error value. This will finally affect the reliability of the kinematic analysis. A ME cut-off level of 0.350 mm is recommended as guideline (38)

The reproducibility of the RSA method was estimated by double measurements performed on the same day, and the precision error was calculated as a theoretical migration between the two sets of X-rays for each individual. Precision is given as absolute mean value and 2SD for translation and rotation along the three axes and MTPM for all double measurements.

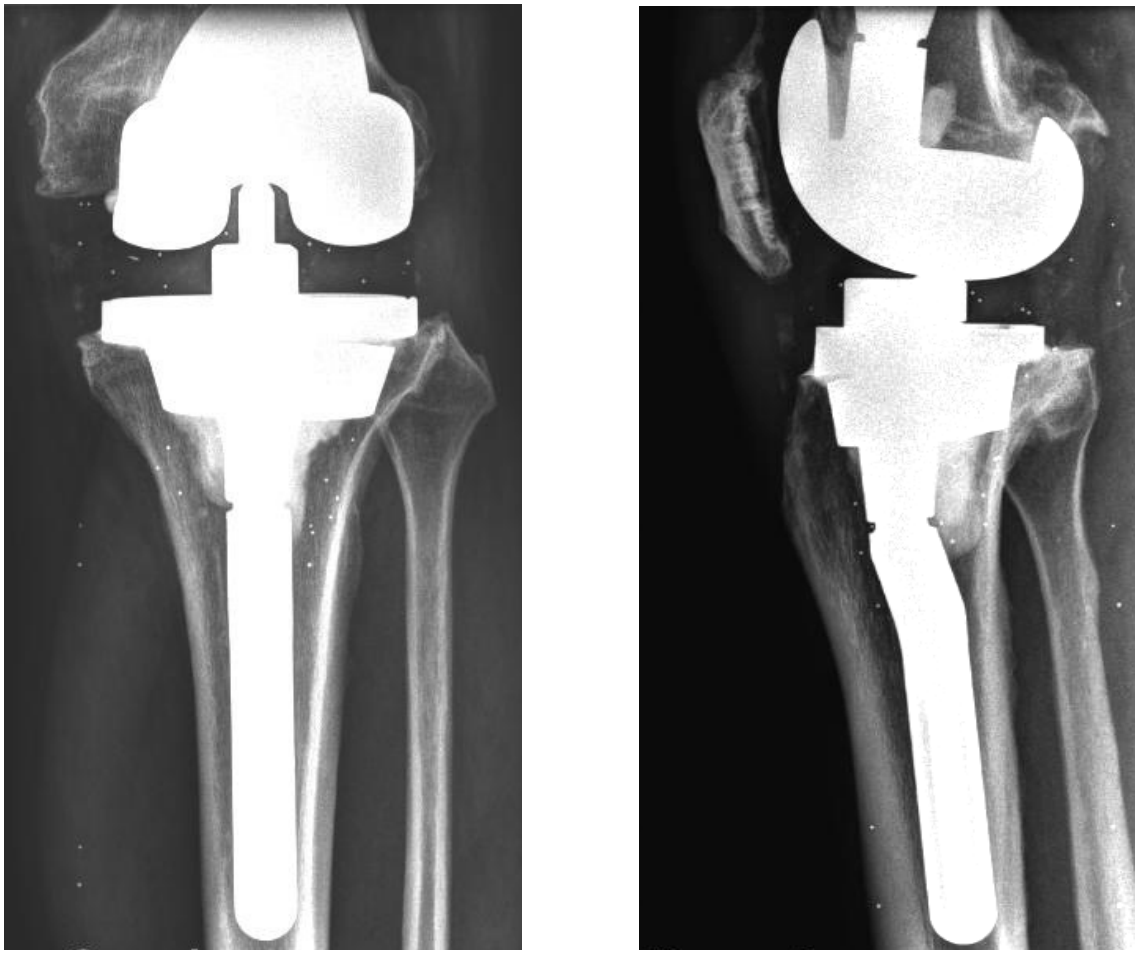

Figure 3. RSA examination showing rTKA with T2b bone loss (Legacy®Knee-constrained condylar (LCCK) with TM Cone) and markers in host bone and PE-insert. Calibration cage markers are also shown.

Dual Energy X-ray Absorptiometry (Study 2 and 3).

The same scanner at the same location was used in study 2 and 3. Measurements of BMD (g/cm^2) were performed by DEXA (21;22) using a Norland XR-46 bone densitometer (Norland Corp. Fort Atkinson, Wis). The diameter of the spot size of the X-ray tube is 1.1 mm. It operates at 100 kV. The two emitted radiation energy peaks are at 47 KeV and 80 KeV. The amount of energy transmitted to each individual is measured by one detector that consists of one high- and one low

energy detector located at different distances from the focal spot. The scanner was calibrated (by scanning of a bone phantom) according to the manufactures guidelines each day.
A custom-made software were used for analysis of DEXA scans (39). The software allows measurements of BMD in close relation to orthopaedic implants, by exclusion of pixels considered by the software as metal. The software exclude the nearest pixels adjacent to the pixel considered as metal. The software allows a variable metal exclusion threshold to be set by the physician. The metal exclusion threshold was set at 4,5 g/cm^2 in study 2 and 3. The pixel size when measuring BMD in study 2 (proximal tibia) and in study 3 (distal femur) was 1.0 mm x 1.0 mm with a scan speed of 45 mm/s. Furthermore, scans of the distal tibia and fibula just above the ankle joint were performed bilaterally with a pixel size of 0.5 x 0.5 mm in both study 2 and 3.

Study 2.
All measurements were performed in the coronal plane of the limb with a scan speed of 45 mm/s using the research scan option. All scans were performed by the same laboratory technician with the patient lying flat on their back, the knee extended and with the ankle in a neutral position pointing straight up. All patients had their first scans performed within the first 2 weeks after surgery and with follow-up after 3, 6, and 12 months.
On the computerized scan plots 7 Regions of Interest (ROI) were selected for measurements of BMD of the proximal tibia and tibial shaft: the lateral tibial condyle (ROI 1), the medial tibial condyle (ROI 2), an area at the level of conjunction of the tibial component and the stem (ROI 3), three ROI along the tibial stem (ROI 4-6), and a distal area below the stem of the tibial component (ROI 7) (Figure 4). In the distal tibia and fibula one ROI was selected 1 cm above the ankle joint line.
The precision of the BMD measurements was measured using double scans of the proximal tibia in 11 patients. Double scans were done consecutively on the same day with full repositioning of the patient with a break of 5 minutes between the scans. The mean precision was calculated in both groups for all ROI and expressed as the mean coefficient of variation (CV) in each ROI.

