OPTIMIZING REVISION TOTAL KNEE ARTHROPLASTY: AN IN-DEPTH ANALYSIS OF 3D PLANNING PREDICTION AND PATIENT-SPECIFIC INSTRUMENTS FOR REVISION SURGERY

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12 Jan 2024

Thesis in partial fulfilment of the requirements for the joint degree of Master of Science in

Technical Medicine

Leiden University ; Delft University of Technology ; Erasmus University Rotterdam

Master thesis project (TM30004 ; 35 ECTS)

Dept. of Biomechanical Engineering, TUDELFT
14-02-2023 TM30004 – 26-01-2024 TM30004

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Abstract

In today's medicine, 3D planning and PSI are not commonly used in revision TKA surgery and little is known about the accuracy and implementation of these techniques in revision TKA. Therefore, the question arises, what are the potential benefits of 3D planning and PSI in revision surgery? The goal of this thesis is to explore the potential benefits of 3D planning and PSI in revision surgery. To achieve this, a retrospective study and a prospective study are performed, and a first design of a 3D printed PSI is created. For both retrospective and prospective study, 3D plannings are made of patients undergoing revision TKA, comparing the pre-operative planning with the post-operative results based on size prediction, augmentation prediction and component placement analysis. The results of the studies conducted in this research align closely with each other, providing similar results for size and augmentation prediction and component placement analysis. All in all, these studies indicated consistency and reliability of the 3D prediction in different scenarios, affirming the potential of 3D planning in revision TKA surgery. Additionally, the first design for a PSI, a 3D-printed guide, is constructed. This design incorporates several important landmarks for component placement during revision TKA, increasing the outcome of these surgeries, especially if landmarks are missing or unidentifiable during surgery. Together 3D planning and PSI have a bright future in revision surgery, however, future research needs to be conducted to implement 3D planning and PSI in modern-day healthcare.

1. Introduction

Total knee arthroplasty (TKA) has established itself as a cost-effective and highly successful procedure, providing an enhanced quality of life for patients with advanced osteoarthritis[1,2] With implant survivorship rates surpassing 90% over 10 to 15 years, TKA has demonstrated its efficacy in addressing the effects of osteoarthritis.[3-5] However, the prevalence of TKA surgeries has significantly increased in recent decades, a trend expected to continue as the population ages.[6-8] Despite the overall success and advancements in surgical techniques, the incidence of revision TKA (R-TKA) continues to rise globally. The increasing demand for primary TKA inherently leads to a proportional increase in revision procedures.[9,10] The most common cause for revision in the early stages is considered to be infection, whereas, for late revision, aseptic loosening appears to be the most common cause for revision.[8-12] Besides these most common causes for revision, other factors are instability, stiffness, periprosthetic fractures, osteolysis, and malalignment.[8-12] Compared to primary TKA, revision TKA is generally more complex, with challenges such as joint line restoration, implant size selection, and positioning of the implant, stems, and augmentations, leading to a longer operation time, more complications and re-revision rates are considerably higher.[12-14] Consequently, the success of the revision surgery is highly dependent on the surgeon's experience. In addition, the risk of re-revision increases in hospitals with a low volume of annual revision TKA surgeries.[12,13]

In recent years, new surgical techniques have been developed, aimed at enhancing prosthesis positioning, consequently, improving clinical and functional outcomes of revision TKA. Amongst these innovations, 3D planning combined with PSI has gained the most interest, providing a comprehensive, three-dimensional overview of the surgical site and translating this three-dimensional plan to the operating table with the PSI.[15-18] 3D planning and PSI represent an advanced computer-assisted surgical technique, using pre-operative imaging techniques, typically Computed Tomography (CT) scans or Magnetic Resonance Imaging (MRI) and long-leg X-rays of the lower limb of the patient. Detailed 3D models of the patient are constructed from these imaging modalities, wherein anatomical landmarks are identified.[19] Subsequently, key parameters are determined, including alignment, bony resections, implant position, rotation, and size before surgery is performed.[20] After a surgeon confirms the pre-operative plan, engineers design the positioning templates customized to the patient's native anatomy. These templates can guide the surgeon during surgery while still using a standard cutting block.[20] Initially introduced as a less-invasive alternative for primary TKA, the scope of 3D planning and PSI has expanded, demonstrating applicability in complex cases of primary TKA[21-23]. However, literature on 3D planning and PSI in revision surgery remains limited, primarily focusing on revision from unicompartmental knee arthroplasty (UKA) to TKA.[24] The lack of published experiences in revision TKA with 3D planning and PSI emphasizes the need for further exploration and in-depth analysis of the potential benefits and limitations of this method in revision surgery.

To approach this, first, a systematic review was performed to assemble information about 3D planning and PSI in TKA and revision TKA. The systematic review aimed to gather existing evidence, identify relevant information, and assess the overall literature on the use and potential benefits and downfalls of 3D planning and PSI in TKA surgery. A systematic search was conducted across major scientific databases, including PubMed, MEDLINE, and Embase, to identify relevant articles published up to the date of the review. The search strategy included a combination of keywords related to PSI, revision TKA, and 3D planning. The generated articles were screened and included in the subsequent data analysis if they centred on 3D planning and/or PSI in TKA surgery. The identified studies were screened for relevance and quality, with a specific focus on pre and post-operative results using 3D planning and PSI. While some variations were noted in femoral and tibial component alignment using 3D planning, few of the important outcome measurements proved to be significantly different, indicating no difference between 3D planning and PSI, and conventional intervention (CI). Yet, in some cases for TKA surgery, 3D planning and PSI are preferred above CI. In particular, when anatomical landmarks are missing or unidentifiable, 3D planning and PSI can provide valuable insights into the placement of the implant. This would especially be the case during revision surgery, where both factors are often present. 3D planning plays an important role in accurately predicting outcomes of TKA surgery and can consistently acquire high accuracy in replicating pre-operative plans, making it a valuable tool for revision TKA as well. More importantly, the systematic review provided important outcome measurements, such as implant size selection and implant placement, including several important angles like; the Femoral Flexion Angle (FFA), Mechanical Femoral Angle (MFA), anatomical Lateral Distal Femoral Angle (aLDFA), Posterior Tibial Slope (PTS) and mechanical Medial Proximal Tibial Angle (mMPTA). In conclusion, the systematic review emphasizes the significance of 3D planning, while also highlighting the potential benefits of PSI in revision TKA surgery. The complete systematic review can be found in Appendix A.

Given the limitations associated with standard revision TKA, for example, missing or unidentifiable landmarks, 3D planning, and PSI can increase the outcome of revision surgery. However, in today’s medicine, 3D planning and PSI are not commonly used in revision TKA surgery and little is known about the accuracy and implementation of these techniques in revision TKA. Therefore, the question arises, what are the potential benefits of 3D planning and PSI in revision surgery? The goal of this thesis is to explore these potential benefits of 3D planning and PSI in revision surgery. Introducing the application of 3D planning and PSI for revision TKA, in the Department of Orthopedics in the Erasmus MC, providing a method for the 3D planning of patients. To achieve this, the thesis is divided into three parts, a retrospective study, a prospective study, and a first design of a 3D printed PSI. The retrospective study focusses on the gathered operative results of patients who already underwent revision TKA, creating a 3D planning in retrospect. The prospective focusses on gathering results of patients undergoing revision TKA surgery, creating a 3D planning pre-operatively. The 3D planning provides valuable information on joint line restoration, implant size selection, and positioning of the implant, stems, and augmentations. Lastly, a first design for a 3D printed PSI is made, implementing the gathered knowledge learned in this study.

2. Method

The goal of this thesis is to explore the potential benefits of 3D planning and PSI in revision surgery. Introducing the application of 3D planning and PSI for revision TKA, in the Department of Orthopedics in the Erasmus MC, providing a method for the 3D planning of patients. This method contains a developed guide for the 3D planning of revision surgery. The validation of this 3D planning method shall be constructed employing two different investigations, a retrospective study and a prospective study, also known as a mixed methods approach.[25] A mixed-methods approach, combines two methods, leveraging the strengths of both the retrospective and prospective study designs, to explore the potential benefits and implementation of 3D planning for revision surgery. The retrospective study is conducted with minimal risk to the patient population while exploring valuable information and providing crucial insights into the effectiveness and accuracy of 3D planning. In addition, the retrospective study also identifies potential benefits and drawbacks associated with 3D planning of revision surgery.[26] Subsequently, a prospective study is conducted to validate the hypothesis in real-time, while also gaining feedback on the practical implementation of the 3D planning method. In addition, the gained information from the retrospective study will be implemented in the prospective part of the study, improving the outcome of the implemented 3D planning.[27,28]

During the retrospective study, a 3D planning is made of patients who already underwent revision TKA in the Erasmus MC. These 3D plannings are then compared to the results of the real surgery, to verify if a 3D planning can accurately predict the outcome of a revision TKA. During the prospective study, a 3D planning is constructed for patients that are planned to have a revision TKA in the Erasmus MC. This planning can assist the surgeon in revision surgery, to improve the outcome of the surgery, while also decreasing operation time and malpositioning[29,30]. Combining these results will lead to a recommendation for future 3D planning in revision surgery. In addition, a design is made for a 3D-printed surgical guide. The guide will not be used as a cutting guide, but as a reference tool, which the surgeon can consult during surgery if anatomical landmarks are missing. This will assist the surgeon in accurately following the 3D planning, which consequently will lead to an improved outcome of the revision TKA.[31,32]

The patient population suited for this investigation in revision TKA surgery consists of both patients undergoing R-TKA surgery this year and patients who already underwent R-TKA surgery in the past years in the Erasmus MC. Both patient populations provide valuable information in different aspects of this study and are therefore included in this study.
For the prospective part of this investigation, the patient population consists of patients who underwent revision surgery in the past years in the Erasmus MC. In the selection of these patients, patients who did not have a CT or MRI scan before revision surgery were excluded. In addition, if no long-leg X-ray was made before surgery, these patients were also excluded from this study. All patients who underwent revision surgery in the past year and have a long-leg X-ray and CT or MRI scan available are included in this review.
For the retrospective part of this investigation, the patient population consists of patients that are planned to undergo revision surgery at the Erasmus MC this year (2023). The inclusion criteria for this patient population were identical to the prospective patient population: the patients must have a long-leg X-ray and a CT or MRI scan available. All patients who are

planned to have revision TKA surgery in 2023 and have a long-leg X-ray and CT or MRI scan available are included in this investigation.

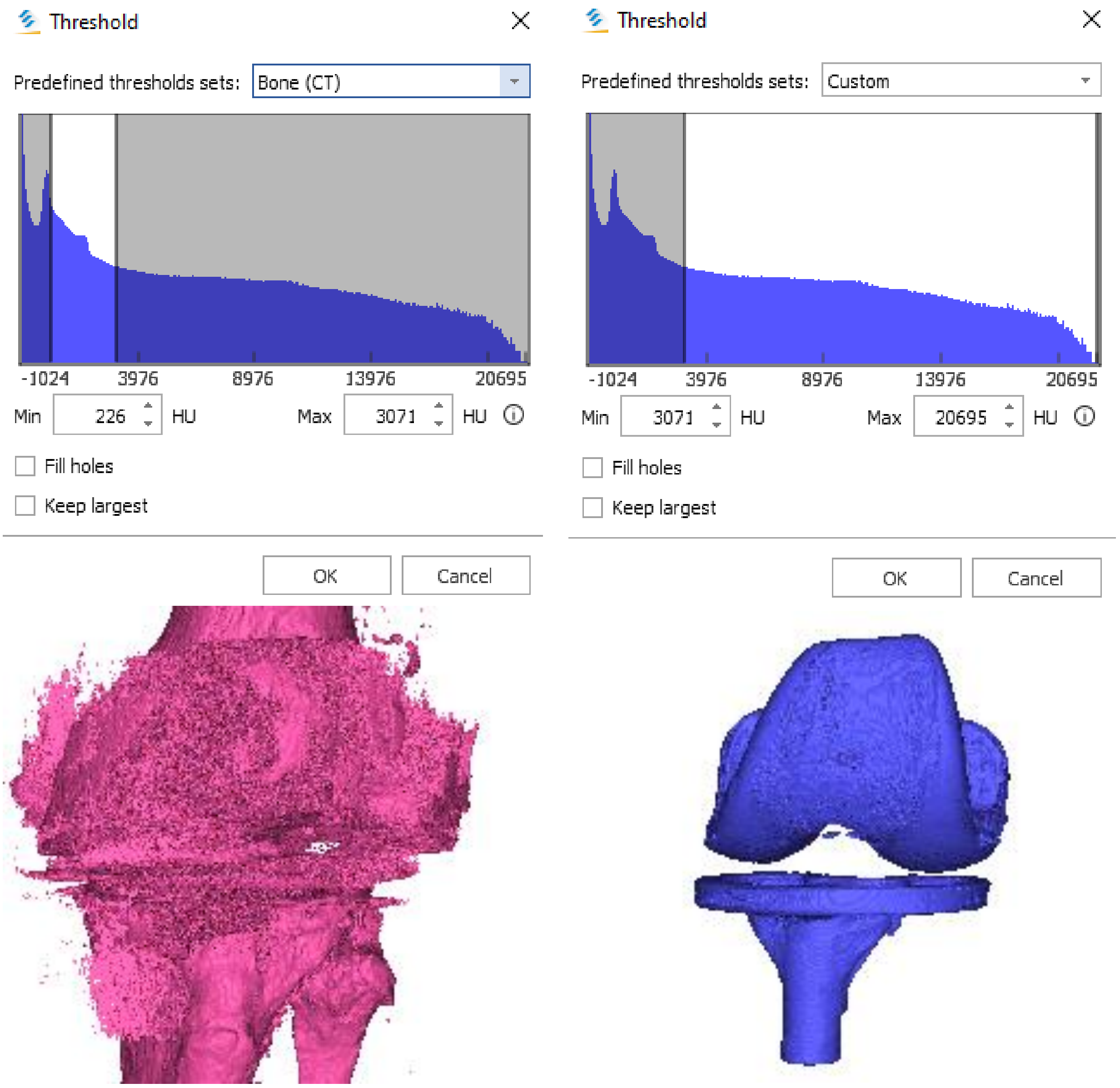
To gather data on the different patient populations, a database must be formed, including all the patients who underwent revision TKA in the last year and all the patients that are planned to undergo revision TKA this year. However, no such database existed at the Department of Orthopedics in the Erasmus MC. Therefore, the Intergraal Capaciteitsmanagement of the Erasmus MC was called for help. This department plays an important role in the capacity of the operation rooms planning all surgeries and guaranteeing a certain flow within the hospital. Both a database of the revision TKA surgeries of the last year as well as a database of the planned revision TKA surgeries this year were requested from the ICM department. In total, the databases contained more than 50 patients that could be included in this investigation. However, not all patients had both a long-leg X-ray and a CT or MRI scan available for this research. An X-ray and CT or MRI scan are proven to be extremely helpful in establishing a diagnosis and assisting a surgeon in making a valid plan for TKA surgery.[33] The long-leg X-ray is a valid tool, still used in today’s healthcare, to outline the placement of the prosthesis in the patient's knee. In addition, a CT or MRI scan is necessary to make a 3D image of the patient's leg. Both radiology images are therefore essential in this investigation. Therefore, all patients in the database were scanned and excluded from this study if either one of the radiology images was missing or unavailable. If both radiology images were available for this investigation, the patients were included, and placed in either the retrospective or prospective study based on time of surgery. In total, the database for the retrospective investigation contained ten participants, while the database for the prospective investigation contained 15 participants.

The next step is gathering all the required radiology images, long leg X-ray, and CT or MRI scan data, from all the patients in the two patient populations. All the radiology images of all the patients treated in the Erasmus MC are gathered in HiX, an Electronic Medical Record (EMR). This electronic medical record can be consulted to find all the patient information needed for this investigation. In HiX, the most recent long-leg X-ray and CT or MRI scan is viewed and validated. The long-leg X-ray consists of a few images of the entire leg of the patient, which are later used to validate the mechanical and anatomical axis of the 3D planning. The CT or MRI scans consist of multiple different images, series, and planes. However, not all these images and series are required for this study. Only the coronal images of the CT or MRI scans are needed for this investigation, from these images all the other planes can be recreated. An important aspect of the validation of the CT or MRI scans is the number of metal artefacts in the images. Since these patients all undergo or underwent revision surgery, a knee prosthesis is already present in the scans, causing a lot of scatter due to the metal artefacts. Ultimately, the coronal image with the least amount of scattering due to metal artefacts is selected and added to the database.
To use the selected CT and MRI scans, the data must be extracted from the HiX database. During the extraction process, the data from the CT and MRI scans is anonymized. The anonymization process is needed, because data derived from patient scans, should not be traceable to the patient. The anonymized CT and MRI data is then extracted to a hard drive only accessible by the researcher, via password. All to protect the patients' security according to the new General Data Protection Regulation (GDPR) law.[34]

In addition to the derived data from the CT and MRI scans, STL files of the different parts of the knee prosthesis are needed to make a 3D plan of the placement of the prosthesis. An STL file describes a raw, unstructured triangulated surface by the unit normal and vertices of the triangles using a three-dimensional Cartesian coordinate system.[35] These STL files are stored in a database managed by Stryker, the manufacturer of the parts. In consultation with Stryker, the different parts of the prosthesis needed for making a 3D planning are transferred to the hard drive managed by the investigators. These parts consist of: Femur component, Tibia component, distal Femur augmentations (medial and lateral), posterior Femur augmentations (medial and lateral) and Tibial augmentations (medial and lateral). With these STL files, a 3D plan of the placement of all the important components of a knee prosthesis can be accurately constructed.

A 3D planning software is needed to make valid planning for revision TKA. The software used during this investigation is Materialise Mimics and 3-Matic. Materialise is a medical 3D image-based engineering software that offers tools in various steps, from image to 3D models and enables scaling from R&D to high-volume clinical operation. Important features of Materialise are effective segmentation of anatomy, analyzing anatomy features, 3D plan procedure before surgery and automatization of the workflow.[36] The segmentation and analysis of anatomical landmarks and 3D planning of procedures are vital features in this study.
There are two different applications of Materialise 3D planning software, Mimics and 3-Matic. Materialise Mimics covers the segmentation and analysis of anatomical landmarks. Mimics is a 3D software in which multiple CT or MRI scans can be imported. These imported 3D images can be used to construct a 3D image of the patient using the segmentation of these images. The segmented 3D images can then be used for the 3D planning of the components. This is done in 3-Matic, which covers the procedure planning of the Materialise software. 3-Matic provides an environment in which multiple STL files can be imported and used for placement planning of different components in a 3-dimensional space. In addition, 3-Matic enables clean-up of rough data and optimisation of model and scanned data by making design modifications, which enhances the models for 3D printing and planning.[37]

When all the CT data is gathered, anonymized and extracted, the data can be imported into Mimics, where the data segmentation is performed. Data segmentation is an important step in providing a 3D image of the patients' scans, which is necessary to make a 3D planning. The first step in the segmentation of the CT data is selecting the right threshold of Houndsfield Units (HU), as every CT scan is different and will consist of a wide variation of HU. In this case, the standard threshold for Bone (CT) is used, 226 to 3071 HU. This is provided by Mimics as a standard threshold and is accurate in most of the cases. If the segmentation is not deemed accurate, the threshold is manually customized until the segmentation is considered to be suitable for the next step. Additionally, another threshold is set, based on the previous bone set. This set contains all the HU above the set 3071 HU. This results in a threshold containing all the HU above the bone threshold, leading to a segmentation of the prosthesis, as the prosthesis always has a higher HU than bone. This is visualized in Image I.