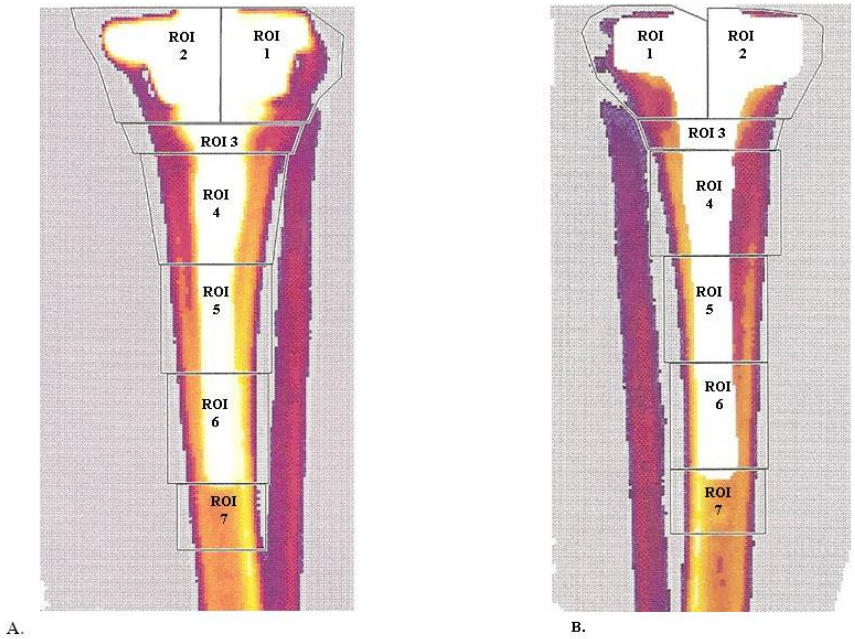

Figure 4. The 7 ROI´s. A. DEXA with TM Cone (Right tibia) B. without TM Cone (left tibia)

Study 3.

All measurements were performed in the coronal plane of the limb with a scan speed of 45 mm/s using the research scan option. Scans were performed of the distal femur and along the femur shaft in close relation to the femur component. All scans were performed with the patient lying flat on their back, the knee extended and with the ankle in a neutral position pointing straight up. All patients had their first scans performed within the first 2 weeks after surgery and with follow-up after 3, 6, and 12 months. On the computerized scan plots 5 Regions of Interest (ROI) were selected for measurements of BMD of the distal femur and femur shaft. The femur stem was divided into 3 ROI´s of the same size; a distal ROI (ROI 1), an intermediate ROI (ROI 2) and a proximal ROI (ROI 3). ROI 4 was defined as a total ROI that counted for the 3 ROI along the stem. At the tip of the stem a distal ROI was defined as ROI 5. (Figure 5). In the distal tibia and fibula one ROI was selected 1 cm above the ankle joint line.

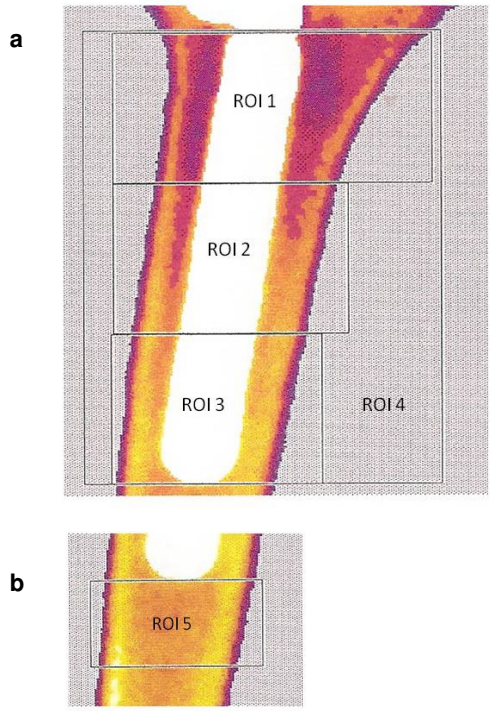

Figure 5. DEXA scan plots of the distal femur showing the 4 ROI´s. along the stem (a), and the 5th ROI at the tip of the stem (b).

Precision.

Study 1

The reproducibility of the RSA method was estimated by double measurements performed on the same day in 10 knees, and the precision error was calculated as a theoretical migration between the two sets of x-rays for each individual. Precision is given as absolute mean value and 2 Standard Deviation (2SD) for translation and rotation along the three axes and MTPM for all double measurements.

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Study 2

The precision of the BMD measurements was measured from double scans of the proximal tibia in 11 patients. Double scans were done consecutively on the same day with full repositioning of the patient with a break of 5 minutes between the scans. The mean precision was calculated in both groups for all ROI and expressed as the mean coefficient of variation (CV) in each ROI.

The coefficient of variation (CV = (SD/mean) x 100 %) was calculated to evaluate the precision of the BMD measurements in the various ROI and given together with range and 95 % confidence limits (95-% CL).

Statistics

Statistical analysis was done by the use of SPSS statistics 17.0 and p-values below 0.05 were considered significant in all studies.

Study 1

Since no previously published RSA studies evaluating migration of the tibial component after rTKA existed when planning the present study, we used standard deviation (SD) values from a study by Toksvig-Larsen et al. (40) for calculation of sample size. In this study the specification of the SD was very clear and four different primary tibial components (n=62) were examined. An average SD of 0.7 mm for the parameter MTPM at 2 years of follow-up was used for our sample size calculations. We planned to be able to measure a significant difference (minimal relevant difference) between the 2 groups of 1.0 mm. With a type 1 error of 5% and a type 2 error of 10% the calculated sample size was 10 in each group.

The data for rotation and translation are given as mean together with SD and 95%-CL, and un-paired t-test was used to test for differences between the two groups.

The data for MTPM, which is per definition not normally distributed, are given as mean and SD (and on the graphical presentation with standard error of mean (SE)), and non-parametric test for un-paired data (Mann-Whitney) are used to test for differences between groups.