Threshold

Predefined thresholds sets: Bone (CT)

Min 226 HU Max 3071 HU

☐ Fill holes

☐ Keep largest

Threshold

Predefined thresholds sets: Custom

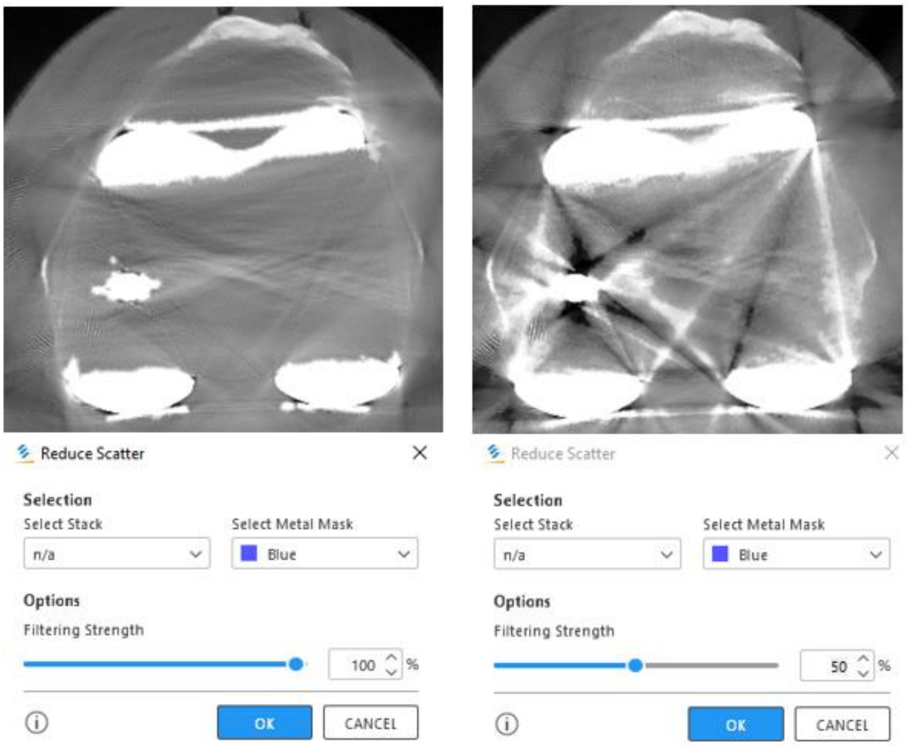
Min 3071 HU Max 20695 HU

☐ Fill holes

☐ Keep largest

Image I: a) Segmentation tab with the given standard values for bone, ranging from 226 HU to 3071 HU. b) Segmentation tab with the threshold set for all the HU above 3071 HU, resulting in the segmentation of the prosthesis. c) Visualization of the results of the standard bone segmentation. d) Results of the segmentation with the threshold set to all the values above 3071 HU.

After selecting the right threshold, the 3D image constructed is evaluated based on noise and metal artefacts. Most of the time, the 3D image contains a lot of noise or metal artefacts. These artefacts are present because of the already implanted knee prosthesis, which is made of metal. Metal can cause severe artefacts and noise in a CT and MRI image and can obstruct a clear view of the region of interest. Therefore the next step performed is called metal artefact reduction. This metal artefact reduction method is supplied by Mimics and can be selected in the *Menu – Image – Scatter Reduction*. This program provides an automatic Scatter Reduction filter, which can be adjusted by the magnitude of the metal artefacts. This filter can be adjusted between 0% and 100%. With the scatter reduction filter set to 100%, the image will be unreadable, since a lot of important bony structures are filtered out by the filter. However, with a low scatter reduction filter, almost nothing will happen and the image will be difficult to interpret. Therefore, a balance must be found between the scatter reduction and bony structures. Most of the time, a scatter reduction of 50% is sufficient.



Reduce Scatter

Selection

Select Stack: n/a

Select Metal Mask: Blue

Options

Filtering Strength: 100 %

Reduce Scatter

Selection

Select Stack: n/a

Select Metal Mask: Blue

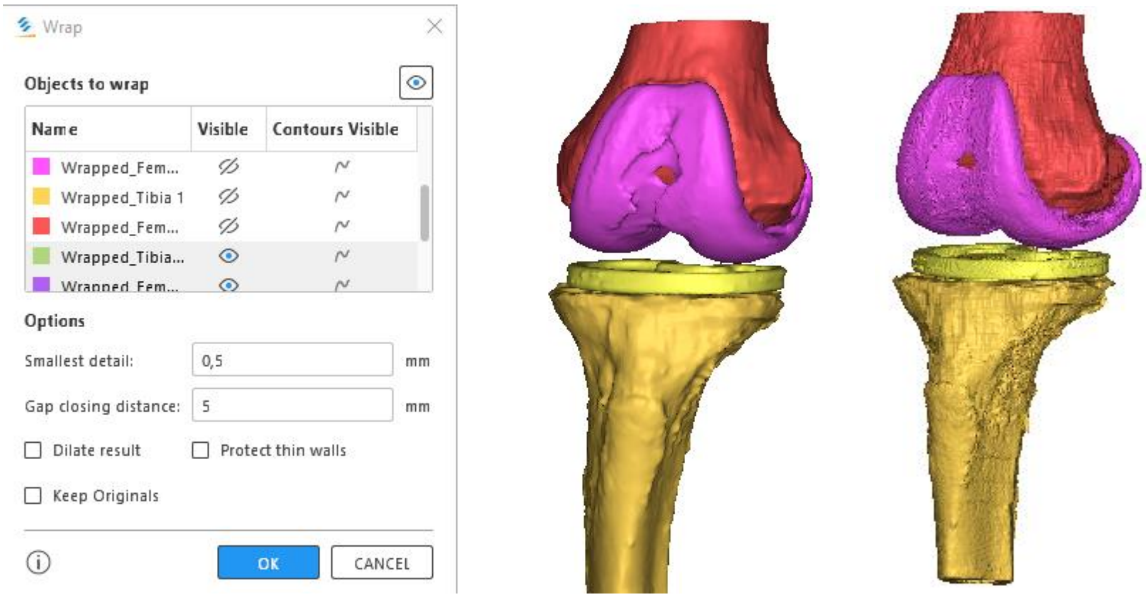
Options

Filtering Strength: 50 %

Image II: a) Image rendered with 100% scatter reduction, yielding an image almost unreadable due to the deleted important structures. b) Image rendered with 50% scatter reduction, leading to less scatter in the image, where the bony structures are still visible.

Different structures can be identified in the created 3D image. The different structures that are identifiable are: Femur, Tibia, Femur Component, Tibia Component and unaffected leg. The Femur and Tibia are used during the 3D planning as a reference for the patient's affected leg, while the two components are used as a reference for the placement of the old knee prosthesis. This reference can be used for the placement of the new components. The unaffected, or healthy leg can used as a guide for several calculations on the affected leg, such as medial condyle high calculation and surgical epicondylar axis prediction. These five different structures are all identified and labelled as different structures.

After the segmentation of the different structures, most of the time, these are filled with small holes and imperfections. These imperfections can make it difficult to identify anatomical landmarks. Therefore smoothing and wrapping procedures are released on the structures. Smoothing flattens the surface and gets rid of the sharp peaks on the surface of the 3D image. Wrapping is used to fill small holes on the surface of the structure as if a small layer is wrapped around the image. Both these procedures create a smoother surface, which more closely resembles the surface of the recreated surfaces. The smoothing method is used under Menu – Segmentation – Smoothing. For this method, no specific filters are used. The wrapping option is based under Menu – 3D Tools – Wrapping. Wrapping has two different parameters which can be varied, smallest detail and gap closing distance. The smallest detail refers to the new triangle size of the mesh after wrapping. The smallest detail is kept relatively small, to protect the detail in the image. The gap closing distance refers to the size of the holes that the wrap function will fill in. This distance is set higher than the smallest detail because larger holes in the bone need to be filled. Therefore for all the segmentation in this study, the smallest detail is set to 0.5mm and the gap closing distance to 5mm. This is based on the parameters given in Mimics Innovation Suite Training Guides[36] When the created structures are smoothed and wrapped they are exported from Mimics.



Wrap

Objects to wrap

Name	Visible	Contours Visible
Wrapped_Fem...		
Wrapped_Tibia 1		
Wrapped_Fem...		
Wrapped_Tibia...		
Wrapped_Fem...		

Options

Smallest detail: 0,5 mm

Gap closing distance: 5 mm

☐ Dilate result ☐ Protect thin walls

☐ Keep Originals

Image III: a) The wrapping tab facilitates the selection of various structures to be wrapped. The smallest detail is set to 0.5mm, while the gap closing distance is set to 5mm, leading to the image given in b. b) Image after wrapping. c) Image before wrapping, with large holes and sharp edges.

The created structures in Mimics are imported in 3-Matic for the placement planning of the new knee prosthesis components. For the 3D planning of a new patient, the femur and tibia bone, as well as the old femur and tibia component are imported into a new workspace. In this workspace, the STL files of the new components are imported as well. These components are the new parts that are placed in the 3D image of the patient, creating a new 3D prediction of the placement of the components. As the STL files are imported into the workspace, each component has a different orientation in the coordinate system. This sometimes creates a distance between the old component and the newly important component. For this reason, translation and rotation play an important role in the placement of the new components on the 3D image of the patient's bone. Translation is a rigid transformation in which the location of the object is changed, but not its size, shape or orientation. The translation is always performed over one of the axes, X, Y or Z-axis.[38] Rotation is a rigid transformation in which the location of the object is rotated around a fixed point or axis, but its size and shape are not changed. Rotation is always performed over one of the axes, X, Y or Z-axis.[38] With translation and rotation, the placement of the component can be changed to the desired location. In addition, there are two methods built into Mimics, which can automatically translate and rotate, N-point Registration and Global Registration. N-point Registration is a registration method, that requires the input of several corresponding points across a structure. For this method, the Iterative Closest Point (ICP) registration is used. For this registration, a difference is measured between two predefined corresponding points. Then an iteration is performed, minimizing the distance between these two points. When the iteration finds the minimum distance for all the points after several iterations, the registration is complete. The results for N-point Registration are visualized in image IV.

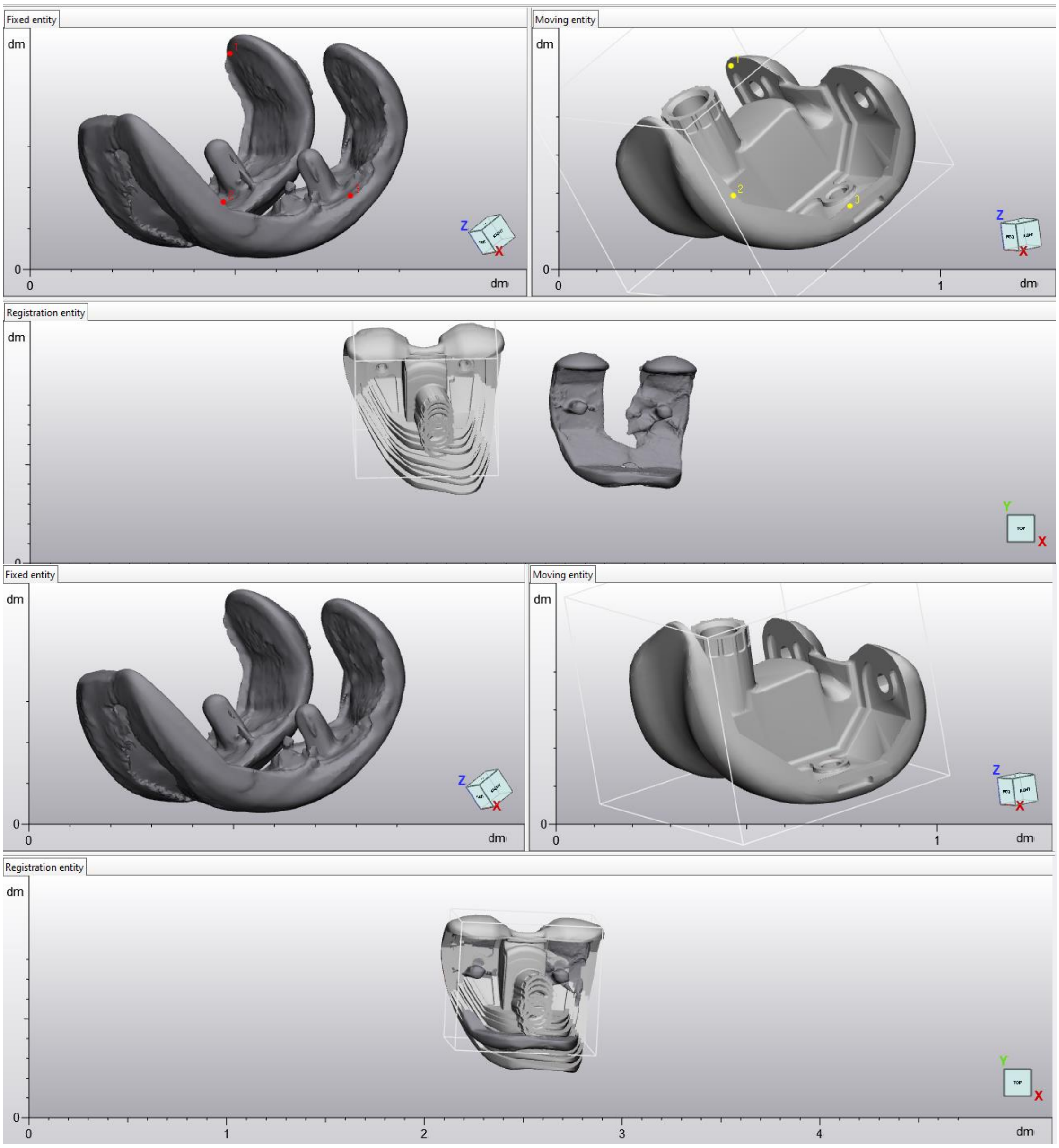


Image IV: a) N-point Registration method, where three points are both located on the fixed image on the left and the moving image on the right. b) After registration the points the images are overlayed.

After N-point Registration, the components are placed around the same point as the old component, however, the registration can be optimized. This is done by performing a Global Registration on the different components. Global Registration, an average distance error is calculated and in every iteration, the component is repositioned. If the average distance error decreases, the new components are repositioned better compared to the old component. If the average distance error increases, the new components are repositioned worse compared to the old component. If the average distance error cannot be improved, the ideal position is found. Based on these positions the size of the components is compared to the old component. There are several sizes of the femoral and tibial components. The Femur and Tibia components can vary from size 1 to size 8 for both the left and right knee. For the global registration, all sizes are translated to the orientation of the old component. The old component is then used as a reference for the new component, as both components are almost always approximately the same size. Based on the previous size, a selection of possible sizes is made, varying from one size smaller and one size bigger.

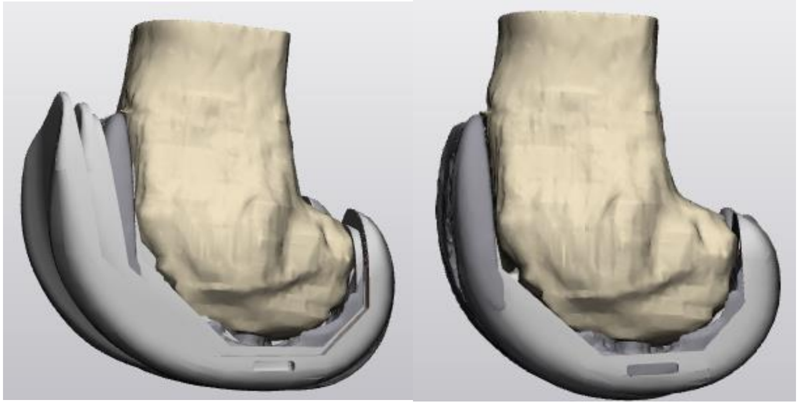


Image V: After N-point Registration, not all components are aligned perfectly. After Global Registration, the components align more precisely. The component most similar to the old component, is registered almost perfectly, indicating this size of the component is most likely to be ideal.

The selection of three femur and three tibia components is then used to determine the correct size of the new component. For the tibia component, the most important factor for the prediction of the size is overhang of the component. This problem can arise if the chosen tibia component is too big for the tibial bone of the patient. Both medial and lateral overhang need to be avoided, however, medial overhang is deemed more important, as the soft tissue on the medial side is closer to the tibial bone.[39-41] This can cause the soft tissue to be damaged by the medial overhang. The biggest size with no medial and lateral overhang is considered to be the proper size for this specific patient. An example of medial overhang is given in Image VI.

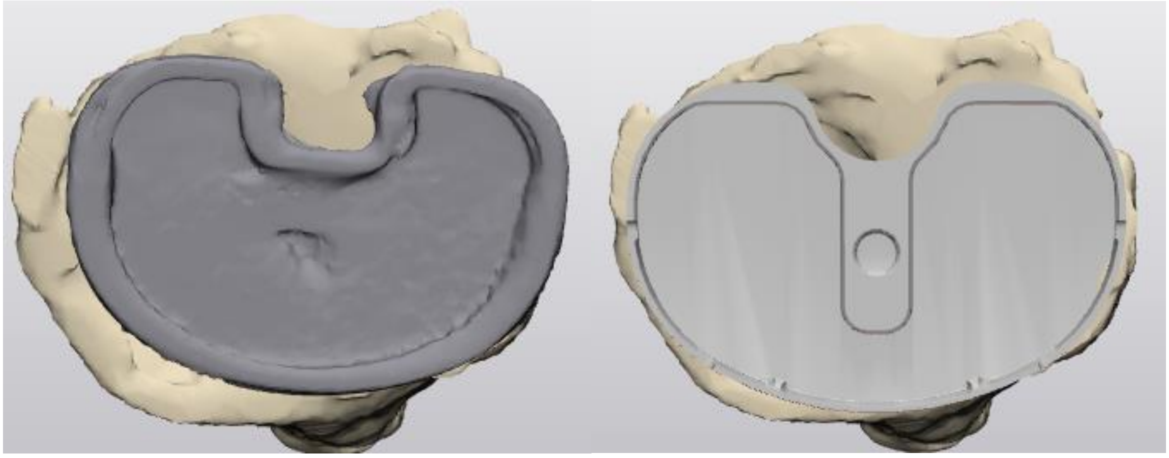


Image VI: The primary tibia component is loosened, and shifted to the medial side. Looking at the components from above, it is seen that the old component has a medial overhang. This is corrected in the placement of the new component, with neither medial nor lateral overhang.

After determining the tibia component size, the femur size can be determined. There is a relationship between the size of the tibia and the femur component. According to a defined rule, the femur component size must align with the prescribed tibia size. For instance, if the prescribed tibia size is 6, the permissible range for the femur component spans from 5 to 7. Based on this rule and the predefined tibial component size, an accurate prediction can be made of the desired femur component size. Additionally, the bone defects are taken into consideration. Due to the bone irregularities, adjustments may be necessary to overcome these bone defects, leading to a different size.[42]

Following the prediction of the component size, the placement and positioning of the component is the next important step. First, the placement of the tibia component is determined, and subsequently the placement of the femur component. This is performed in the same sequence as a surgery procedure for revision TKA, to follow the same steps. To determine the correct position of the component, firstly, the axis needs to be determined. The mechanical and anatomical axis of the patient's knee can be calculated based on the long-leg X-ray. The mechanical axis of the knee is a line extending from the centre of the femoral head to the centre of the ankle and in normal conditions it crosses the centre of the knee joint.[43] The anatomical axis is a line placed from the centre of the knee through the shaft of the femur and the shaft of the tibia. The anatomical axis of the femur is, normally, 6° from the mechanical axis while the anatomical axis of the tibia is in line with the mechanical axis. These axes provide the basis on which the placement of the components is determined.[44]

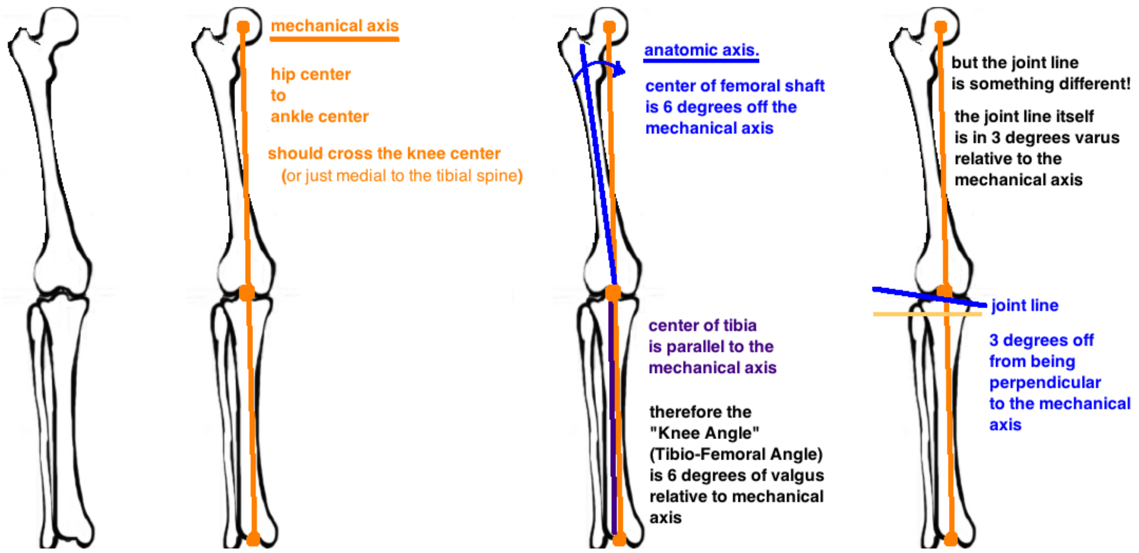


Image VII. a) Long-leg X-ray faced from AP, where the mechanical axis is visualized by a line going from center of the hip, through center of the knee to the center of the ankle. b) Long-leg X-ray AP, where the anatomical axis is visualized, by making a 6 degree angle between the mechanical axis.

The mechanical and anatomical axis can be determined by the long-leg X-ray of the patient, as the CT scan lacks the information to determine these axes. However, to translate the long-leg X-ray axis to the axis of the 3D image in 3-Matic, these images need to be superimposed, by putting a picture of the long-leg X-ray on top of a picture of the created 3D image. These images are then adjusted until the images overlay perfectly. The 3D image axis is adjusted based on the superimpose, as a result of which the axis of the long-leg X-ray and 3D image are now identical.

Based on this, the mechanical axis and anatomical axis can be calculated in the 3D image. With the mechanical axis determined, the joint line can be calculated as well. The joint line of the tibia is a line perpendicular to the mechanical axis, on the height of the knee joint, creating a 90˚ angle between the mechanical axis and joint line, correcting the mMTPA (mechanical Medial Tibia Proximal Angle) for any previous varus or valgus tibia angles. The height of the joint line is based on the previously placed tibia component, as this is placed in the correct place during primary TKA. Therefore the new tibia component is placed in the same place, otherwise, the flexion and extension gap will increase, leading to a displacement of the joint line. The flexion gap is the space between the posterior coronal cut on the distal femur &

transverse cut on the proximal tibia, while the knee is in flexion. The extension gap the is space between the transverse cut on the distal femur & the transverse proximal tibial cut while the knee is in complete extension.[45-47] Both these gaps contain the transverse cut of the proximal tibia, therefore accurate restoration of joint line height in TKA has been shown to be an important factor in post-operative range of movement and function. [48] A deviation of more than 2mm in joint line height has also been shown to have a negative impact on post-operative range of movement [1,4,5,24,25]. [48].

In addition, the posterior tibial slope (PTS) needs to be included in the 3D planning. The posterior tibial slope is the slope of the tibial plateau, from anterior to posterior relative to its longitudinal axis. The posterior tibial slope affects knee joint stability, ACL ligament and the flexion gap, which are associated with a wide range of knee motions.[49,50] The optimal slope for the tibial plateau is considered to be between 3° to 9° for primary TKA, however with revision TKA, the posterior tibial slope is placed at 0° slope.[51]

Lastly, the rotation of the tibia component needs to be applied to the planning. Two methods can be applied to calculate the correct position of the rotation. The first method is rotating the component so that the middle of the component is aligned with the medial third of the tibial tuberosity. Referencing the tibial rotation on a line from the medial third of the tibial tuberosity to the centre of the tibial tray resulted in a better tibial rotational alignment than using the medial border of the tibial tubercle as a landmark.[52] The second method is internally rotating the centre of the tibia component 18˚ from the middle of the tuberosity.[53] This will lead to the same internal rotation as the first method. The middle of the tuberosity is more easily recognizable than the medial third of the tuberosity, therefore the second method is used as a reference to determine the tibial rotation during this investigation.

The tibia component is placed in the correct position based on the previously noted angles. However, proximal tibial bone deficiencies are not an uncommon appearance in revision TKA surgery. For these cases, tibial augmentation is introduced. Augmentations are little metal blocks or wedges, that can be placed on the components, covering a small bone deficit.[54] These augmentations are either 5mm or 10mm and can be placed medial or lateral on the tibia component. To see if any augmentations are needed, the bone stock on which the tibia component will rest is visualized by the 3D planning. If enough bone stock is present, no augmentations are needed. However, if the bone stock is insufficient, augmentations will be placed below the component until the bone deficiency is completely covered.[55] Afterwards, the 3D planning of the tibia component is finished and the planning of the femur component can start.

After determining the position and placement of the tibia component, the positioning and placement of the femur component is next. Some of the steps needed for the positioning of the femur component have already been performed during the positioning of the tibia component. Just like the tibia component the mechanical and anatomical axis need to be determined. However, as previously mentioned, the mechanical and anatomical axes are not identical, as was the case with the tibia. The anatomical axis of the femur is, normally, 6° from the mechanical axis.[44] The joint line of the femur is a line perpendicular to the mechanical axis, on the height of the knee joint, creating a 90˚ angle between the mechanical axis and joint line, correcting the mLDFA (mechanical Lateral Distal Femoral Angle) for any previous varus or valgus femur angles.[56] The femoral joint line is positioned at the same height as the primary femur component, as this is placed in the correct place during primary TKA and therefore corrects the flexion and extension gap in the placement of the primary TKA. However, in addition, the flexion gap can be altered by the size of the femur component. If the size of the femur component increases, the flexion gap decreases, leading to a different outcome of the surgery. Therefore it should always be checked if the joint line on the posterior side of the component is also the same as the primary component.[57] Not only the size of the femur component can influence the flexion gap, but also the flexion the component is placed in can have an impact on the flexion gap. Even a small flexion of the femoral component leads to a reduction of the flexion gap and thus potentially limited mobility.[58] Therefore, to not affect the flexion gap, the flexion of the femur component is placed at 0°.[59] Another useful parameter is the distance to the medial epicondyle, which is roughly 28mm on the medial side. However, this may vary per person.[60]

Lastly, the rotation of the femur component needs to be included in the 3D planning. The femur rotation is based on the surgical transepicondylar axis. The surgical transepicondylar axis is a line connecting the sulcus of the medial epicondyle and the most prominent point of the lateral epicondyle.[61] These bony landmarks can be used during surgery to identify the surgical transepicondylar axis, and based on these landmarks the rotation of the femur component is corrected. The femur component is placed parallel to the axes. However, with revision surgery, the bony landmarks are sometimes missing or not identifiable. Therefore, in the 3D planning, the anterior cut is compared to the surgical transepicondylar axis. Based on the this cut, the femur component rotation is calculated and translated to the surgical plan.

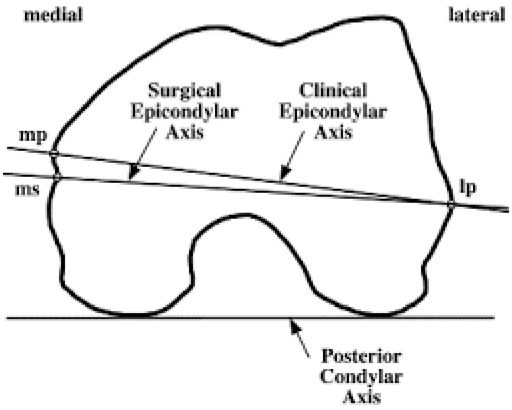


Image VIII: Representation of the Surgical Epicondylar axis, based on the anatomical landmarks of the femur, going from the tip of the lateral condyle to the center of the valley of the medial condyle

To complete the 3D planning for a revision surgery, any bone deficiencies need to be inspected and corrected. These bone deficiencies can be overcome by placing metal augmentations in these defects.[62] Femoral defects most often occur on the posterior surfaces and metal augmentation can also be used to increase femoral component rotation and to maintain the balance between flexion and extension gap. [42] These augmentations can be placed on the distal and posterior part of the component, on both the medial and lateral side, with a length of 5 mm or 10 mm creating multiple different outcome possibilities. Predictions of which augmentations are needed are included in the 3D planning, finishing the 3D planning for both the tibia and femur.

During this investigation, multiple 3D plannings will be made, for both the retrospective and prospective parts of this study. All the 3D planning made will be controlled by either one of the orthopaedic surgeons performing the revision TKA, Jakob van Oldenrijk or Wout Veltman. The surgeons will inspect the 3D planning and give feedback based on their experience of the procedure. The given feedback will be incorporated into the 3D planning, increasing the probability of a correctly predicted revision TKA. In the systematic review was found that the accuracy of the planned prosthesis size increases from 79.8% to 93.9% for the femur component and from 82.6% to 91.1% for the tibia component, if the planning was made by a surgeon instead of an engineer. Therefore all the created 3D plannings are checked by an orthopedic surgeon.

For the data production of the retrospective part of this investigation, a comparison is made between the 3D planning and the results gathered from the already performed revision TKA surgery. The results of the revision TKA surgery are all gathered in the Electronic Medical Record, HiX. From HiX the surgical report is collected, in which the surgeon gives a summary of the performed surgery, including the implanted materials, condition of the patient, difficulties during surgery and any other remarks observed during the surgery. Furthermore, in this report is the size of each component and the added augmentations noted. These are used to compare the predicted sizes and augmentations to the implanted sizes and augmentations of the femur and tibia component. In addition, post-operative imaging is collected, mostly an X-ray made 1-day post-op.

The results from the post-operative imaging are gathered in the same way as the axes are determined on the 3D planning, by superimposing the post-operative X-ray and the 3D image combined with the pre-operative long-leg X-ray. By tweaking and improving the superimpose until the images align, the margin of error is minimized. After aligning the images, different angles can be calculated. In the previously mentioned systematic review, several imported angles were highlighted. These angles are the Femoral Flexion Angle (FFA), Mechanical Femoral Angle (MFA) or mechanical Lateral Distal Femoral Angle (mLDFA), anatomical Lateral Distal Femoral Angle (aLDFA), Posterior Tibial Slope (PTS) and mechanical Medial Proximal Tibial Angle (mMPTA). All these angles are both calculated in the 3D image and post-operative imaging, providing different angles to make a comparison between the pre and post-operative results.

First, the superimpose of the AP X-ray image is used to calculate the MFA/mLDFA, aLDFA and mMPTA. The MFA or mLDFA is calculated by taking the angle between the joint line of the femur and the centre point of the hip, usually 90˚ in neutral stand for knee revision surgery. The aLDFA is calculated by taking the angle between the joint line of the femur and the shaft of the femur, which normally varies 6˚ from the mLDFA, 84˚. Lastly, the mMPTA can be calculated by taking the angle between the joint line of the tibia and the centre of the ankle joint, normally creating a 90˚ angle.[63]
Subsequently, the superimpose of the sagittal X-ray image is used to calculate the FFA and PTS. The FFA is calculated by taking the angle of the femur component, compared to the curvature of the shaft of the femur. Usually, the FFA is between the 0˚ and 8˚, however, during this investigation, the FFA was set to 0˚.[63-65] Besides the FFA, the PTS was calculated by taking the angle between the slope of the tibia plateau from anterior to posterior relative to the sagittal axis going through the diaphysis of the tibia. During primary TKA, this angle varies between 3° to 9°, however, for revision surgery, this angle is set to 0°.[51,66]

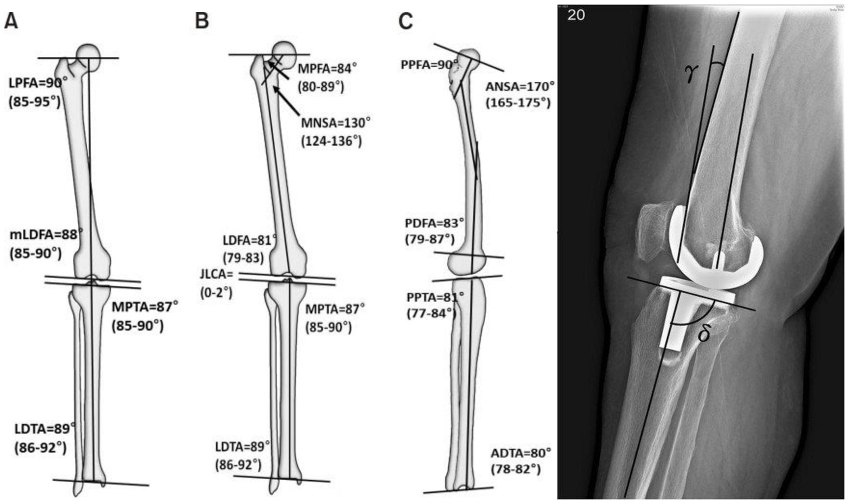


Image IX: Visualization of all the previously mentioned angles. In the first image the mLDFA, aLDFA, MPTA are visualized. In the second image the gamma is the FFA and the omega is the PTS.

After calculating and collecting all the different angles for both the results of the revision surgery and the prediction of the 3D planning, these results can then be compared to each other. Comparing the pre and post-operative results can provide valuable information on the predictive values of the 3D planning and the translation of the planning to the revision surgery, concluding the retrospective part of this investigation.

Besides the retrospective study, a prospective study is also performed. During this investigation, a 3D planning for a patient is made, before the patient goes for surgery. This 3D planning could then be consulted before and during the surgery, as an additional tool for the surgeon. However, during surgery, the surgeon was not obliged to follow the 3D planning, as it is provided as a guidance tool. The results of the surgery are then recorded in the EMR in HiX. The results from the surgery are gathered from the surgical report, such as the implanted size and used augmentations. In addition, post-operative imaging is collected, mostly an X-ray made 1-day post-op. The post-op imaging is then superimposed over the fused 3D image with the pre-operative long-leg X-ray, in the same way as the retrospective study. The post-operative imaging superimpose can be used to calculate all the different angles. These angles are the same as for the retrospective results, Femoral Flexion Angle (FFA), Mechanical Femoral Angle (MFA) or mechanical Lateral Distal Femoral Angle (mLDFA), anatomical Lateral Distal Femoral Angle (aLDFA), Posterior Tibial Slope (PTS) and mechanical Medial Proximal Tibial Angle (mMPTA).
The 3D planning made is identical to the 3D planning made in the retrospective study. This is to compare the results of the retrospective study with the prospective study. Thus first, the superimpose of the AP X-ray is used to calculate the MFA/mLDFA, aLDFA and the mMPTA. The MFA or mLDFA is set to 90˚, as the aLDFA is set to 84˚, varying 6˚ from each other. The mMPTA is set to be 90˚. Furthermore, the sagittal superimposed image is used to calculate the FFA and the PTS, where the FFA and PTS are both set to 0˚.[51,63-66]

After calculating the different angles, the data is collected in an Excel sheet. In this sheet, the results of the pre-operative 3D planning are collected as well as the results of the revision surgery. Then these results can be compared with each other to find information on the accuracy of the 3D planning. In addition, the results of the retrospective and prospective studies can be compared, to find the differences between these investigations.