Study 2

Since no previously published studies evaluating the changes in BMD of the proximal tibia following rTKA existed, when the study was planned and sample size calculated, we used the SD from a recently published 2-year follow-up study (32), where measurements of BMD were performed of the proximal tibia in patients with uncemented primary TKA. In that study a relatively large difference in SD (5.59%-12.40%) was found in the different (ROI) used for BMD measurements, and our sample size calculations were based on an average SD from 4 different ROI of 7.53%. We planned to be able to measure a significant difference (minimal relevant difference) between the 2 groups of

10%, and with a type 1 error of 5% and a type 2 error of 10% the calculated sample size was 11 in each group.

The changes in BMD are given as the mean percent change together with total range and SD. For evaluation of the intra-group changes 95%-CL were calculated (t-test for paired data). The potential differences in BMD changes between groups were evaluated using unpaired t-test.

Study 3

The changes in BMD are given as the mean percent change together with total range and SD. For evaluation t-test for paired data with calculation of the 95%-CL were performed and p-values below 0.05 were considered significant.

Results

Study 1

Precision error

The mean precision error and range for the RSA measurements of rotation and translation along the x-, y-, and z-axis was 0.11° (0.0° - 0.59°), 0.36° (0.0° - 2.95°), and 0.45° (0.0° - 4.26°) for rotation and 0.39mm (0.0mm - 3.56mm), 0.23 mm (0.0mm - 2.0mm), and 0.2 mm (0.0mm - 1.75mm) for translation. The mean precision error of MTPM was 0.16mm (0.05mm - 0.28mm).

	ROTATION			TRANSLATION			Mean Error		Condition nr		Markers	
	X	Y	Z	X	Y	Z	Ref	Cur	Ref	Cur	Ref	Cur
MEAN	0.11	0.36	0.46	0.38	0.23	0.20	0,08	0,06	95	66	4.4	3.7
2SD	0.34	1.82	2.68	2.24	1.22	1.08						

	MTPM (mm)
Mean	0.16
2SD	0.12

Tabel 3. Precision error given as absolute mean values and 2SD for segment motion (rotation and translation) and point motion (MTPM). Mean ME, CN and markers are also shown for the reference and current segment.

X-translation (lateral-medial migration)

The net-direction of migration along the lateral-medial axis was for both groups lateral after 12 months. On average the implants in the NO TM Cone group had moved the most (1 mm), but no significant difference was found between the two groups (Table 4).

Y-translation (subsidence and lift-off)

A slight lift-off at 3 months of follow-up (0.03 mm) was turned into subsidence at 12 months of follow-up (0.23 mm) in the NO TM Cone group. The pattern was opposite in the TM Cone group where a subsidence of 0.1 mm was turned into a marginal lift-off of 0.09 mm. No statistically difference was found between the two groups (Table 4).

Z-translation (anterior-posterior migration).

Apparently the tibial implant in the TM Cone group had moved the most, although no statistically difference was found. The net direction in both groups was migration in the anterior plane (Table 4).

Rotation around the transverse (x-) (anterior/posterior tilt) and vertical axis (y-)(internal/external rotation)

A marginal posterior tilt (0.17°) was found at 3 months of follow-up in the TM Cone group compared with 0.4° anterior tilt in the NO TM Cone group. At 12 months a slight posterior tilt was found in both groups (0.03° and 0.07°). In both groups the main direction of micromotion was internal rotation which was most pronounced in the NO TM Cone group measuring 1.02° at 12 months. No statistical significant differences were found comparing anterior/posterior tilt or internal/external rotation in the two groups. (Table 2).

Rotation around the sagittal (z-) axis (varus and valgus rotation)

Both groups had rotated in a varus position after 3 months (0.1° and 0.28°). The TM Cone group increased the mean varus rotation at 6 months to turn to a mean valgus rotation at 12 months, compared to the NO TM Cone group that faster (at 6 months) turned into valgus rotation (0.96°) to settle at 1.3° at 12 months. No statistically significant difference was found between the two groups (Table 4).

	X-AXIS Months			Y-AXIS Months			Z-AXIS Months		
	3	6	12	3	6	12	3	6	12
TM Cone Rotation									
Mean	-0.17 °	0.05 °	-0.03 °	-0.07 °	0.18 °	0.29 °	-0.10 °	-0.20 °	0.20 °
SD	0.39	0.41	0.41	0.4	0.44	0.53	0.24	0.44	0.39
CL95	-0.96-0.41	-0.40-0.81	-0.65-0.60	-0.73-0.44	-0.35-0.85	-0.45-1.37	-0.54-0.2	-0.93-0.25	-1.0-0.25
n	8	9	8	8	9	8	8	9	8
NO TM Cone Rotation									
Mean	0.4 °	0.11 °	-0.07 °	0.41 °	1.31 °	1.02 °	-0.28 °	0.96 °	1.30 °
SD	0.64	0.54	0.72	1.34	2.22	2.38	0.61	2.90	3.11
CL95	-0.20-1.67	-0.6-0.66	-1.0-1.06	-0.78-3.07	-0.17-4.57	-0.49-5.8	-1.47-0.07	-0.88-5.27	-0.62-7.60
n	6	4	6	6	4	6	6	4	6
T-test	0.09	0.86	0.93	0.43	0.39	0.50	0.51	0.48	0.29
TM Cone Translation									
Mean	0.02 mm	0.10 mm	-0.2 mm	-0.10 mm	0.05 mm	0.09 mm	-0.06 mm	0.09 mm	0.32 mm
SD	0.27	0.21	0.51	0.19	0.20	0.30	0.35	0.41	0.81
CL95	-0.54-0.37	-0.29-0.40	-1.14-0.47	-0.52-0.12	-0.21-0.46	-0.21-0.89	-0.51-0.69	-0.41-0.89	-0.42-2.36
n	10	9	11	10	9	11	10	9	11
NO TM Cone Translation									
Mean	0.22 mm	-0.58 mm	-1.0 mm	0.03 mm	0.09 mm	-0.23 mm	0.12 mm	0.05 mm	0.15 mm
SD	0.5	2.38	2.47	0.14	0.23	0.59	0.67	0.42	0.09
CL95	-0.04-1.54	-5.35-1.30	-7.55-0.10	-0.13-0.36	-0.09-0.53	-1.45-0.34	-0.56-1.8	-0.42-0.83	0.06-0.30
n	9	6	9	9	6	9	9	6	9
T-test	0.31	0.51	0.37	0.11	0.72	0.16	0.50	0.84	0.28

Table 4. Mean segment motion values along the three axes at each follow-up.