Following the collection of all the data, data analysis and statistical analysis can be applied on the gathered results. Several statistical analyses were used in this study to explore the relationship within the data. Scatter pots were utilized to visually represent the distribution of the data and potentially identify any patterns or trends within the data, allowing for a quick assessment of the correlation.[67] Following this exploration of data, the Pearson correlation coefficient is calculated to understand the strength and direction of the relationship between two variables. This statistical measurement varies from -1 to 1, with 1 indicating a perfect positive relationship and -1 a perfect negative relationship. 0 indicates no correlation between the data.[68,69] Additionally, Cohen's Kappa statistics were used to assess the agreement between the two variables. Kappa statistics corrects for the possibility of change agreement and contributes to an understanding of a relationship or pattern between data.[70] In addition, this study also incorporated the delta differences of the gathered results, to quantify the magnitude of change. Delta difference, often expressed as Δ, is calculated by subtracting one value from another, providing a measure of the absolute change or difference. The delta difference, alongside the Pearson correlation coefficient and Kappa, adds a practical relevance to the study's findings, as it helps to bridge the gap between statistical significance and actual significance of observed relationships.[71] Furthermore, to assess the significance of differences between the two samples, a two-sided t-test was performed. The two-sided t-test is a powerful statistical tool used to determine whether the means of two groups are significantly different from each other. The t-test produces a p-value, representing the probability of obtaining the observed results by chance alone. A p-value lower than 0.05 indicates statistically significant results. The two-sided t-test provides an investigation with more precise conclusions about the significance observed. All these statistics together enhance the depth, reliability and validity of the findings of this investigation.

In addition to the retrospective and prospective study, the first design of a 3D printed guide is made. This guide can assist the surgeon during revision TKA. However, the guide will not be used as a cutting guide, like most 3D printed guides, but more like a landmark guide. There are two critical landmarks the guide must contain, the joint line, or fresh-up cut of the distal part of the femur, and the rotation of the newly placed femur component.

The design process initiates with a rough sketch of the guide's outlines on the segmented bone of the patient, this will ensure the guides conformity to the unique shape of the patient's bone. This outline is used to create a patient-specific 3D print, which can only be placed conform to the patient's anatomy, creating a PSI that aids the surgeon. To achieve the outline of the guide, the option "Marked Triangles" is used, allowing technicians to selectively mark the desired region of interest, with a brush. The brushed surfaces are added to the total of marked triangles. The marked area is then separated to create a new part, representing the surface of the marked triangles. This is visualized as the green area in Image Xb. The "Uniform Offset" function is employed to convert this 2D surface into a 3D guide, with a specified external offset determining the thickness of the 3D printed guide. The thickness of the 3D print is designed to be 3mm, giving the print a good strength, while also limiting the size of the guide. The results of the Uniform Offset are visualized in Image Xc. In addition, Finish – Smooth Edge, is used to smooth the edges of the created 3D surface, to enhance the aesthetics of the model and remove any sharp edges which can damage the soft tissue in the patient.

The results of the Uniform Offset contain the outlines of the 3D printed guide. However, the height of the joint line and the rotation of the femur component are not yet incorporated in the design. To address this, the 3D-printed guide is cut off at the height of the joint line. The same method is used to cut off the guide at the surgical epicondylar axis. The joint line and surgical epicondylar axis are visualized in Image Xd, with the joint line visualized in red and the surgical epicondylar axis in blue. Multiple designs are made to test which guide would be optimal for revision TKA, offering variations for evaluation. Two designs are made for the femur component placement and two designs are made for the tibia component placement. These designs will be presented to an orthopaedic surgeon, who will give feedback on the presented designs. Subsequently, one definite design is made for both the femur and tibia components, providing a foundation for future research and experimentation.

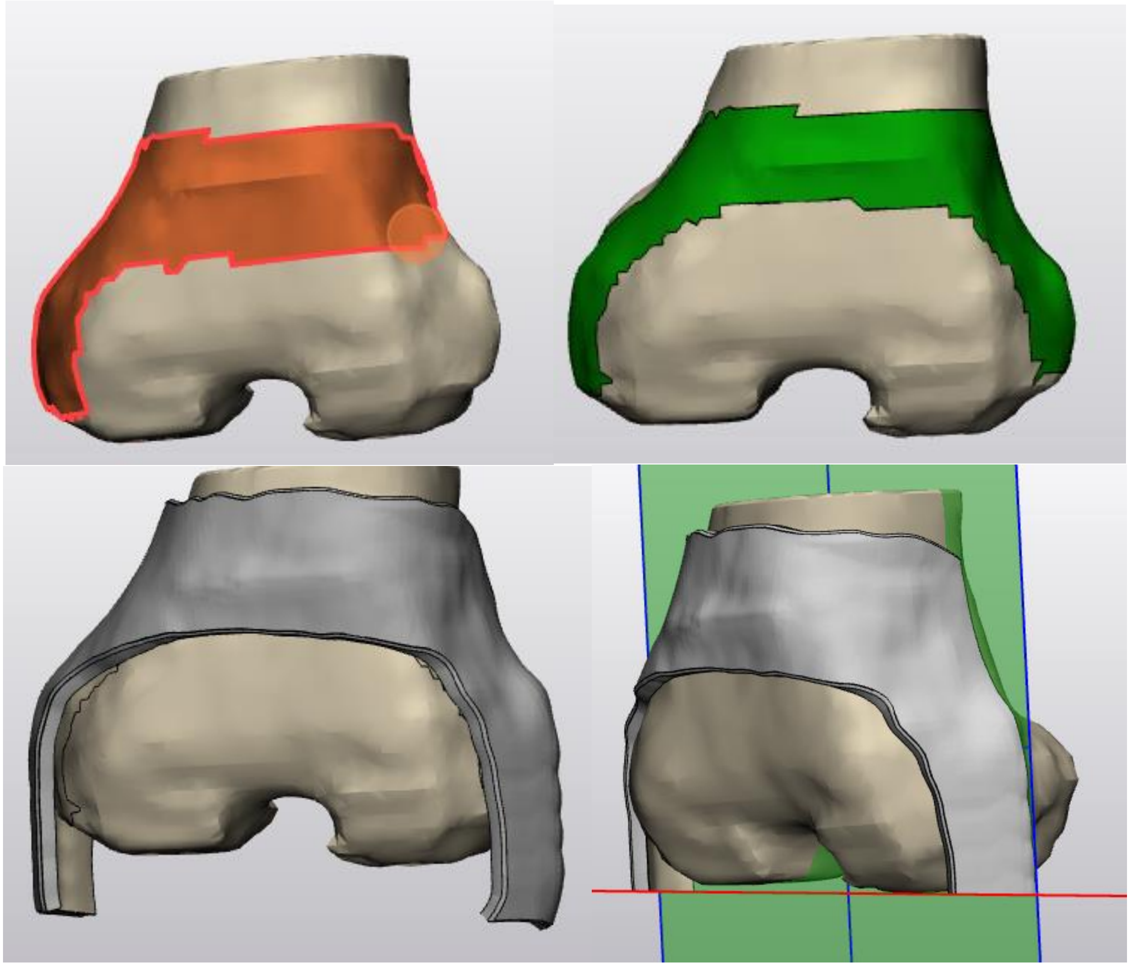


Image X. a) The surface of the new 3D guide, marked with a brush. b) The completed marked surface of the 3Dguide. c) Uniform offset of 3mm given to the selected surface expanding the surface outwards. d) Complete 3D guide with the joint line visualized in red and the surgical epicondylar axis in blue.

Additionally, a 3D-printed guide for the tibia component is crafted using a similar method. The only difference is the determination of the rotation of the component. The rotation of the tibia component is 18° with respect to the middle of the tuberosity. The middle of the tuberosity is visualized in Image XIb as the red line, whilst the blue line represents the tibial rotation, 18° in regards to the red line.

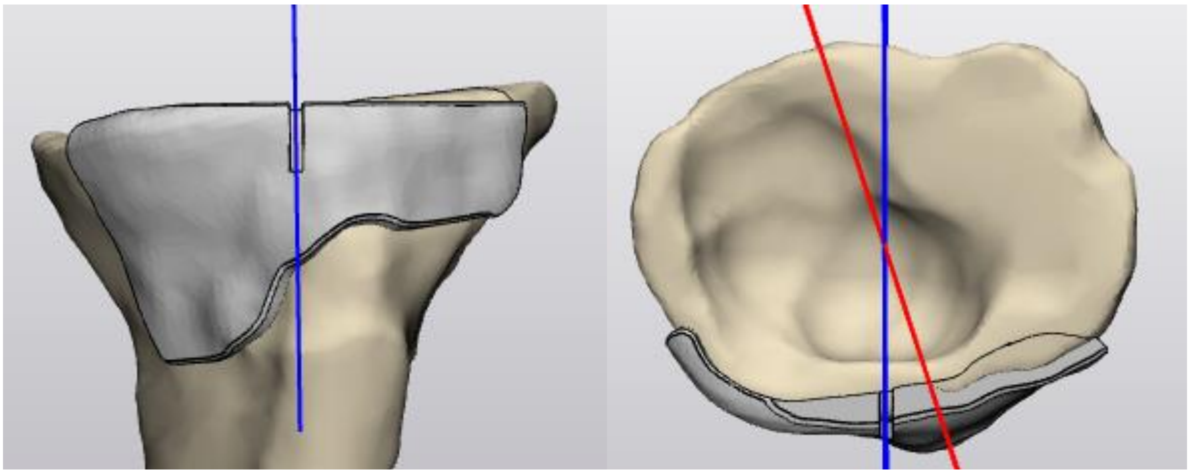


Image XI. a) Frontal visualization of the 3D guide for the tibia, with the rotational axis of the component given in blue. b) Transverse image of the 3D guide, with the middle of the tuberosity visualized in red, given the angle between this and the rotational axis to be 18°

3. Results

Retrospective Study

Femur 3D plan	**Femur Size (-)**		**Distal Augmentation (med - lat)**		**Posterior Augmentation (med - lat)**		**FFA (˚)**		**MFA (˚)**		**aLDFA (˚)**	
Patients	*Pre-op*	*Post-op*	*Pre-op*	*Post-op*	*Pre-op*	*Post-op*	*Pre-op*	*Post-op*	*Pre-op*	*Post-op*	*Pre-op*	*Post-op*
RO01	7	7	5mm - 10mm	5mm - 10mm	5mm - 10mm	10mm - 10mm	0,0	1,0	89,0	88,9	83,0	82,8
RO02	7	7	5mm - 5mm	5mm - 10mm	5mm - 5mm	5mm - 10mm	1,0	1,3	89,5	92,2	84,0	84,9
RO03	5	5	5mm - 10mm	5mm - 10mm	5mm -5mm	5mm - 10mm	0,5	0,4	90,0	92,4	84,0	84,8
RO04	5	5	5mm - 5mm	5mm - 5mm	0mm - 0mm	0mm - 0mm	2,0	4,4	90,5	87,1	83,5	85
RO05	5	6	0mm - 0mm	0mm - 0mm	5mm - 5mm	10mm - 10mm	1,0	1,0	90,0	90,1	84,0	84,1
RO06	7	7	0mm - 10mm	0mm - 10mm	5mm - 5mm	10mm - 5mm	3,0	3,2	90,5	91,8	84,0	83,2
RO07	5	5	5mm - 0mm	5mm - 5mm	5mm - 5mm	5mm - 5mm	1,0	2,6	90,0	90,5	83,0	84,1
RO08	4	4	5mm - 0mm	0mm - 5mm	0mm - 0mm	5mm - 10mm	0,5	1,2	90,0	91,9	84,0	85,6
RO09	4	4	5mm - 5mm	5mm - 5mm	5mm - 5mm	5mm - 5mm	0,5	2,5	90,0	91,6	84,0	83,7
RO10	4	4	10mm - 10mm	10mm - 10mm	5mm - 5mm	5mm - 10mm	1,0	4,2	89,5	90	83,5	84,1

Note: Tabel X

Retrospective Study

Tibia 3D plan	**Tibia Size (-)**		**Tibial Augmentation (med – lat)**		**PTS (˚)**		**MPTA (˚)**	
Patients	*Pre-op*	*Post-op*	*Pre-op*	*Post-op*	*Pre-op*	*Post-op*	*Pre-op*	*Post-op*
RO01	7	6	5mm - 5mm	5mm - 5mm	2,0	2,7	89,0	90,7
RO02	7	7	5mm - 0mm	5mm - 0mm	1,0	3,2	90,0	89,1
RO03	4	4	5mm - 0mm	5mm - 0mm	0,0	-0,9	89,5	91,0
RO04	4	4	0mm - 0mm	0mm - 0mm	0,5	1,1	90,5	90,0
RO05	5	5	0mm - 5mm	0mm - 0mm	0,0	0,4	90,5	90,4
RO06	6	6	0mm - 0mm	0mm - 0mm	2,5	1,0	90,0	90,4
RO07	5	5	0mm - 0mm	0mm - 0mm	0,5	2,7	88,5	89,8
RO08	4	4	0mm - 0mm	0mm - 0mm	2,5	0,9	87,5	86,6
RO09	4	3	0mm - 0mm	0mm - 0mm	0,0	1,1	91,0	88,6
RO10	3	3	5mm - 0mm	5mm - 5mm	2,0	2,4	90,5	91,1

Note: Tabel Y

Prospective Study

Femur 3D plan	**Femur Size (-)**		**Distal Augmentation (med - lat)**		**Posterior Augmentation (med - lat)**		**FFA (°)**		**MFA (°)**		**aLDFA (°)**	
Patients	*Pre-op*	*Post-op*	*Pre-op*	*Post-op*	*Pre-op*	*Post-op*	*Pre-op*	*Post-op*	*Pre-op*	*Post-op*	*Pre-op*	*Post-op*
PO01	6	6	10 mm - 5mm	10 mm - 5mm	10mm - 10mm	5mm - 5mm	0,5	3,5	88,7	89,6	83,6	84,3
PO02	3	3	5mm - 5mm	5mm - 5mm	5mm - 0mm	0mm - 0mm	1,0	1,4	90,0	89,8	84,0	83,3
PO03	3	2	0mm - 0mm	0mm - 0mm	5mm - 0mm	0mm - 0mm	2,0	5,8	90,5	91,4	84,0	82,4
PO04	4	4	5mm - 5mm	5mm - 5mm	0mm - 0mm	5mm - 10mm	1,0	1,8	90,3	89,8	84,3	84,3
PO05	6	7	5mm - 5mm	5mm - 10mm	10mm - 10mm	10mm - 10mm	0,0	2,7	89,5	88,8	83,5	84,7
PO06	6	6	5mm - 5mm	5mm - 5mm	10mm - 5mm	5mm - 5mm	1,0	2,9	90,0	89,4	84,0	84,6
PO07	5	5	0mm - 0mm	0mm - 0mm	0mm - 0mm	0mm - 0mm	2,5	2,4	89,0	90,6	83,0	84,1
PO08	3	3	5mm - 5mm	5mm - 5mm	5mm - 5mm	0mm - 0mm	1,0	2,1	90,0	90,7	84,0	84,8
PO09	7	7	10mm - 10mm	5mm - 10mm	5mm - 5mm	10mm - 5mm	0,0	0,3	89,9	90,5	84,2	85,2
PO10	3	3	5mm - 0mm	5mm - 0mm	0mm - 0mm	0mm - 0mm	0,0	3,1	90,0	91,0	84,0	84,8
PO11	5	5	5mm - 0mm	5mm - 0mm	5mm - 0mm	0mm - 0mm	3,5	4,2	90,0	89,8	84,0	84,2
PO12	6	6	0mm - 0mm	0mm - 0mm	0mm - 5mm	0mm - 5mm	1,5	2,1	90,0	90,2	84,0	84,7

Note: Tabel XX

Prospective Study

Tibia 3D plan	**Tibia Size (-)**		**Proximal Augmentation (med - lat)**		**Posterior Tibial Slope (˚)**		**MPTA (˚)**	
Patients	*Pre-op*	*Post-op*	*Pre-op*	*Post-op*	*Pre-op*	*Post-op*	*Pre-op*	*Post-op*
PO01	6	6	0mm - 0mm	0mm - 0mm	2,0	1,1	90,0	89,8
PO02	3	3	0mm - 0mm	0mm - 0mm	0,0	1,8	90,3	89,3
PO03	3	3	5mm - 0mm	5mm - 5mm	1,5	0,2	90,0	90,2
PO04	4	4	5mm - 0mm	5mm - 0mm	0,0	0,4	90,4	90,1
PO05	6	6	5mm - 0mm	5mm - 0mm	0,5	1,5	90,5	89,3
PO06	5	5	0mm - 0mm	0mm - 0mm	0,5	1,2	90,0	90,6
PO07	5	5	0mm - 0mm	0mm - 0mm	1,0	1,2	90,0	89,7
PO08	3	3	0mm - 0mm	0mm - 0mm	0,0	0,5	90,5	90,4
PO09	6	6	5mm - 0mm	0mm - 0mm	1,0	5,7	89,9	89,4
PO10	2	2	5mm - 0mm	10mm - 0mm	0,5	1,1	89,5	88,9
PO11	5	5	5mm - 0mm	5mm - 0mm	0,0	1,6	90,0	90,2
PO12	6	6	0mm - 0mm	0mm - 0mm	0,0	0,5	90,0	89,6

Note: Tabel YY

Creating a validated 3D planning for revision surgery involves a structured protocol, with each step contributing to the overall precision of the plan. A comprehensive view of the steps taken and corresponding results of 3D planning are given below.

The initial step in creating a 3D planning involves determining the size of the component. This is accomplished by importing the segmented parts from the patient's CT scan. These parts include the segmented femur and tibia bone, as well as the implanted femur and tibia components. In addition, the STL files of the new components are imported into the workspace. Based on the dimension of the previously implanted component, the size of the new implant is determined. In addition, for the tibia component, medial or lateral overhang is unacceptable and adjustments to the size are made to ensure there is no overhang. These steps are visualized in Images IV, V, and VI.

Following the prediction of the component size, the placement and positioning of the component is the next important step. The placement and positioning all depend on the axis of the 3D image. The axis can be determined by the long-leg X-ray of the patient, as the CT scan lacks the information to determine these axes. However, to translate the long-leg X-ray axis to the axis of the 3D image in 3-Matic, these images need to be superimposed, by putting a picture of the long-leg X-ray on top of a picture of the created 3D image. The result of the superimpose is visualized in Image XII.

Image XII: Superimpose of the long-leg X-ray and the 3D image, where the 3D image should overlap the X-ray image as good as possible. With this superimpose the axis of the 3D image is created.

Using the superimpose, the axis of the 3D image can be determined. Based on these axes the mechanical and anatomical axis can be calculated. These are the basis for the computation of the angles. In Image XIII, the old situation is depicted, featuring the mechanical axis in red and the anatomical axis in green. Additionally, the joint lines of both the femur and tibia are illustrated. These joint lines are calculated based on the mechanical axis, with the joint line positioned perpendicular to the mechanical axis, visualized by the blue line. The femoral joint line is placed on the bottom of the femur component. In the previous setting, both femur and tibia components were placed at a slight valgus angle. This is improved in the new setting, ensuring that the MFA/mLDFA and the MPTA are both corrected to the desired 90˚ and the aLDFA to the desired 6˚ deviation, so 84˚.

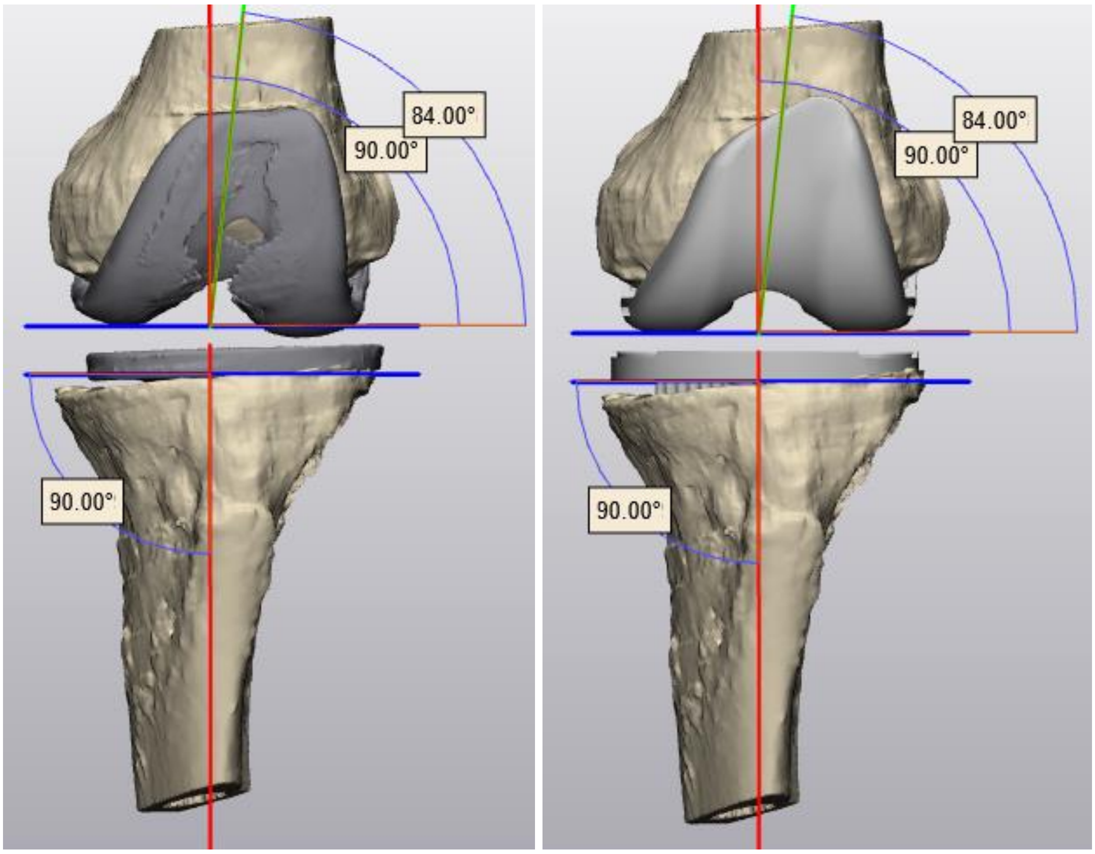


Image XIII: AP view of the 3D image, with the mechanical axis given in red, the anatomical axis in green and the femoral and tibial joint line in blue.

A complete file of a 3D planning of a patient follows the same steps. First, an X-ray image or CT image of the original situation is depicted, including a 3D image of the original setting. In this original image, all the important angles are calculated so the setting is visualized for the surgeon. After this, an image will be included of the new total setting, including all the angles and measurements. Next, the 3D planning contains parts of the total planning, specified. This consists of; anterior images of the femur, both old and new situations, including distance to the medial epicondyle and potential distal augmentations. Sagittal images are included to determine the Femoral Flexion Angle and potential posterior augmentations and bony defects. The last images for the femur contain the transverse image, on which the rotation of the femur component can be determined. For the tibia component, first, the old and new situations are sketched, mostly from an anterior view, including the angles and measurements. In addition, the transverse image of the tibia is depicted, on which not only the medial and lateral overhang are visible, but also the potential augmentations and rotation of the tibial component. A complete 3D planning of a random patient is included in this thesis, in Appendix B.

The retrospective study enrolled a total of 10 participants, all underwent a revision TKA surgery at the Erasmus MC. Of these patients, a 3D planning was made, predicting the placement of the knee prosthesis. The results of the pre-operative prediction and the post-operative results of the surgery for the femur component and tibia component can be found in Tabel X and Y respectively. The distribution of all the scores appears to be approximately normal, as illustrated in Figure I. The values for kurtosis between -2 and +2 are considered acceptable to prove normal univariate distribution. However, some articles even argued that data is considered to be normal if skewness is between -2 to +2 and kurtosis is between -7 to +7. [72-74] The skewness of the FFA, MFA, aLDFA, PTS and MPTA is calculated to be .99, -.31, .46, .01, and -1.23 respectively. The kurtosis of the FFA, MFA, aLDFA, PTS and MPTA was found to be -.01, .93, .23, -1.03, and 1.19 respectively, indicating a normal distribution of these variables.

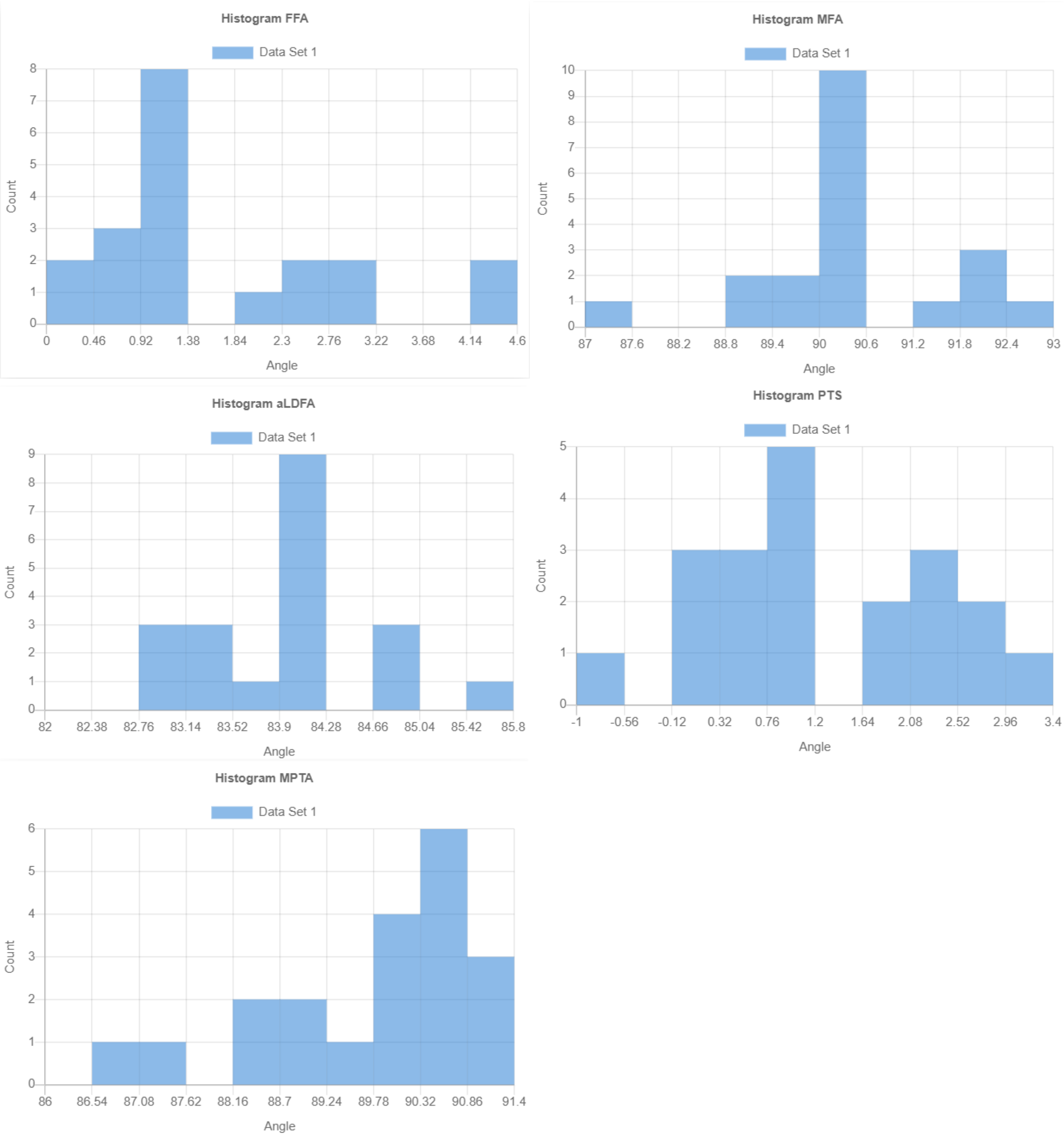


Figure I. Histogram of the FFA, MFA, aLDFA, PTS and MPTA, where for all the variables the distribution of the scores appears to be normal.

The findings of the comparison of pre-operative 3D planning with the implanted results suggest a high level of accuracy in predicting the size of the femur component. Specifically, 3D planning can accurately predict the size of the femur component in 90% of the cases, indicating a strong alignment between the planned size and the actual implanted size during surgery. As for the tibia component, the 3D planning can accurately predict the size of the component in 80% of the cases. While slightly lower than the observed accuracy of the femur component, the accuracy of the tibia component still suggests a strong alignment between the planned size and the actual implanted size during surgery. These results highlight the importance and reliability of the pre-operative planning process for both the femur and tibia components, providing a valuable tool for predicting implant sizing.

In addition to the size prediction, the 3D planning also includes augmentation prediction, which is documented in Tabel X and Y. The comparison between pre-operative 3D planning and the implanted augmentations reveals a notable accuracy, specifically, in 16 out of 20 cases, the 3D planning accurately predicts the distal augmentations of the femur component. This results in an 80% accuracy rate. This high level of precision indicates the efficacy of the 3D planning method in the implementation of distal augmentations during revision TKA. However, when examining the predictions for posterior femoral augmentations, the accuracy dropped. In 11 out of the 20 cases, the 3D planning correctly predicted the posterior femoral augmentation, yielding a 55% accuracy rate. This accuracy suggests there may be some challenges in predicting and implementing posterior augmentations for the femur component. As for the tibia component, the 3D planning can correctly predict the tibial augmentations in 18 of the 20 cases, resulting in a 90% accuracy rate, demonstrating a high level of accuracy. This level of precision in implementing tibial augmentations underlines the effectiveness of the 3D planning process.
Collectively, these findings for the retrospective study, indicate the capability of 3D planning, not only in predicting the implant sizes but also in anticipating specific augmentations during revision TKA surgery. The accuracy rates for different types of augmentations provide valuable insights for refining and improving the 3D planning process, contributing to more precise and accurate revision surgery.

Besides the prediction of the size and augmentations, the ideal placement of the components is visualized in the 3D planning. To assess the accuracy of the component placement, specific angles are calculated within the 3D planning system. Post-operative, these angles are calculated again based on the post-operative imaging, creating a comprehensive comparison between the predicted pre-operative 3D planning angles and the post-operative results. These detailed findings of these angles are recorded in Tabel X and Y.

Firstly, the Femoral Flexion Angle (FFA), is measured pre and post-operative, revealing some variation between the predicted and actual outcomes. The mean prediction of the FFA is 1.05˚, while the post-operative outcome yields a mean of 2.18˚, resulting in a delta difference of 1.15˚. Looking at the results in Tabel X, some outliers are noted. However, none of these outliers surpass 3.2˚. Considering that the normal range for FFA is targeted to be around 0-3˚, most of the observed outliers fall within this acceptable range, suggesting that the differences between predicted and post-operative FFA are clinically insignificant.[75] The small delta difference and the absence of clinically relevant outliers underscore the reliability of the 3D planning in accurately predicting the FFA in the placement of the component.

Secondly, the Mechanical Femoral Angle, also known as the mechanical Lateral Distal Femoral Angle (mLDFA), is calculated leading to a predicted pre-operative mean of 89.9˚, compared to the post-operative results, with a mean of 90.65˚. This results in a delta difference of 1.45˚. The limited deviation of the surgery compared to the predicted values indicates the effectivity of the 3D planning in predicting the intended mechanical alignment of the femoral component. Like the FFA, some MFA outliers are recognized, however, these outliers do not surpass the 3˚ range on the MFA, suggesting these results are less clinically relevant.[56].
Third, the anatomical Lateral Distal Femoral Angle (aLDFA), is pre-operatively planned with a mean of 83.7˚, resulting in an 84.23˚ aLDFA post-operatively, leading to a delta difference of 0.79˚. This delta difference is even smaller than the delta difference for the FFA and MFA, with the highest outlier of 1.6˚, indicating even less variance in predicting this angle. Therefore the 3D planning of all planned femoral angles are deemed accurate and the outliers are considered to be clinically irrelevant.

In addition to the femoral angles, several tibial angles are planned and measured as well, the Posterior Tibial Slope (PTS) and Medial Proximal Tibial Angle (MPTA) respectively. The mean of the pre-operative planning for the PTS is 1.1˚, showing minimal deviation from the post-operative results calculated to be 1.46˚ The delta difference between the pre and post-operative values is 1.16˚, suggesting little variance in the PTS measurements. However, an interesting observation is made: one of the results displays a negative PTS, indicating an unusual negative slope in the posterior tibial angle. The targeted range for the PTS is set between -1˚ and 3˚, as these specific PTS values are associated with notably improved post-operative results.[66] The outliers observed in both the predicted 3D planning and post-operative results largely align with this specified range.
Besides the PTS, the MPTA angles are calculated. The mean of the pre-operative 3D planning was 89.7˚, while the post-operative results of the TKA revision surgery were 89.77˚, varying only 0.07˚. However, the delta difference between the pre and post-op results was estimated to be 1.03, with outliers up to 2.4˚. Importantly, these outliers did not surpass the accepted normal mechanical axis deviation of 1.56 ± 1.48 mm.[76] These findings together suggest that while there is a slight variation in pre-operative 3D planning and post-operative PTS and MPTA angles, the observed outliers remain within an acceptable range, indicating the overall effectiveness of the prediction of the 3D planning for both the femoral and tibial component sizes, augmentations and placement angles.

The study included a cohort of 12 participants, all undergoing a revision TKA surgery this year at the Erasmus MC. For each patient, a 3D planning was constructed, predicting the placement of the knee prosthesis. This 3D planning could be consulted before and during the surgery. The detailed results of the pre-operative predictions and the post-operative outcomes for the femur and tibia components can be found in Tables XX and YY, respectively. The distribution of all the values appears to be approximately normal, as illustrated in Figure II. The skewness of the FFA, MFA, aLDFA, PTS and MPTA was found to be .75, -.03, -.83, -.99 and -.60 respectively. The kurtosis of the FFA, MFA, aLDFA, PTS and MPTA is estimated to be .68, .39, 1.45, 2.50 and -.07 respectively, indicating normally distributed variables. Even though the kurtosis of the PTS is above the threshold of 2, many articles determined that a kurtosis below 7 is also believed to be normally distributed[72-74].

First of all, a comparison is made between the predicted size of the pre-operative 3D planning and the gathered post-operative results. For the femur component, the prediction of the size of the component yields an 83% accuracy, where only 2 of the 12 sizes were wrongly predicted. However, one of these false predictions did not have a femur component replacement, therefore, these results are not included in this study, leading to a correctly predicted size in 10 of the 11 cases, yielding a 91% accuracy. For the tibia component, all the component sizes were correctly predicted, resulting in 100% accuracy. These results together observe a high accuracy of size prediction, suggesting a connection between the predicted size and the actual implanted size. A pre-operative 3D planning is therefore an accurate and reliable tool for predicting implant sizing and can be implemented in the pre-operative planning process of revision TKA.

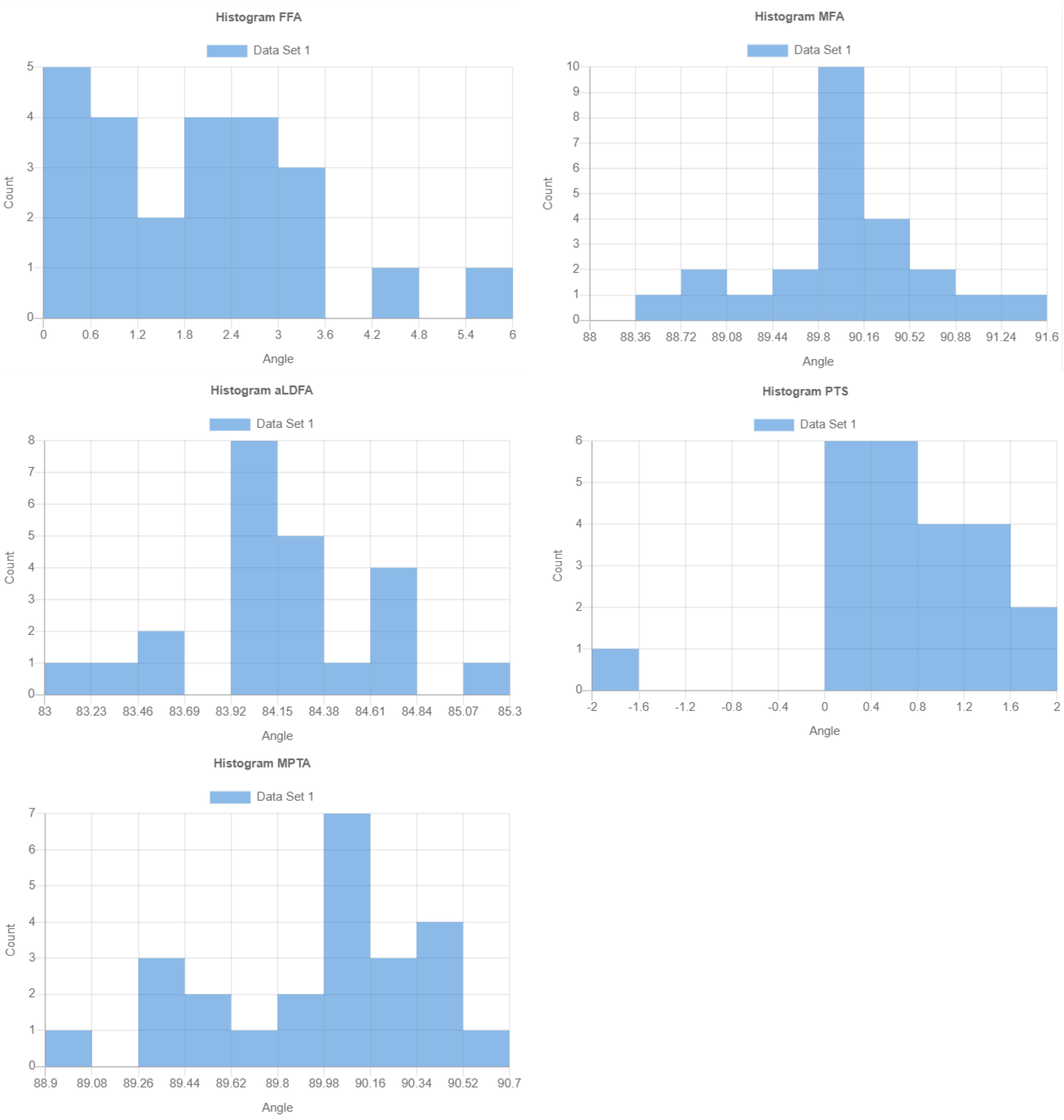


Figure II. Histogram of the FFA, MFA, aLDFA, PTS and MPTA, where for all the variables the distribution of the scores appears to be normal. Only the PTS histogram seems to be negatively skewed.