MTPM

MTPM showed a slightly divergent pattern in the two groups. The MTPM was at 3 months around 1 mm in both groups. MTPM in the TM Cone group then decreased to become relatively stable between 6 months (0.63 mm $\pm$ 0.45mm) and 12 months (0.77 mm $\pm$ 0.78 mm). MTPM in the NO TM Cone group continued to migrate slightly up to 6 months before being relatively stable between 6 and 12 months (2.28 mm $\pm$ 3.69mm). No statistically significant difference between MPTM in the two groups was found (Figure 6).

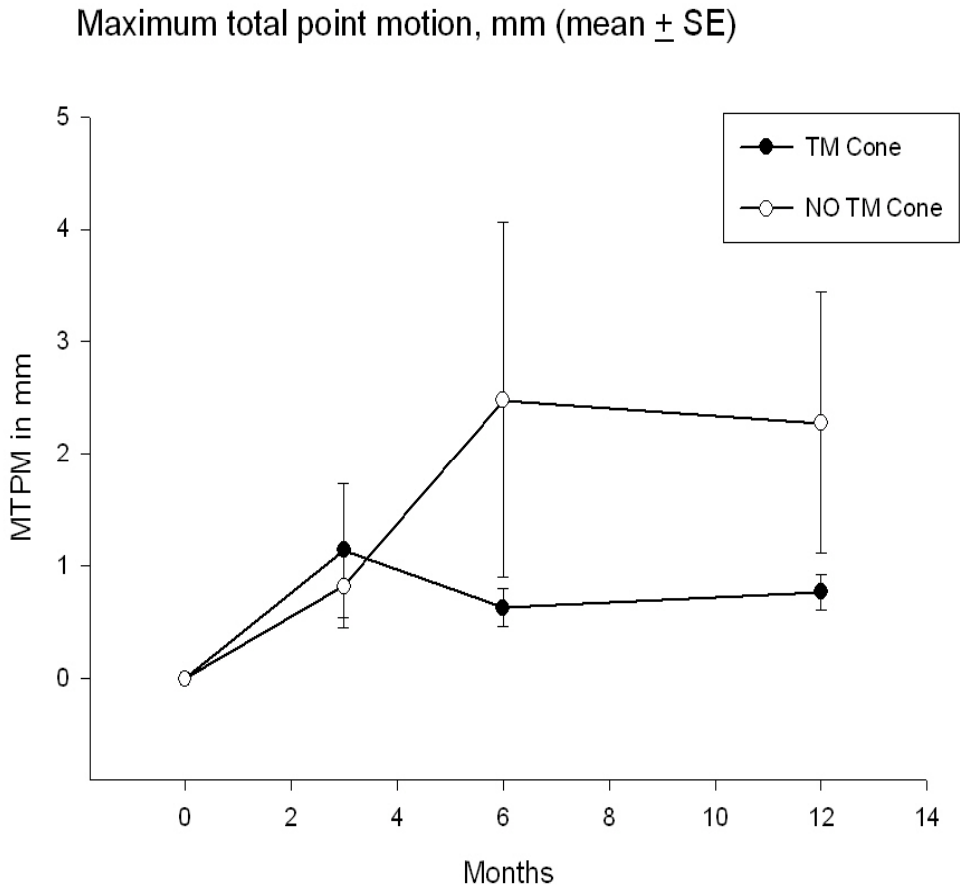

Figure 6. The movement of the single marker that moves the most.

Study 2

The average precision for measurements of BMD in the various ROI in close relation to the tibial components of the two study groups was 3.6% and 2.1% for respectively the TM Cone and NO TM Cone group (Table 2).

Study group	n	ROI 1	ROI 2	ROI 3	ROI 4	ROI 5	ROI 6	ROI 7	**All ROI**
TM Cone									
Mean	5	7.1	8.9	1.4	2.3	2.5	1.4	1.4	**3.6**
Range		2.30-11.80	1.90-19.90	0.30-2.90	0.80-4.20	0.80-4.40	0.94-2.00	0.05-2.83	1.4-8.9
95%-CL		2.71-11.45	-0.80-18.68	0.06-2.65	0.63-4.0	0.55-4.48	0.88-1.88	-0.0034-2.81	0.7-6.5
NO TM Cone									
Mean	6	2.0	2.3	2.9	1.7	1.8	2.8	1.2	**2.1**
Range		0.09-3.80	0.08-8.30	1.20-4.50	0.09-4.5	0.05-4.40	0.15-5.20	0.59-2.98	1.2-2.9
95%-CL		0.43-3.57	-1.02-5.58	1.41-4.29	-0.31-3.70	0.20-3.45	0.82-4.70	0.30-2.19	1.6-2.6

Table 2**.** Precision expressed as mean CV (%) with range and 95 %-CL.

For all patients (n=36) the measured clinical effect of the rTKA showed that the average knee score and function score improved from 37 to 76 (p=0.005) and from 22 to 57 (p=0.005) respectively. An identical improvement (p = 0.0005) of the knee- and function scores were observed also in both individual study groups (Table 1c), and no statistically significant difference between the improvements of the knee score (p=0.36) and function score (p=0.75) was found between the TM Cone and NO TM Cone groups. Surgical times using the TM Cone were significantly longer (p = 0.004) than that of the conventional method with an average time difference of 42 minutes (Table 5).

Duration of surgery	**Total**	**TM Cone**	**No TM Cone**
N	36	17	19
Mean, Range	174 min (85 – 355) min	193 min (135 - 355)min	151 min (85 – 250) min

Table 5. Duration of surgery in study two with or without TM Cone.