In addition to size prediction, the 3D planning integrates augmentation predictions, documented in Tables XX and YY. The comparison between pre-operative 3D planning and the implemented augmentations reveals an accuracy of 91.6%, for the distal augmentations of the femur component. The observed high accuracy in distal augmentations implies that 3D planning may be an effective method for predicting and implementing these augmentations in revision TKA. Despite the high accuracy achieved with distal augmentations, the accuracy significantly falls for posterior femoral augmentations. In 13 out of the 24 cases, the 3D planning accurately predicted the correct augmentations, leading to a lower accuracy of 54.2%, suggesting challenges to overcome in the prediction of the posterior augmentations. Lastly, the augmentations of the tibia component were correctly predicted in 21 of the 24 cases, leading to an 87.5% accuracy. Overall, the observed levels of accuracy for the distal femoral and tibial augmentations suggest an important role for 3D planning in predicting revision TKA augmentations. However, for the prediction of posterior femoral augmentations, additional research is necessary to address existing challenges and improve predictive accuracy.

Overall, the outcomes of the retrospective study indicate a great potential for 3D planning in accurately predicting implant sizes and augmentations for revision TKA surgery. The accuracy rates for the various augmentations offer valuable understandings for the enhancement of the 3D planning process. Altogether, contributing to the advancement in the field of revision surgery, by refining and increasing the effectiveness of the 3D planning method.

Moreover, the best possible placement of the components is calculated and implemented in the 3D planning. To evaluate the precision of the 3D planning, specific angles of the components are calculated. Post-operatively, these angles are recalculated based on imaging, creating a comparison between the pre-operative 3D planning and the post-operative results. These results are documented in Tables XX and YY.

Identical to the retrospective study, the FFA, MFA, aLDFA, PTS and MPTA are used for the placement of the components. The results of the comparison between the pre-operative planning and the post-operative results of the surgery reveal that the mean prediction of the FFA is 1.15˚, while the post-operative outcome has a mean of 2.73˚. The results lead to a delta difference of 1.6˚. Some outliers are noted in Tabel XX, with the largest outlier being 5.8˚. In total one pre-operative planning and four post-operative outcomes exhibit FFA angles exceeding the normal range of 0˚ to 3˚.[75] Therefore further observations of these specific cases are necessary to draw valid conclusions about the reliability of 3D planning. However, the small delta difference, despite the outliers, still indicates a high accuracy, suggesting 3D planning can effectively predict the outcome of a revision TKA surgery.

The predictions for the MFA yield a mean angle of 89.9˚, while the outcomes for the revision surgery result in a mean angle of 90.65˚. This translates to a delta difference of 1.45˚, showcasing a high level of accuracy in predicting the outcomes of revision TKA surgery with 3D planning. The most significant outlier noted in Table XX, 91.4˚, does not surpass the normal variance of 3˚ for the MFA, further supporting the notion of a reliable and accurate prediction made by the 3D planning.[56]

The pre-operatively planned aLDFA angle has a mean of 83.86˚, whereas the post-operative results show a mean of 84.21˚, resulting in a delta difference of 0.81˚. Similar to the retrospective study, the prospective study also yields the smallest delta difference for the aLDFA compared to the FFA and MFA. The largest outlier of the aLDFA being 1.6˚, further indicates little variance in the prediction accuracy of this particular angle. All these findings together, highlight the consistent and accurate prediction of the 3D planning method in both the retrospective and prospective assessment.

Besides the femur component, various angles are planned and calculated for the tibial component, including the PTS and MPTA, similar to the retrospective study. The pre-operatively planned posterior slope had a mean of 0.65˚, in comparison to the post-operative results, which had a mean of 1.15˚. This results in a delta difference of 1.3˚, which indicates a negligible variance between the pre and post-operative results as the targeted range for the PTS is set between -1˚ and 3˚.[66] However, one outlier exceeded the targeted range, leading to a PTS of 5.7˚.
In the case of the MPTA, the pre-operative 3D planned angles have a mean of 90.11, while the post-operative results show a mean of 89.73˚, resulting in a delta difference of 0.46˚. This low delta difference signifies a low variance between the pre-operative 3D plan and post-operative results, indicating a high level of accuracy in the 3D planning process for MPTA. The precision in predicting and achieving the PTS and MPTA further strengthens the overall reliability and effectiveness of the 3D planning system in guiding tibial component placement during revision TKA.

To test if there were significant differences between the pre and post-operative groups, a statistical analysis was performed. First, the statistical analysis of the retrospective study is performed. The statistical analysis consists of t-test analysis, scatter plot analysis, Pearson Correlation Coefficient analysis and Cohen’s Kappa Statistics analysis.

A paired t-test was performed to compare the pre-operative positioning of the implant and the post-operative results of revision TKA for several angles calculated in the retrospective study. For the Femoral Flexion Angle, the pre-operative planning (M = 1.1, SD = 0.9) significantly differs compared to the post-operative results (M = 2.2, SD = 1.4), revealing a significant difference in implant positioning for the femoral component, t(9) = 3.2, p = .011. However, no significant difference was observed for the other femoral angles. No remarkable changes are observed between the pre-operative planning (M = 89.9, SD = 0.5) and the post-operative results (M = 90.7, SD = 1.7) for the Mechanical Flexion Angle, t(9) = 1.4, p = .207. The anatomical Lateral Distal Femoral Angle demonstrated no significant differences between the pre-operative planning (M = 83.7, SD = 0.4) and post-operative results (M = 84.2, SD = 0.9), t(9) = 2.1, p =.066. In addition to the femoral angle, a paired t-test was performed on the tibial angles as well. No significant difference was found between the pre-operative planning (M = 1.1, SD = 1,0) and the post-operative results (M = 1.5, SD = 1,3) for the Posterior Tibial Slope, t(9) = 0.8, p = .421. Finally, the results of the comparison between the pre-operative planning (M = 89.7, SD = 1.1) and the post-operative results (M = 89.8, SD = 1.4) yielded no significant difference for the Medial Proximal Tibial Angle, t(9) = 0.2, p =.868.

A paired t-test was employed to compare the pre-operative placement of the implant and the post-operative placement of revision TKA surgery for several angles calculated in the prospective study. The results from the pre-operative planning (M = 1.2, SD = 1.1) and post-operative results (M = 2.7, SD = 1.4) for the Femoral Flexion Angle indicate a significant alteration in implant positioning between the planned and the post-operative placement, t(11) = 4.1, p = .002. For all the other angles calculated during the prospective study, no significant differences were found. The Mechanical Flexion Angle demonstrated no noteworthy change between pre-operative planning (M = 89.8, SD = 0.5) and post-operative outcomes (M = 90.1, SD = 0.7) (t(11) = 1.4, p = .180). No significant difference was found between the pre-operative planning (M = 83.9, SD = 0.4) and post-operative results (M = 84.3, SD = 0.8) for the anatomical Lateral Distal Femoral Angle, t(11) = 1.7, p = .120. Exploring tibial angles, the mean value of the pre-operative planning (M = 0.6, SD = 0.7) was not significantly different than the post-operative results (M = 1.1, SD = 1.7) of the revision surgery for Posterior Tibial Slope, t(11) = 1.1, p = 0.300. Lastly, no significant difference is found between the pre-operative planning (M = 90.1, SD = 0.3) and post-operative results (M = 89.8, SD = 0.5) of the Medial Proximal Tibial Angle, t(11) = 2.1, p = .064.

To analyze if there is an association between different variables, scatterplots are used to identify certain relationships between the variables. Firstly, the scatterplots of the retrospective investigation are drawn, see Figure III. Scanning these scatterplots, a strong positive relationship is noticed between the pre and post-op angles calculated for the FFA angle. However, for the MFA angle, almost no relationship is noticed, as the variables are scattered throughout the plot. For the aLDFA, PTS and MPTA a positive relationship is noticed between the pre and post-op angles, yet this relationship seems weak.

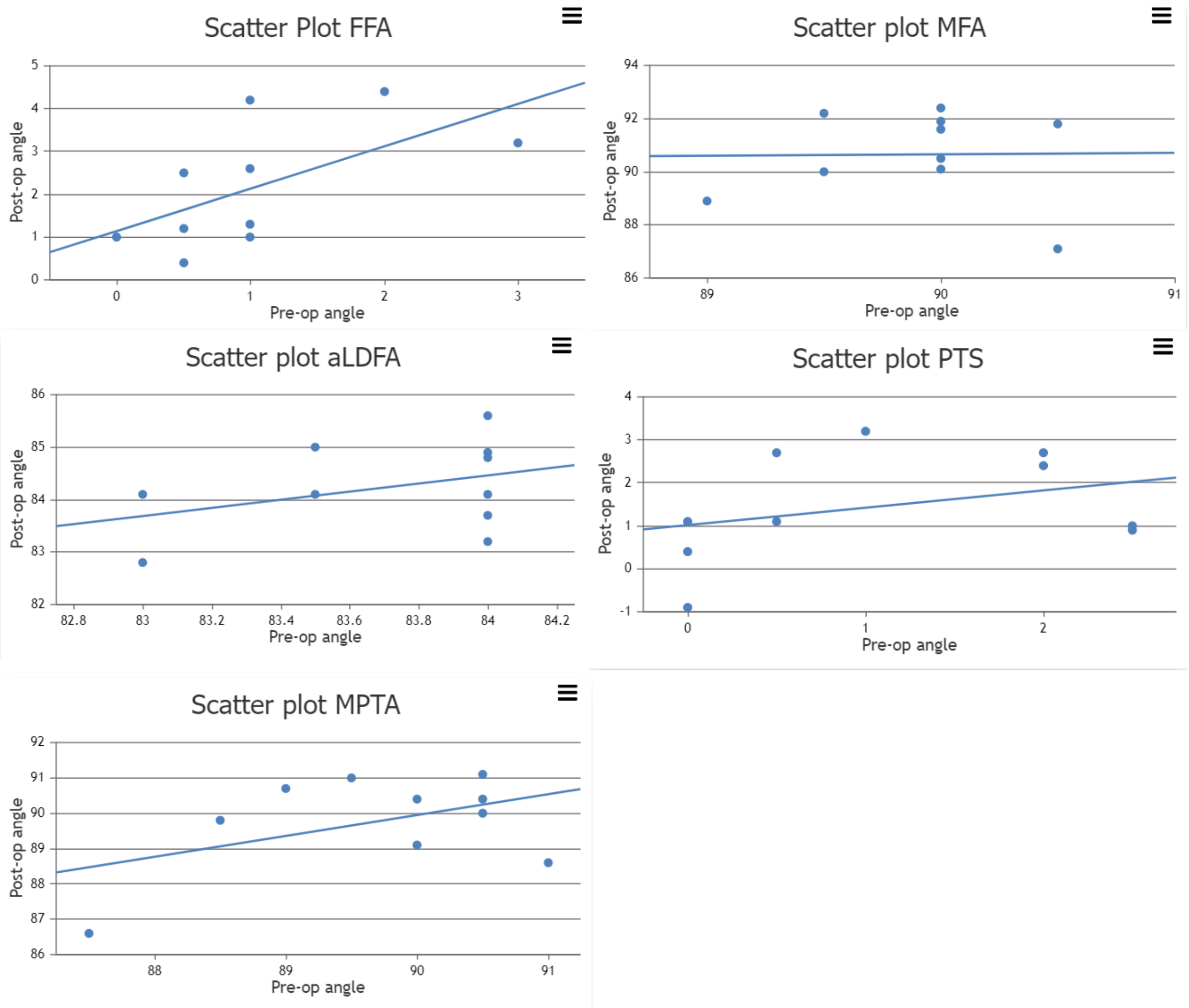


Figure III. The scatter plots of the different calculated angles for the retrospective investigation, where the relationship between pre and post-op angles seems to be the strongest for the FFA and the weakest for the MFA.

In Figure IV, the scatterplots of the prospective investigation are shown. These scatterplots show a weak positive relationship between the pre and post-op results for the FFA, MFA, PTS and MPTA, as for the aLDFA almost no relationship is noticed.

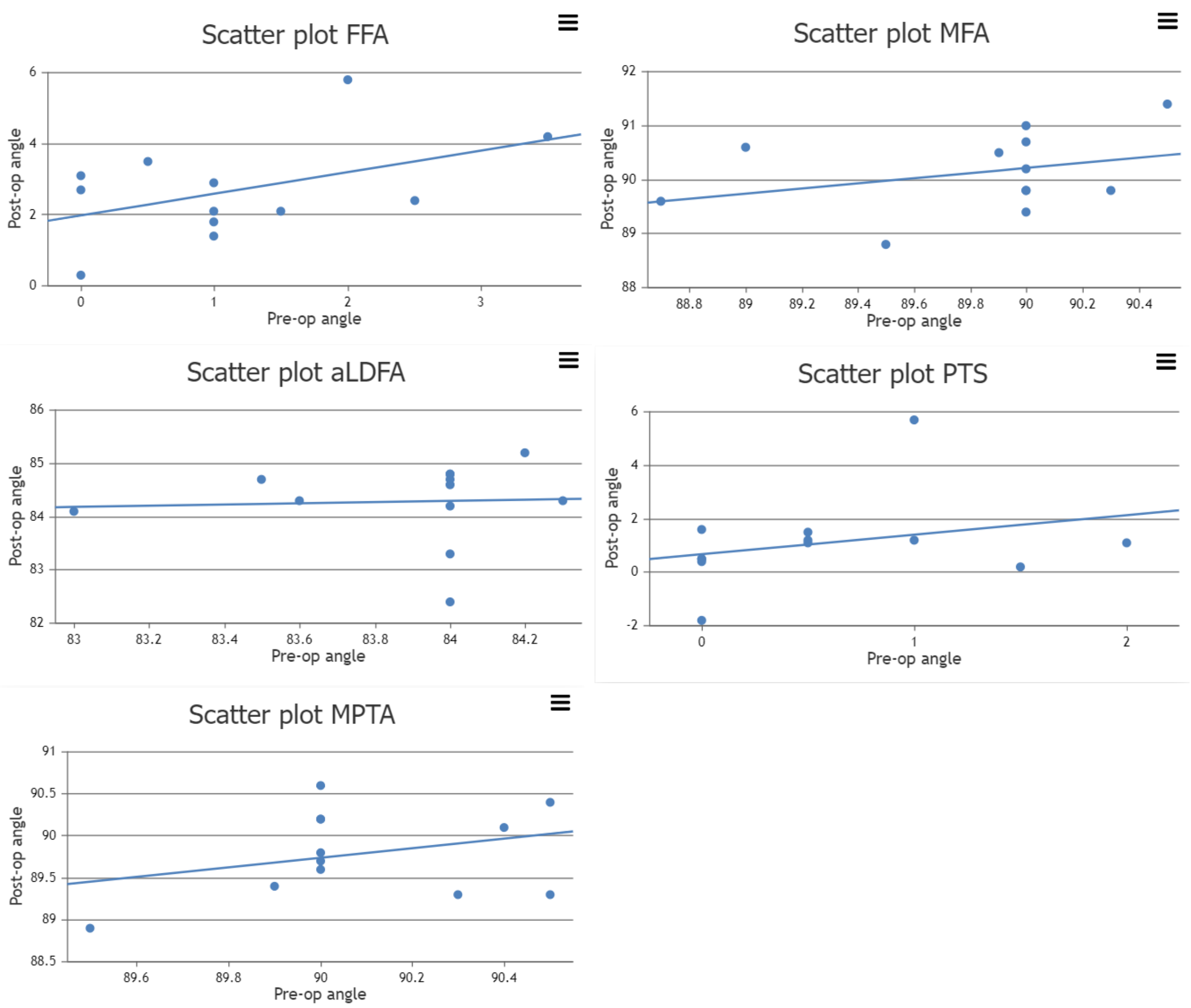


Figure IV. The scatter plots of the different calculated angles for the prospective investigation, where the relationship between pre and post-op is weak for the FFA, MFA, PTS and MPTA, as the relationship between these angles seems nonexistent for the aLDFA.

In addition to the scatter plot analysis, a Pearson Correlation Coefficient (PCC) was computed to determine whether there is a relationship between the pre-operative planning and the post-operative results. The value determines how strong the linear relationship between these variables is, with -1 a strong negative relationship, 0 no relationship and 1 a strong positive relationship. For the angles in the retrospective study, a Pearson Correlation Coefficient was performed. The results of the Femoral Flexion Angle indicated a strong positive correlation between the pre-operative planning and post-operative results, r(8) = .605; however, the relationship was deemed not significant, p = 0.064. A Pearson Correlation Coefficient was also performed for all the other angles in the retrospective study. The results for the Medial Proximal Tibial Angle indicate a moderate positive correlation between the two variables, r(8), = .468; however, the association was not significant, p = .172. The results for the anatomical Lateral Distal Femoral Angle and Posterior Tibial Slope both indicate a weak positive correlation between the pre-operative planning and post-operative results, r(8) =

.379, r(8) = .333, respectively; however, the relationship for both angles was deemed to be not significant, p = .280 for aLDFA and p = 0.346 for PTS. Lastly, the relationship between the pre-operative planning and post-operative results for the Mechanical Femoral Angle is calculated, indicating a very weak positive correlation between the two variables; however, this relationship is not significant.