The changes in BMD within the two study groups were quite similar with statistically significant decreases in BMD after one year of 6 – 8.6 % in ROI along the stem (ROI 3, ROI 4 and ROI 5). In the most distal ROI along the stem (ROI 6) and in the ROI below the stem (ROI 7) no statistically significant changes were found in any of the groups at one year of follow-up. In the two most proximal ROI, BMD after one year showed a statistically significant decrease of 12.1% medially (ROI 2) in the TM Cone group, while no statistically significant changes were seen in this ROI in the NO TM Cone group or in the lateral ROI (ROI 1) in any of the groups (Table 6). The percentage

changes in BMD in the 7 ROI of the proximal tibia and along the tibial shaft seen within the two study groups were not statistically different after 3, 6, or 12 months respectively.
The BMD value in the distal tibia of the operated legs decreased in both groups, but this decrease was significant only after 6 months of follow-up in the TM Cone group (6.0%, 95%-CL: -11.0% - 1.0%), and the BMD changes in the contralateral (not operated leg) distal tibia showed only minor insignificant changes from baseline during the 12 months of follow-up. The percentage changes in BMD of the distal tibia within the two study groups after 3, 6, and 12 months respectively were not statistically different.

	BMD *(g/cm²)* Postoperative **TM Cone**	BMD *(g/cm²)* Postoperative **NO TM Cone**	Δ BMD *[%]* 0-3 months **TM Cone**	Δ BMD *[%]* 0-3 months **NO TM Cone**	P	Δ BMD *[%]* 0-6months **TM Cone**	Δ BMD *[%]* 0-6 months **NO TM Cone**	P	Δ BMD *[%]* 0-12 months **TM Cone**	Δ BMD *[%]* 0-12months **NO TM Cone**	P
ROI 1											
Mean	0.860	0.874	-6.6	0.6		-3.0	3.0		-0.4	-3.4	
Range	0.465-1.615	0.589-1.587	-45 – 42.6	-16.5 – 17.9	**0.20**	-23.3 – 19.7	-17.8 – 21	**0.17**	-21.2 – 21.8	-28.4 – 18.7	**0.56**
SD	0.28	0.26	19.0	10		13.1	10.9		13.9	14.2	
95%-CL			-17.2 ; 4	-4.5 ; 5.7		-10.3 ; 4.2	-2.7 ; 8.9		-7.9 ; 7	-11.3 ; 4.4	
ROI 2											
Mean	0.852	0.917	-6.5	-1.4		-4.3	-0.6		-12.1	-2.8	
Range	0.533-1.659	0.572-1.344	-22.9 – 10.5	-26.2 – 31.9	**0.23**	-34.1 – 15.8	-24.5 – 30.3	**0.54**	-44.5 – 11.7	-29.5 – 27.2	**0.15**
SD	0.29	0.28	9.7	13.5		16.7	15.9		18.3	16.6	
95%-CL			-11.9 ; -1.1	-8.3 ; 5.5		-13.5 ; 4.9	-9.1 ; 7.8		-22 ; -2.4	-12 ; 6.3	
ROI 3											
Mean	1.093	0.972	-7.8	-3.7		-8.8	-6.0		-7.2	-7.0	
Range	0.663-1.742	0.722-1.485	-18.1 – 17.6	-21- 10.7	**0.25**	-16 – 7.4	-24.9 – 14	**0.38**	-25.4 – 12.4	-20.1 – 23.6	**0.95**
SD	0.26	0.25	10.2	9.4		6.6	10.2		10.6	10.9	
95%-CL			-13.5 ; -2.2	-8.6 ; 1,1		-12.4 ; -5.1	-11.5 ; -0.6		-12.9 ; -1.6	-13.0 ; -0.9	
ROI 4											
Mean	1.146	0.983	-4.8	-2.8		-5.5	-4.7		-7.5	-6.0	
Range	0.627-1.983	0.533-1.394	-12.1 – 4.1	-15.5 – 5.9	**0.30**	-14.9- (-0.2)	-22.3 – 3.4	**0.70**	-20.4 – 1.3	-26.6 – 5.2	**0.53**
SD	0.37	0.25	4.9	6.1		4.1	7.0		5.8	7.9	
95%-CL			-7.6 ; -2.1	-6.0 ; 0.4		-7.8 ; -3.2	-8.4 ; -0.9		-10.6 ; -4.4	-10 ; -1.6	
ROI 5											
Mean	1.229	1.064	-6.5	-4.0		-7.1	-5.3		-8.6	-8.0	
Range	0.743-2.027	0.508-1.526	-17.1 – 2.5	-19 – 4.6	**0.32**	-19.6 – 2.0	-20.8 – 4.6	**0.48**	-31.8 – 2.2	-21.5 – 1.6	**0.81**
SD	0.35	0.3	6.2	7.0		6.9	6.9		9.1	6.7	
95%-CL			-9.9 ; -3.1	-7.7 ; -0.4		-11 ; -3.2	-9.0 ; -1.6		-13.5 ; -3.8	-11.6 ; -4.2	
ROI 6											
Mean	1.158	0.993	-7.8	-3.5		-6.7	-4.6		-9.2	-4.0	
Range	0.619-2.195	0.414-1.338	-22.6 – 0.1	-21.5 – 17.8	**0.13**	-23.1 – 5.4	-26.3 – 5.1	**0.56**	-38.1 – 3.8	-25.1 – 6.5	**0.15**
SD	0.40	0.3	6.6	8.9		9.2	9.7		11.3	8.5	
95%-CL			-11.5 ; -1.6	-8.1 ; 1.1		-11.8 ; -1.6	-9.8 ; 0.6		-15.2 ; 3.2	-8.6 ; 0.7	
ROI 7											
Mean	1.385	1.272	-0.9	-0.3		1.8	-1.2		1.5	-1,6	
Range	0.844-2.027	0.701-1.272	-19 – 8.6	-8.7 – 10.5	**0.80**	-13.3 – 13.5	-14.7 – 6.6	**0.17**	-14.3 – 12.5	-13.6 – 5.5	**0.15**
SD	0.34	0.28	7.4	4.8		6.3	5.5		6.0	5.5	
95%-CL			-5.0 ; 3.2	-2.8 ; 2.2		-1.7- 5.3	-4.2 – 1.7		-1.7 ; 4.7	-4.6 ; 1.5	

Table 6. Changes in BMD of the proximal tibia and tibial shaft around the rTKA.

Study 3

Knee- and function scores improved significantly (P=0.005) from the preoperative values of 37 and 24 to 78 and 61 at one year of follow-up. In ROI1-4 a significant increase in BMD reaching 3.5-6.0% after 6 months was seen during the first 3-6 months after surgery. This increase only remained significant in ROI4 (4.0%, p = 0.01) at 1 year of follow-up (Table 7). In ROI5 no significant changes was observed during the first postoperative year.