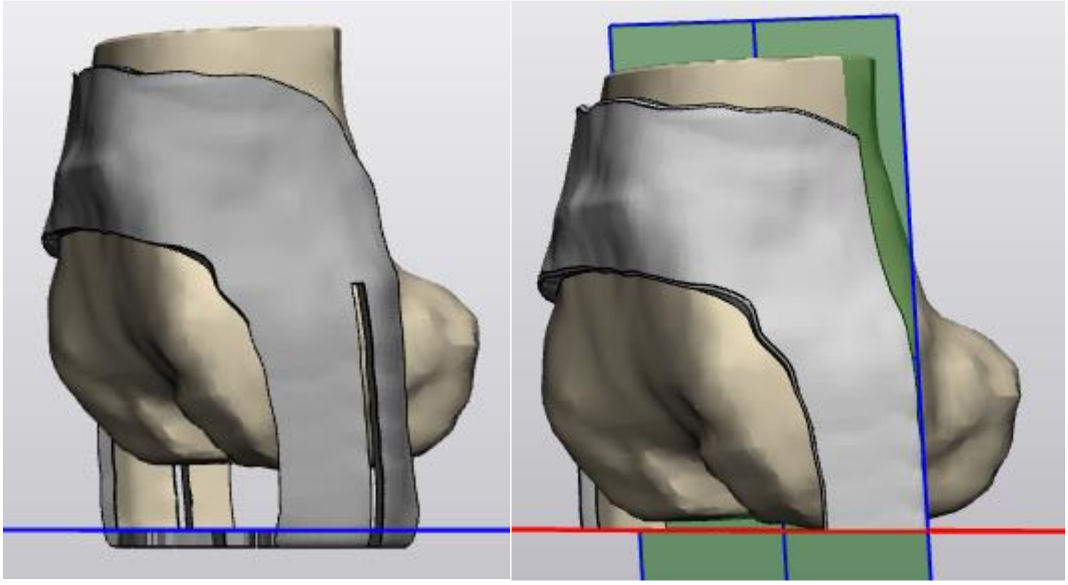
In the prospective study, the correlation of the angles was conducted using the Pearson Correlation Coefficient. For the Femoral Flexion Angle and the Medial Proximal Tibial Angle, a moderate positive correlation between pre-operative planning and post-operative results was observed, with respective correlation coefficients of r(10) = 0.486 and r(10) = 0.420. However, neither of these results are deemed significant, with p-values of .154 and .228, respectively. The Mechanical Flexion Angle and Posterior Tibial Slope exhibited slightly lower correlation coefficients, indicating a weak correlation between the variables (r(10) = 0.391 and r(10) = 0.246). Nonetheless, both correlations were not statistically significant, p = .264, and p = 493, respectively. Finally, the results of the anatomical Lateral Distal Femoral Angle, indicate a not significant, very weak positive correlation between the two variables, r(10) = 0.019, p = 0.959.

Furthermore, in assessing the reliability of predictions made during pre-operative planning, Cohen's Kappa Statistics were employed to determine the accuracy of predicting augmentations compared to their post-operative placement. In the retrospective study, the reliability of the Distal Femur Augmentations was found to be Kappa = .840, indicating an almost perfect agreement between the pre-operative planning and post-operative results. In contrast to the high agreement of the Distal Femur Augmentations, the Kappa of the Posterior Femur Augmentations was found to be Kappa = .274. This value for Kappa only suggests a fair agreement between the pre-operative planning and post-operative results. In addition, tibial augmentations are also predicted in the pre-operative planning. The reliability of the Tibial Augmentations was found to be Kappa = .750, which indicates a substantial agreement between the pre and post-op.
For the prospective study, the same predictions for the augmentations are made. The Distal Femur Augmentations generate a Kappa score of = .829, which is considered to be an almost perfect agreement. The Kappa score for Posterior Femur Augmentations is considerably lower, which was found in the retrospective study as well, with Kappa = 0.219, indicating a fair agreement between pre-operative planning and post-operative results. Lastly, the Kappa of the Tibia Augmentations is calculated, which was found to be Kappa = 0.775, similar to the retrospective study, indicating a substantial agreement between the two variables.

Two distinct designs were developed for both the femur and tibia components, each incorporating either the joint line or the fresh-up cut and component rotation. The four designs are depicted in Image XIV(a-d). The joint line is represented by the blue horizontal line, the fresh-up cut as the red horizontal line and the surgical epicondylar axis as the blue vertical line.

The first design of the femur component, Femur_guide_1, depicted in Image XIVa, uses the joint line as the main landmark to base the placement of the component on. The joint line is visualized as a blue line. This line rests on the lowest base of the created design, visualizing the joint line for the surgeon during revision TKA, indicating where the component should be placed. In this design, the surgical epicondylar axis is depicted as a sleeve on both sides of the

3D printed guide, parallel to the surgical epicondylar axis. The sleeve can be used to mark the surgical epicondylar axis on the bone using the diathermy. This will assist the surgeon in determining the rotation of the femur component. The second design of the femur component, Femur_guide_2, visualized in Image XIVb, uses the fresh-up cut instead of the joint line to determine the placement of the femur component. The fresh-up cut is the cut the surgeon must make to achieve the most ideal height of the joint line. The surgeon can use the bottom of the 3D printed guide as a reference to the fresh-up cut. Based on this, the surgeon can determine where he wants to make the first cut. The rotation of the component is again, based on the surgical epicondylar axis. However, instead of a sleeve, the side of the 3D-printed guide is cut off at the surgical epicondylar axis. This eliminates a part of the guide, making it smaller, and limiting the chance of hinder from soft tissue.



Imagev XIV. a) Femur_guide_1, with the surgical epicondylar axis represented by the vertical sleeve and the joint line visualized as the blue line. b) Femur_guied_2, with the sleeve cut off and the lowest point of the guide representing the fresh-up cut.

The designs of the tibia 3D printed guides follow the same principle as the femur counterparts. The first design of the tibia, Tibia_guide_1 uses the joint line of the tibia as the first referential landmark, represented as the blue line in Image XVa. The sleeve in the middle of the design represents the 18˚ angle from the middle of the tuberosity. This sleeve can be used to mark the bone with the diathermy. This can be used to align the middle of the tibia component with this line.

Lastly, in the second tibia design, Tibia_guide_2, the placement of the component is not based on the joint line, but on the fresh-up cut, visualized as the red line in Image XVa. The determination of the rotation of the component is the same as the previous design, focusing on the 18˚ angle from the middle of the tuberosity.

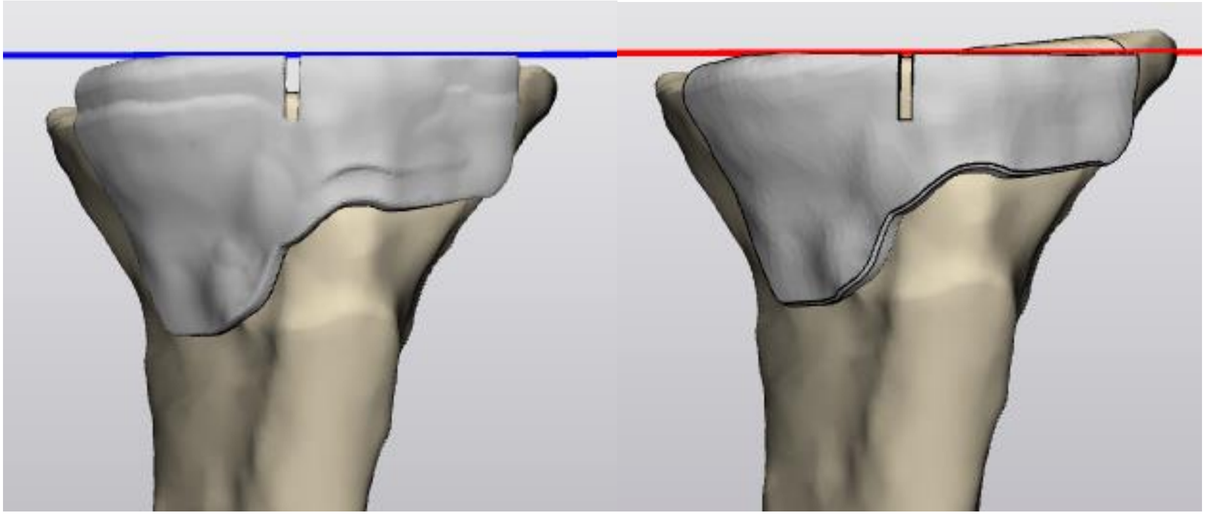


Image X. a) Tibia_guide_1, with the blue line representing the joint line. This in combination with the vertical sleeve in the middle, visualizing the component rotation. b) Tibia_guide_2, cut off at a lower point, the red line, which represents the fresh-up cut.

4. Discussion

Missing or unidentifiable landmarks can pose major issues with standard revision TKA surgery, leading to increased difficulty in surgery. 3D planning and PSI may provide increased outcomes for revision surgery, however, in present healthcare, these techniques are not commonly used and little is known about the implementation of these methods in revision TKA surgery. Therefore the goal of this thesis is to introduce 3D planning and PSI in revision TKA providing a method for the 3D planning of patients. This is achieved by providing results for both a retrospective and prospective investigation, called a mixed-methods approach, leveraging the strengths of both study designs, to explore the potential benefits of 3D planning for revision surgery. In addition to both studies, a first draft design is made for a PSI, implementing the gathered knowledge in this 3D printed guide.

The systematic review conducted in this study provides valuable insights into the use of 3D planning and PSI in revision TKA surgery. The review examined a vast database of existing literature, focusing on pre and post-operative outcomes of component alignment. Results generated by the different articles provided key outcome measurements for this thesis, such as different femoral and tibial angles and component size prediction. One notable observation from the review is the preference for 3D planning and PSI over CI in specific cases of TKA surgery. Notably, in challenging cases, where anatomical landmarks are missing, 3D planning and PSI appear as valuable tools for accurate implant placement. In short, the systematic review underscores the role of 3D planning and PSI in achieving high precision and accuracy during TKA procedures. The systematic review suggests that the ability to customize 3D templates based on the patient's anatomy allows for a tailored approach, addressing challenges posed by revision surgery. While revision TKA is a complex and time-consuming surgery, 3D planning and PSI could contribute to operational efficiency, leading to a decrease in operation time.

The retrospective study executed in this study demonstrated a remarkable accuracy for both the femur and tibia component size prediction of 90% and 80% respectively. These high accuracies showcase a strong alignment between the planned and implanted sizes during surgery. Distal femur augmentations and tibia augmentations both achieved a high accuracy as well, 80% and 90% respectively. However, with posterior femur augmentations, the accuracy dropped to 55%, suggesting potential challenges in predicting and executing posterior augmentations. Even though some outliers were noted in component placement angles, all observations fall within the acceptable range and no significant difference between pre-operative prediction and post-operative results was observed.

Different statistical analyses have been performed on the retrospective data. The distribution of all angles was found to be a normal distribution, with skewness and kurtosis values within the acceptable ranges. Therefore a paired t-test could be conducted, leading to a significant difference between the pre-operative planning and post-operative results of the FFA, p = .011, indicating notable changes in femoral component positioning. No significant differences were found for the remaining femoral and tibial angles. In addition, a scatter plot analysis and Pearson Correlation Coefficient both found a strong positive correlation for the FFA, however, not statistically significant. For the prediction of the distal femur and tibial augmentations, a high Kappa value was constructed, as the posterior femur augmentations gathered a low Kappa score.

The prospective study implemented in this study illustrated similar results for size prediction as the retrospective investigation, yielding an accuracy of 91% for femur component prediction and 100% for tibia component prediction. The augmentation prediction showcases high accuracies for the distal femur and tibia augmentations as well, with 91.6% and 87.5% accuracy respectively, yet the accuracy drops to 54.2% for the posterior femur augmentations, indicating the same challenges are present in the prospective study. Minimal variances between pre-operatively planned and post-operative results are observed for the component angles, highlighting the clinical insignificance of these differences.
The overall reliability and effectiveness of the 3D planning system, in both the retrospective and prospective study, was evident, emphasizing the potential to enhance surgical precision in revision TKA.
For the prospective data, the distribution of all angles was found to be normally distributed, with skewness and kurtosis values within the acceptable ranges. The paired t-test performed, lead to a significant difference observed for the FFA, p = .002, indicating changes in femoral component positioning between pre-operative planning and post-operative results. No significant differences were found for the other femoral and tibial angles. Pearson Correlation Coefficient found some moderate positive correlation for the FFA and MPTA, however, none of the generated results are statistically significant. Lastly, the Kappa value was constructed, leading to a high Kappa value for the distal femur and tibia augmentation, indicating high reliability and accuracy in augmentation prediction.

The retrospective study conducted in this research provides significant insights into the accuracy and performance of 3D planning in revision TKA. The remarkable accuracies for both the femur and tibia components underscore the success of 3D planning in predicting implant sizes. This is in line with the results generated by Franceschi et al., Müller et al. and Schotanus et al. who all reported a high prediction accuracy for both the femur and tibia components for primary TKA.[17,22,77] These results indicate that 3D planning can accurately predict the implant size of both components, implicating its usefulness in revision TKA surgery. The distal femur and tibia augmentation prediction exhibited similar accuracy rates, indicating the same usefulness in revision TKA. This is supported by the calculated Kappa statistics, providing a statistical level of agreement. The Kappa scores for both augmentations suggest an excellent level of agreement between pre-operative planning and post-operative results.[78] However, the prediction accuracy of posterior augmentations was observed significantly lower, indicating potential challenges in predicting the surgical outcome for the posterior augmentations. One of the causes of this problem could be the large amount of scatter on the CT scan, generated by the previous implant. These metal artefacts are most prominent around the proximal condyles, creating difficulties in segmenting the bone. This may cause differences between segmented and actual bone, creating differences between pre-operative planning and post-operative results. In addition, restoring the posterior condylar offset may be carried out by posterior translation of the femur component. Posterior translation creates a space between the component and posterior bone, requiring different augmentations. Both approaches may cause differences in the prediction of posterior augmentations. Addressing these challenges in future research is of vital importance for optimizing the use of 3D planning.

Despite the presence of some outliers in component placement angles, it is reassuring that all observations fell within an acceptable range. The absence of a significant difference between pre-operative predictions and post-operative results indicates high accuracy in predicting surgical outcomes with 3D planning. The findings of the statistical analysis further underscore the strength of 3D planning, generating only one statistical difference between pre-operative planning and post-operative results. This indicates that the 3D planning can accurately predict the placement of both the femur and tibia components. The only significant difference was in the prediction of the FFA. However, the FFA can intentionally be alternated to balance the flexion-extension gap. In more than 90% of primary TKA cases, intentional flexion was necessary to achieve equal flexion-extension gaps.[64] This could explain the significant difference of the FFA, between pre-operative planning and post-operative results.

All in all, the study's comprehensive results highlights the effectiveness and reliability of 3D planning in predicting implant sizes, specific augmentations and optimal placement angles during revision TKA surgery. The observed high accuracy rates emphasize the significance of incorporating 3D planning in the pre-operative phase, to decrease the operation time, and increase the surgical outcome of revision TKA surgery, especially in cases where anatomical landmarks are compromised.[77,79]

The prospective investigation conducted in this research aligns closely with the retrospective investigation, with both investigations underscoring the reliability and effectiveness of 3D planning in revision TKA. Notably, the size prediction of the 3D planning is extraordinarily high, even higher than the prediction accuracies of the retrospective investigation. This may be caused by the surgeons having access to the pre-operative plan before surgery. Therefore, unknowingly, changing the intended size of the implant to the pre-operatively predicted size, consequently changing the outcome of the surgery. This may also be the case for the predictions of the augmentation, scoring a similarly high prediction accuracy. This is in line with the increase in distal femur augmentation accuracy, going from 80% to 91.6%. However, for the tibial augmentations, the accuracy of the prediction drops slightly, contradicting the influence of the pre-operative plan on the decision-making of the surgeon. This is in line with the prediction results of the posterior femur augmentations, going from 55% to 54.2%, remaining nearly identical. These results underscore the potential of 3D planning to successfully predict the size and augmentation outcome of a revision surgery

For the prediction of the component placement, a paired t-test was performed. Only the difference between pre-operative planning and post-operative results for the FFA are deemed significant, indicating no significant difference between the rest of the placement angles. This indicates an agreement between the pre-operative planning and post-operative results on the placement of both the femur and tibia components. As was previously mentioned, the FFA can be adjusted to balance the flexion-extension gap, explaining the significant difference.[64] These results are identical to the outcomes of the component placement analysis of the retrospective study, indicating that 3D planning can accurately predict the outcome of a revision TKA in multiple cases and settings. This symbolizes the predictive power of 3D planning. All in all, the prospective study provided nearly identical results as the retrospective study, indicating consistency and reliability of the 3D prediction in different scenarios. This affirms the potential of 3D planning in revision TKA surgery.

The four created designs of the 3D guides were presented to an orthopaedic surgeon and a medical technician, to be reviewed based on their experience in the field of medicine. First, the femur designs were discussed, which are depicted in Image XIVa and XIVb. Both designs contained interesting points, but neither of the designs were optimal. Femur_guide_1 had an interesting approach to the depiction of the surgical epicondylar axis, as a sleeve could be used to draw the axis on the bone with the diathermy. However, questions arose whether this sleeve would be strong enough to withstand all forces, as the back part of the guide becomes very thin. This problem is tackled in Femur_guide_2 as the back part and the sleeve is cut off, compared to the previous design. This makes the design more wieldable and less fragile. The second difference between the designs is that Femur_guide_1 landmarks the joint line, while Femur_guide_2 landmarks the fresh-up cut. Both approaches were reviewed to add an extra dimension to the revision surgery, as the joint line gives the surgeon a good reference of the flexion and extension gap, whereas the fresh-up cut gives a good reference of where the first cut must be made, while also quickly showing the surgeon if any augmentations are needed to cover bone defects. Both viewpoints contain valuable information, therefore both approaches should be included in the final design of the 3D-printed guide. An additional remark was placed, as it should be possible to use the 3D guide even when the new component is in place, to check if the joint line is restored correctly.

Second, the tibia designs were reviewed, which are shown in Image XIVc and XIVd. The rotation of the tibia component is addressed similarly in both designs, as the sleeve in the middle of the guide can be used to draw a line on the bone using the diathermy. This line represents the middle of the tibia component. This method was reviewed to be a valid approach and easily achievable in revision surgery, making it an important addition to the 3D-printed guide. Tibia_guide_1 focuses on the tibial joint line, while Tibia_guide_2 focuses on the fresh-up cut. Even though both approaches highlight an important landmark, the fresh-up cut was deemed to be more important for the tibia 3D guide. This is because the tibia component is placed first, therefore limiting the use of the joint line, as the flexion and extension gap cannot be calculated yet. In addition, the fresh-up cut can be used to mark a line on the bone with the diathermy, which can be used as a reference for the first cut. This yields essentially the same results as Tibia_guide_1 when the tibia component is placed. Therefore Tibia_guide_2 was reviewed to be preferable over Tibia_guide_1. One question occurred during the review, whether the guide was not too large, as the patellar tendon attaches to the tibial tuberosity. However, the guide is made small enough to fit in the space between the attachment of the patellar tendon and the tibia plateau. During surgery the tendon is bent to the lateral side, creating space for the guide to be placed.