	BMD *(g/cm²)* Postoperative	**Δ BMD** *[%]* 0-3 months	**P**	**Δ BMD** *[%]* 0-6 months	**P**	**Δ BMD** *[%]* 0-12months	**P**
ROI 1							
Mean	0.848	4.5		6.0		3.4	
Range	0.634 - 1.112	-5.3 - 16.4	**0.03**	-3.9 - 15.7	**0.01**	-3.4 - 10.8	**0.07**
SD	0.153	5.9		5.8		4.9	
95%-CL		0.5 ; 8.5		2.1 ; 9.9		-0.3 ; 7.2	
ROI 2							
Mean	1.014	3.1		4.1		3.4	
Range	1.285 - 1.014	-5.0 - 9.6	**0.06**	-4.7 - 16.1	**0.03**	-7.7 - 14.4	**0.12**
SD	0.193	4.7		5.6		5.7	
95%-CL		-0.1 ; 6.2		0.4 ; 7.9		-1.0 ; 7.8	
ROI 3							
Mean	1.236	2.2		3.5		2.8	
Range	0.718 - 1.657	-3.3 - 5.6	**0.03**	-1.6 - 11.9	**0.02**	-9.6 - 15.0	**0.27**
SD	0.251	2.8		4.0		6.9	
95%-CL		0.3 ; 4.0		0.80 ; 6.1		-2.6 - 8.1	
ROI 4							
Mean	0.998	3.4		4.7		4.0	
Range	0.641 - 1.310	-0.8 - 10.3	**0.01**	1.9 - 9.7	**0.00**	-0.7 - 10	**0.01**
SD	0.184	3.7		2.9		3.1	
95%-CL		0.9 ; 5.8		2.8 ; 6.6		1.5 ; 6.3	
ROI 5							
Mean	1.276	-0.7		-0.8		0.4	
Range	0.640 - 1.988	-5.6 - 3.9	**0.63**	-5.3 - 3.9	**0.42**	-6.7 - 8.3	**0.84**
SD	0.352	3.7		3,0		4.8	
95%-CL		-3.8 ; 2.4		-3.0 ; 1.4		-3.7 ; 4.4	

Table 7. Changes in BMD of the Distal femur around the rTKA. The given p-values are the results of Students t-test.

BMD changes of the distal tibia showed a temporary decrease of 4.4% (p=0,03) in the operated legs but this increase was not significant at the 1-year follow-up. In the contra lateral distal tibia no significant changes in BMD was seen (Table 8)

ROI	*BMD (g/cm^2) POST*	*Δ BMD [%] 0-3 months*	*P*	*Δ BMD [%] 0-6 months*	*P*	*Δ BMD [%] 0-12 month*	*P*
OPERATED							
Mean	0.693	-2.5		-4.4		-1.3	
Range	0.184 - 1.032	-24.1 – 11.4		-17.6 - 3.3		-16.3 - 12.3	
SD	0.23	9.5		5.6		7.7	
95%-CL		-8.2 ; 3.2	0.39	-7.8 ; -1.1	0.03	-5.7 ; 3.2	0.39
NOT OPERATED							
Mean	0.678	-1.6		1.84		1.6	
Range	0.284 – 1.024	-18.5 – 12.6		-10.64 - 18,47		-16.4 – 23.7	
SD	0.226	8.8		8.44		13.1	
95%-CL		-6.5 ; 3.3		-2.8 ; 6.5		-5.3 ; 8.6	
			0.35		0.51		0.77

Table 8. BMD changes in the distal tibia of the operated (rTKA) legs and contralateral legs.
P = unpaired and paired t-test.

Discussion

Study 1

This is the first published RSA data evaluating migration of the tibial component after rTKA. Proper insertion of the Tantalum markers was difficult because of the relatively large rTKA and not least TM Cone implants, occupying the space for marker insertion. In addition, it was difficult to produce and reproduce X-rays with the same marker configuration (at least 3 markers in each segment) visible on both the anterior-posterior and lateral radiographs as the big implants were hiding markers. The result was a high discard of examinations (24%) and exclusion of patients (37 %). However, technical problems in relation to insertion of Tantalum markers and difficulties with sufficient marker visualisation on the radiographs during RSA studies are a well know problem also in primary TKA (19;41;42). A marker free RSA system could in the future remedy these technical problems (43;44). The precision data from previous RSA studies are presented in different ways, which makes direct comparison difficult with our study. None of the following studies reported the precision error of measurements of MTPM. Garling et al. (45) reported a precision error after performing double measurements (TKA) on rotation (n=22) and translation (n=16) expressed as the upper limits of CI-95 % of rotation and translation along x-, y-, and z-axis of 0.45°, 0.42°, 0.16° and 0.07mm, 0.06mm, 0.28mm. Önsten et al. (46) examined the precision error of 56 TKA knees and found a precision error expressed as mean absolute error, close to zero in all six directions (rotation and translation). Regnér et al. (47) found in a TKA RSA study the precision error given as, 95 % confidence limits, of their RSA setup to be 0.16mm for subsidence and 0.24° 0.36° 0.31° for

rotation (27 double examinations). Nilsson et al. reported the precision of measurements as the absolute mean value of all recorded differences between 2 double examinations with an SD of 2.58 representing the total error of the determinations at the 99 % level of significance (48). We expected and found the precision error in our study to be higher than the precision errors published on RSA in primary TKA-studies, because of the technical difficulties with proper visualisation of the Tantalum markers.

Since previously published studies evaluating migration of the tibial component after rTKA does not exist, the magnitude of migration of the present study can only be compared to migration after primary TKA. Ryd et al. (19) found in a series of 143 primary TKA, that was not later revised for aseptic loosening, an average migration expressed as MTPM after the first postoperative year of 0.7 mm for cemented tibial components and 1.7 mm for uncemented components. Later studies found that the average MTPM of the tibial component in uncemented TKA could be reduced almost to the level of cemented implants, when using hydroxyapatite coated implants (40) or trabecular metal tibial components (49). The MTPM of the TM Cone group of the present study was on the same level as what is normally seen after cemented primary tibial implants, while the MTPM of the NO TM Cone group was higher than normally seen after even uncemented tibial components. This finding is probably due to the rigid construct created by proximal cementation of the tibial implant into the press-fitted TM Cone. The cement is equally distributed in the TM Cone creating a rigid construct in relation to the tibial implant compared with the often depleted cancellous bone in the proximal tibia in rTKA patients. The rigid construct prevents the stemmed tibial implant to subside, which is crucial and beneficial for bone ingrowths and fixation of the prosthesis (TM Cone).

The TM Cone group migration pattern with little migration and early stabilisation is consistent with the findings of Henricson et al. (49) They found in a randomised RSA study comparing an uncemented Trabecular Metal monoblock with a cemented tibial component for the use of TKA, that the TM monoblock showed a considerable migration during the first three months before stabilizing, except for the external rotation which first stabilized at 12 months.

The hypothesis of our study was that the use of the TM Cone implant would cause the tibial component of the rTKA to show less migration as a consequence of a better fixation of the tibial component compared with the conventional rTKA technique for reconstruction of bone loss in the proximal tibia. However, even though the difference between the mean MTPM of the two study groups was almost 2 mm, we could not detect this as a significant difference between the two

groups because the SD of the NO TM Cone group was surprisingly large and more than 5 times higher than expected from our sample size calculations performed before the start of the study. RSA has shown that tibial components in primary total knee arthroplasty migrate during the first year but then stabilize (50). Ryd et al. (19) were the first to show that RSA can be used to identify primary total knee prostheses at risk of mechanical loosening, when they showed that continuous migration with MTPM-values that exceeds 0.2 mm from the first to the second year after surgery. RSA has therefore been considered a beneficial tool, when testing new implants before wide spread clinical use. It is unknown if the migration between 1 and 2 years postoperatively could also be used for prediction of later mechanical loosening in rTKA.

Study 2

Knee Society knee- and function scores improved significantly (37 to 76 and 22 to 57) from approximately the same baseline values to the same level at 1 year of follow-up in both groups. The finding is consistent with Meneghini et al. who followed 15 patients, who had rTKA with TM Cone for an average of 34 months. They found an increase in Knee Society clinical score from 52 to 85 points (Knee function scores not reported). Peters et al. examined the clinical results of 47 rTKA operated with insertion of metaphyseal cemented femoral and tibial components with press-fit stems at a mean of 36 months of follow-up. They did not describe the extent of bone loss of the proximal tibia, but they found overall good to excellent results. Studies on clinical outcome after rTKA with the use of structural bone grafting also report good results (51;52).

The reproducibility of our BMD measurements expressed as the average precision was in this study 3.6% and 2.1% for measurements in knees with and without TM Cone. This is consistent with other DEXA studies on BMD changes after knee replacement surgery, where the precision ranges from 0.9 - 8.3 % (27;29;53;54). The slightly higher precision error in the TM Cone group was caused by a significantly higher CV for repeated measurements of the two proximal ROI´s (ROI 1 and ROI 2). The area of ROI 1 and 2 are small which increases the CV (55).

Studies on BMD changes in the lower extremity after different physiological and traumatic influences are many. A decrease in BMD is often observed after immobilisation and reduced mobility (56), after ankle- (57), tibia- and femoral-shaft fractures (58), and a postoperative decrease in BMD ranging from nearly unchanged to 27 % have been measured one year after TKA (23;27-29;33;34;59;60), THA (61;62) and osteotomia of the tibia (63).

Järvinen et Kannus (1997) has described three factors that that are thought to be involved in the process of bone loss: 1) the injury itself, 2) the operative trauma and 3) post-traumatic immobilization. In our study, the initial decrease in BMD is probably due to the response of the organism to the surgical trauma and continued reduced mobilisation. All patients included in this study had a period of physical inactivity because of the failed TKA. In addition 10 patients had a period of immobilisation of the affected limb in relation with stage one (spacer status) of the two-stage revision because of infection. These circumstances in combination with the cause of knee prosthesis failure (e.g. infection, wear etc.) and previous surgery have been increasing bone resorption resulting in initial low BMD values prior to rTKA. Entering the study with low BMD values, could be an explanation for the fact that large decreases in BMD are absent due to the already depleted bone stock.

At 12 months of follow-up significant decreases in BMD were found in ROI 3, 4 and 5 in the NO TM Cone group. Significant changes in the TM Cone group were found in ROI 2, 3, 4, 5. These results imply, that bone resorption occur along the tibial stem. In the literature no published data from studies measuring BMD using DEXA after rTKA exists, however experimental strain studies have been published. Completo et al. (2008) performed an experimental quantification of strain shielding in the proximal synthetic tibia following rTKA. They tested the use of a revision tibial component with cemented (proximal and distal cementation) stem (13 mm x 60mm) and press-fit (proximal cementation) stem (14 mm x 115 mm) of the proximal tibia. They found that the cemented stem induced a pronounced stress shielding effect of the proximal tibia close to the base plate of the tibial component, while the press-fit stem showed a minor effect of strain shielding along the stem. Both the cemented and press-fit stems transferred load to the bone at the tip of the stem. We believe that the results of the experimental stain study of the press-fit stem model are in god agreement with the bone remodelling pattern found in the present study with a moderate bone loss in ROI along the stems, but not of the bone at the tip of the stem. The significant decrease in BMD of the most proximal ROI in the medial tibial condyle seen only in the TM Cone group could be the result of a bone remodeling pattern as described for a cemented stem, but also the poor precision of the small proximal ROI in the TM Cone group may play a role.

This is the first published study on BMD changes after rTKA. We have compared rTKA with or without the use of TM Cone. The bone remodelling pattern was almost the same in the two groups and no significant difference in changes in BMD between the groups was found. The Bone remodelling pattern is probably due to the strain forces along the stem. Further investigation with a

longer period of follow-up will reveal if the overall decrease continues or changes in another direction.

Study 3

The clinical outcome of the present study after one year of follow-up are comparable with other studies on rTKA with considerable bone loss, where bone loss at the proximal tibia and/or femur has been reconstructed with stemmed femoral implants and impaction bone grafting (51;64) with or without metal augments (5). We found at 6 months of follow-up a significant increase in BMD of 3.5 % - 6 % in all ROI along the stem. However, after 1 year the increase (4%) in BMD was only significant in ROI 4. In ROI 5 above the stem no significant changes in BMD was observed.

To our knowledge there exists no published studies on BMD changes at the distal femur after rTKA. Existing knowledge comes from finite element studies on stemmed femoral implants and from studies evaluating the changes in BMD around the femoral component without stem after TKA.

In a finite element study Van Lenthe et al. (65) studied bone loss and remodelling patterns of 4 femoral components; two primary TKA and two stemmed revision prostheses with stem diameter of respectively 18 mm and 12 mm. They found that the revision prostheses tend to cause more bone loss than the primary implants, especially in the distal regions. They also found that prostheses with a thick press- fit stem comparable to the implants in the present study would be expected to lead to an increased bone loss of the most distal femur due to increased stress shielding. However, in the ROI proximally along the stem comparable to the ROI used in the present study they found stresses and strains slightly higher than in the femur without TKA or rTKA, and thus predicted minimal increase in BMD in most proximal ROI.

Our results, in this present study, are consistent with the findings made by Van Lenthe et al. (65) We believe that the increase in BMD along the proximal parts of the femur stem is caused by an increase in strain created by altered mechanical load. This remodeling of the periprostetic bone is well known and a result of Wolff´s law (66); the bone remodel and model to adapt to altered mechanical loads (the adaptive bone remodeling). The adaptive bone remodeling are quantified and described after THA and TKA in many other studies.

Prospective studies on BMD changes after THA reports a tendency of decrease in BMD during the first year after surgery. The decreases are greatest in the proximal ROI´s (calcar region), unrelated

to the method of fixation and ranges from 11.5 % - 28 %. The decrease in BMD diminishes distally to the tip of the stem (67-72) or show small gain in BMD (73-75).

Studies on BMD changes at the distal femur after TKA, reports decreases in BMD ranging from 2.6 % to 36 % at two years of follow-up (30;34;35;76). The bone loss is typically located behind the anterior flange of the femoral implant and claimed to be caused by stress shielding. The ROI behind the anterior flange is located at the distal part of the femur, whereas the ROI´s in this present study are located at the more proximal parts of distal femoral shaft. Even though most studies on changes in BMD after TKA have shown loss of bone mineral with time (30;34;76), Petersen et al. (32) have previously reported a significant increase (6,1%) in BMD at the lateral tibia condyle 2 years after TKA with uncemented tibial components without hydroxyapatite. Initial temporary increases in BMD within the first operative year after TKA have been seen in another study (26). The patients participating in our study have all suffered from failed TKA´s, that resulted in periods of reduced mobilization or long-term immobilization e.g. in patients undergoing two-stage revision surgery. Given the fact that immobilization and reduced mobility suppresses the BMD (77), the increase in BMD seen in this study is probably the result of increased mobility and load of the extremity after implantation of a well-functioning rTKA, thus stimulating the femoral bone to bone formation.

Conclusion

Study 1

Knee score and function score improved in both groups, but no significant changes between the groups were found. At 1 year follow-up, the tibial implants from both groups had migrated in the same direction except for the translation along the vertical axis. The tibial implants with TM Cone showed a tendency towards less migration compared to the NO TM Cone group. Subsidence was found in the NO TM Cone group at 12 months of follow-up compared to a marginal lift off in the TM Cone group. No statistically significant differences between the patterns of migration were found. MTPM in both groups seemed to stabilize between 6 months and 1 year, but the NO TM Cone group on a higher level at 12 months of follow-up (2,28 mm versus 0,77 mm). The difference was not statistically significant. We believe that this migration pattern is due to the rigid construct created by proximal cementation of the tibial implant into the press-fitted TM Cone. The cement is equally distributed in the TM Cone creating a rigid construct in relation to the tibial implant compared with the often depleted cancellous bone in the proximal tibia in rTKA patients. The rigid construct prevents the stemmed tibial implant to subside, which could be beneficial for bone ingrowths and fixation of the prosthesis

However, these preliminary RSA results shows no significant difference in migration pattern between the groups. The tibial implants with TM Cone showed a tendency towards less migration compared to the NO TM Cone group.

Study 2.

Knee score and function score improved in both groups, but no significant changes between the groups were found. The bone remodelling pattern was almost the same in the two groups after one year. Initial low BMD values, could explain the fact that large decreases in BMD are absent due to the already depleted bone stock. At 12 months of follow-up significant decreases in BMD were found in ROI 3, 4 and 5 in the NO TMC group. Significant changes in the TM Cone group were found in ROI 2, 3, 4, 5. These results imply, that bone resorption occur along the tibial stem. The significant decrease in BMD of the most proximal ROI in the medial tibial condyle seen only in the TM Cone group could be the result of a bone remodeling pattern as described for a cemented stem, but also the poor precision of the small proximal ROI in the TM Cone group may play a role.

The bone remodelling pattern was almost the same in the two groups. No significant difference in changes in BMD between the groups was found. The Bone remodelling pattern is probably due to the strain forces along the stem (stress shielding).

Study 3

Knee- and function scores improved significantly (P=0.005) from the preoperative values to 1 year of follow-up. In ROI 1 - 4 a significant increase in BMD (3.5-6.0%) after 6 months was seen. This increase only remained significant in ROI4 (4.0%, p = 0.01) at 1 year of follow-up.
The increase in BMD is probably the result of increased mobility and load of the extremity after implantation of a well-functioning rTKA. We believe that the increase in BMD along the proximal parts of the femur stem is caused by an increase in strain created by altered mechanical load according to Wolff´s law.

In summary

The results from study 1 and 2 shows that the use of TM Cone in rTKA gives the same short term clinical results and a tendency (not significant) of less migration of the tibial implant which could be beneficial for long term fixation of the implant construct.

Future research

This PhD-thesis is based on the results of the data collected after 1 year of follow-up. However, all patients included in study 1, 2 and 3 are followed for at least 2 years. Further investigation are therefore warranted. Of special interest is the tibial migration pattern in the two groups. We still don´t know if tibial rTKA prosthesis that shows continuous migration over 0.2 mm between the first and second year after rTKA are at risk of future aseptic loosening. Long term follow-up of 5 to 10 years could give us the crucial data of the feasibility of migration assessed by RSA for prediction of long term survival of the prosthesis. We are also interested in finding out, if there exists any link between the migration pattern of the tibial component and the bone remodelling pattern of the proximal tibia.

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