A new 3D guide design is made, with all the given feedback taken into account. For the final design of the 3D-printed femur guide, the designs of both guides are combined. The Femur_guide_1 is used as the base of the 3D print. Firstly, the sleeve is cut off, to make the guide more stable and less fragile, yielding the same representation of the surgical epicondylar axis as Femur_guide_2. In addition to the joint line landmark, the fresh-up cut must be included in the design, as this optimizes the overview for the surgeon. This is managed by creating a cylinder with a diameter of 1.5mm, the average diameter of a K-wire.[80]. The holes created with this cylinder can be used to insert a K-wire in, during surgery. This method is chosen, so the K-wire can be removed at any time, or else the 3D guide may be in the way, for example when the new femur component is placed. In addition, the wings at the bottom of the 3D guide representing the joint line, are shortened. This is because the wings may be too big for the 4-in-1 cutting block to fit in. Lastly, the guide is placed slightly higher, compared to the previous designs, as now the new femur component can be placed on the patient's bone without interference from the 3D-printed guide. The results of the newly created design are shown in Image XVI.

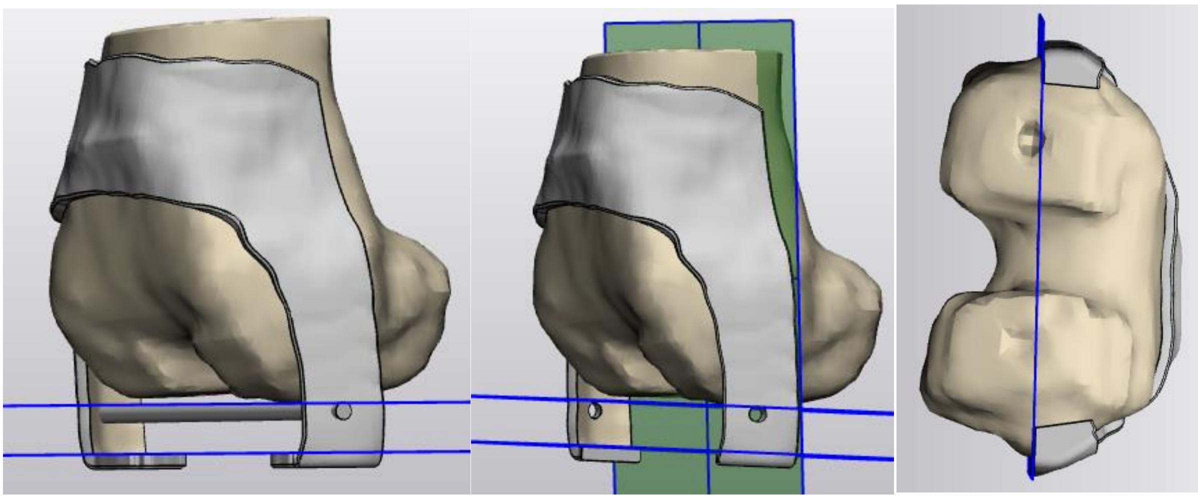


Image XVI. a) The first draft of the new design, with the cylinder representing the K-wire. b) Final design of the femur component, with the lowest horizontal line representing the joint line, the highest the fresh-up cut and the vertical blue line the surgical epicondylar axis. c) Transverse visualization of the femur 3D guide, with the smaller wings on the bottom, making the space big enough to fit the new component.

For the final design of the Tibia guide, Femur_guide_2 was used, as this guide was preferred over Femur_guied_1. However, one small change was made, as the guide is placed in a slightly endorotated position. In this position, a smaller part of the guide falls below the patellar tendon, creating more space for the guide. Altogether, the created 3D guides for the femur and tibia provide a solid base for future research. The final design of the created 3D-printed guides is shown in Image XVII.

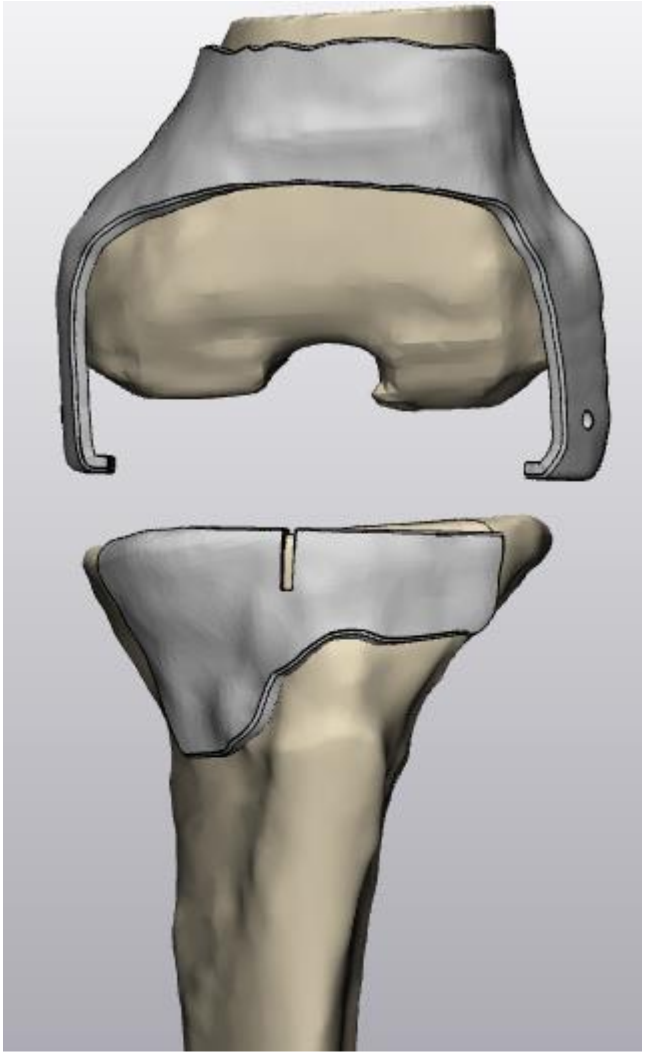


Image XVII. Final design of both the femur and tibia 3D guide.

While the results of the retrospective and prospective studies provide valuable insights into the effectiveness of 3D planning in revision TKA, it is crucial to acknowledge several limitations of these studies. These limitations should be considered when interpreting the results. One of the limitations of both the retrospective and prospective study is the relatively small number of participants included in the cohort. The study enrolled a limited number of participants because the number of patients undergoing revision TKA at the Erasmus MC, on a yearly basis, is relatively small. In addition, not all the patients undergoing revision TKA had a long-leg X-ray or CT scan available, excluding these patients from this study. The small sample size introduces the potential for selection bias and may not capture the diversity of cases and variations of surgical outcomes. Therefore, caution should be taken when generalizing the findings to a broader population, and future studies with larger cohorts are warranted to validate the current observations.

Besides the small sample size for both studies, another significant limitation is the lack of existing literature studies, specifically exploring the application of 3D planning and PSI for revision TKA surgery. The current literature predominantly focuses on primary TKA, leaving a gap in knowledge regarding the efficacy and challenges associated with revision TKA. The absence of said research limits the ability to compare the study's findings with other literature. Future investigations should address this gap, conducting more research dedicated to 3D planning and PSI in revision TKA surgeries.

The process of superimposing the pre-operative imaging onto the 3D image relies on intricate alignment, mostly based on anatomical landmarks. However, the superimposition made of these images is not infallible, and its precision may vary between the cases. The superimpose can vary in accuracy, leading to false angle calculations and can nullify any comparison made with these incorrect superimpositions. In addition, a superimpose of the post-operative results and 3D planning is also constructed, where the intraoperative changes to q patients can introduce new uncertainties in the accuracy of the superimpose. Altogether these conditions may contribute to deviations between the planned and actual outcomes of the surgery. Consequently, this variability can cause some of the outliers visible in the data, influencing the overall interpretation of the results. However, no other method was available to compare the created 3D planning with post-operative results, as X-ray imaging cannot be imported in Mimics and 3-Matic. One way to negate these variations is if future research contains post-operative CT imaging negating the variations caused by the superimpose, as the pre-operative planning and post-operative CT can be imported into the same workspace.

Revision TKA still remains a complex procedure, and the long-term success of the component placement is influenced by various factors, including implant survival, patient-specific factors, and potential complications that may arise over time. However, due to the relatively short duration of this study, a comprehensive analysis of the long-term outcomes is beyond the scope of this investigation. In addition, the outcomes of the post-operative results are assumed to be optimal. Yet sometimes post-operative results may not be optimal, as ideal placement cannot be achieved intraoperatively. This may lead to a large variance between the pre-operative planning and post-operative results. Future research should aim to extend the follow-up of the patients, enabling extended observation and contributing valuable insights into the performance of the new surgical techniques addressing the complexities of revision TKA.

Another limitation of this study could be the potential for sample bias, as the Erasmus MC primarily handle difficult cases, the study’s results may be skewed towards a population with unique medical conditions or complexities. However, it is important to acknowledge that revision TKA, which are typically challenging surgeries, often require the expertise available at a medical centre. As a result, the study’s focus on cases handled by this institution is justified given the nature of the surgeries, reducing the risk of sample bias.

The absence of a questionnaire addressing the most optimal design for the 3D guide is another limitation of this study. Due to time constraints, a comprehensive survey could not be incorporated, missing valuable information and insights into the preferences of healthcare professionals, such as orthopaedic surgeons and medical technicians. Specific features that could potentially increase the effectiveness and acceptance of the 3D-printed model are missed. Therefore future research should include a comprehensive investigation into the preferences of medical professionals about the latest design of the 3D-printed femur and tibia guides. Therefore the findings of this study should be approached with a nuanced understanding of these limitations, recognizing potential downfalls and interpreting the results in context with these findings.

The investigation revealed that 3D planning and PSI can offer potential benefits to the outcome of revision TKA. On this basis, it is recommended that future research should incorporate a larger cohort of patients. Research-based on a larger cohort can yield a better observation and stronger conclusion of the potential benefits of 3D planning and PIS. In addition, a long-term investigation of the outcomes of revision TKA should be conducted. In this investigation, Conventional Intervention is compared to the new 3D planning and PSI technique. This comparative study tries to unravel the short and long-term benefits of 3D planning and PSI in revision TKA compared to CI.

Building upon the findings of the current investigation, future research should add post-operative CT scans. These CT scans eliminate the limitations of superimposing 3D plans with 2D X-ray imaging, as post-operative CT scans can be imported into the same workspace as the 3D plan. This increases the accuracy of the comparison between pre-operative planning and post-operative results. Furthermore, a questionnaire should be included in future research, to explore the perspectives of several healthcare professionals on optimal 3D guide design, increasing the effectiveness of the 3D guide. Besides this questionnaire, a comparative investigation should be conducted to explore the potential benefits of 3D planning and PSI in revision TKA even further. As this study only yields a 3D design, future research should optimize this design and test it during revision TKA, to explore its upsides and downfalls. Additionally, the integration of artificial intelligence (AI) in revision TKA could be a promising approach. The integration of AI should focus on optimizing automatic segmentation structures of patient's CT scans. In addition, AI could optimize and automate component size prediction and component placement. Both approaches increase time efficiency and reduce human error in planning patients for revision TKA. All this will contribute to the continuous improvement of precision and automation for revision TKA surgeries.

The goal of this thesis was to explore the potential benefits of 3D planning and PSI in revision surgery. The retrospective and prospective study both showed huge potential and effectiveness for 3D planning in revision TKA. Both studies provided nearly identical results, highlighting the uniformity of 3D planning in diverse scenarios. This consistency reinforces the notion that 3D planning can be a valuable tool for enhancing precision and predictability in revision TKA surgery. 3D planning offers several potential benefits, including predicting the total outcome of a revision TKA, including size, augmentations and component placement, reduced operation time and improved surgical outcomes. Altogether providing a solid foundation for the incorporation of 3D planning in revision TKA surgery. A first design for a PSI, a 3D-printed guide, is constructed. This design incorporates several important landmarks for component placement during revision TKA, increasing the outcome of these surgeries, especially if landmarks are missing or unidentifiable. Together 3D planning and PSI have a bright future in revision surgery, however, future research needs to be conducted to implement 3D planning and PSI in modern-day healthcare.

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Appendix A

Optimizing Total Knee Arthroplasty: A Comprehensive Review of 3D Planning and Patient-Specific Instruments in Future Revision Surgery

1. Abstract

This article discusses the increasing use of new surgical techniques in Total Knee Arthroplasty (TKA) including 3D planning and Patient Specific Instruments (PSI), to improve prosthesis positioning and reduce malalignment. The study aims to systematically review existing literature, to evaluate the potential benefits 3D planning and PSI in TKA and its applicability in TKA revision surgery. This will be done by comparing the accuracy of pre-operative 3D planning vs. post-operative CT-scans, MRI-scans and X-rays.

The data search included various databases, with a search performed on December 12, 2022. Specific search terms were used to identify studies investigating 3D planning and PSI in TKA. The generated articles were screened and included in the subsequent data analysis if they centred on 3D planning and/or PSI in TKA and scored at least four points on the quality assessment QUADAS-2 tool. Important outcome measurements of this review include: prediction of planned prosthesis size, femoral rotation angle, mechanical lateral distal femoral angle, mechanical medial proximal tibial angle, posterior tibial slope and tibial rotation.

16 articles were analysed to asses TKA outcomes, with a specific focus on pre and post-operative results using 3D planning and PSI. While some significant variations were noted in femoral and tibial component alignment using 3D planning, PSI demonstrated advantages is sagittal tibia alignment and femoral component rotation. However, few of the important outcome measurements proved to be significantly different, indicating no difference between PSI and conventional intervention (CI). Yet, in some cases in revision surgery, PSI is preferred above CI, in particular when anatomical landmarks are missing or unidentifiable, PSI can provide valuable insights on the placement of the prosthesis.

3D planning plays an important role in accurately predicting outcomes of TKA surgery and together with PSI it can consistently acquire high accuracy in replicating pre-operative plans, making it a valuable tool for revision TKA. More importantly, the review provided important outcome measurements for the thesis, emphasizing the significance of 3D planning and the importance of surgeon involvement in examining the plans, while also highlighting the potential benefits and applicability of PSI in TKA revision surgery.

2. Keywords

Total Knee Arthroplasty (TKA), Revision Surgery, 3D planning, Patient-Specific Instrument (PSI), Prosthesis, Orthopedics, Implant Alignment, Implant Positioning, Pre-operative Planning.

3. Introduction

The number of Total Knee Arthroplasty (TKA) procedures continuously increases, with good results. In the last few years, new surgical techniques have been developed to improve the positioning of the prosthesis, increasing clinical and functional outcomes. One of these new techniques is 3D planning. 3D planning is an increasingly used technique in orthopedics, in which the surgery is pre-operatively planned in a 3D program.**[1]** This pre-operative plan gives the surgeon an overall view of the situation in 3D. However, even with 3D planning, the surgeon relies on mechanical alignment during surgery, which could still lead to malalignment or malpositioning of the implant. Coronal malalignment is the most common cause of revision surgery.**[2]** To tackle the malalignment and malpositioning of the implant, new techniques are on the rise.

Patient Specific Instruments (PSI) is a surgical technique that provides a pre-operative 3D model and custom fit 3D printed guides for the femur and tibia for each patient using bone models based on pre-operative computed tomography (CT) or magnetic resonance imaging (MRI) imaging. This technique reduces operative time and number of instrumentation trays.**[3]** Besides, PSI is expected to increase the accuracy of component positioning in TKA.**[2-4]** This and other research in this field, suggest that 3D planning with PSI could also deliver promising results in TKA revision surgery. Compared to normal TKA surgery, revision TKA is significantly more difficult and the outcome is extremely dependent on the experience of the surgeon.**[2]** As a consequence of these inaccuracies, PSI is suggested to be an interesting approach to revision surgery.

However, to our knowledge, no systematic review has yet been published focusing on the potential added value of 3D planning in combination with PSI in the field of TKA revision surgery. Additionally, almost no articles are yet published, focusing on the combination of 3D planning, PSI and revision arthroplasty. Due to the lack of articles, this review will focus on 3D planning and PSI in primary TKA surgery and the advantages and downsides of this technique. These findings will then be used on further research in this thesis, on 3D planning, PSI in revision TKA.

This study aims to increase the knowledge of 3D planning and PSI in (revision) TKA, in order to better understand the upsides and downfalls of this new technique. In addition, this study also aims to systematically review all available literature regarding the potential of 3D planning using and PSI in TKA. This will be done by comparing the accuracy of pre-operative 3D planning vs. post-operative CT-scans and X-rays. In addition the accuracy of the placement and size prediction of 3D planning is compared to the outcome of the conventional intervention. All in order to understand the possibilities and limitations of 3D planning and PSI in TKA surgery and translating these possibilities and limitations to the use of 3D planning and PSI in revision TKA.

4. Methods

Data search

In this study all studies in which 3D planning of the TKA is compared to either itself (pre-operative 3D planning vs. post-operative CT-scan/MRI-scan/X-ray) or one or more standard modalities for evaluating the accuracy and outcome of these modalities were included. The databases used in this review was Medline ALL, Embase, Web of Science Core Collection and Cochrane Central Register of Controlled Trials. The literature search was performed on December 12., 2022. The first selection was done by using the following combination of search terms for the databases:

Medline ALL

(Arthroplasty, Replacement, Knee / OR * Knee Prosthesis/ OR ((total ADJ3 knee ADJ3 (arthroplast* OR replacement* OR prosthe*)) OR tka OR tkr).ab,ti. OR (knee ADJ3 (arthroplast* OR replacement* OR prosthe*)).ti.) AND (Patient-Specific Modeling / OR ((Models, Biological/) AND (Printing, Three-Dimensional/)) OR (((patient-specific* OR 3D OR 3-D OR 3Dimension* OR 3-Dimension* OR three-Dimension* OR personalized* OR personalised*) ADJ6 (guide* OR model* OR template* OR instrument* OR alignment*)) OR cutting-guide* OR ((patient-specific* OR personalized* OR personalised*) AND ((3D OR 3-D) ADJ3 print*))).ab,ti. OR patient-specific*.ti.) NOT (*Robotic Surgical Procedures / OR (unicompart* OR uni-compart* OR robot*).ti.) AND english.la. NOT (exp animals/ NOT humans/)

Embase

('total knee arthroplasty'/de OR 'knee replacement'/mj OR 'knee prosthesis'/mj OR 'knee arthroplasty'/mj OR ((total NEAR/3 knee NEAR/3 (arthroplast* OR replacement* OR prosthe*)) OR *tka OR tkr):ab,ti OR (knee NEAR/3 (arthroplast* OR replacement* OR prosthe*)):ti) AND ('patient specific instrumentation'/de OR 'patient specific instrument'/de OR ((model/de OR 'biological model'/de OR 'prosthetic alignment'/de) AND ('three dimensional printing'/de)) OR (((patient-specific* OR 3D OR 3-D OR 3Dimension* OR 3-Dimension* OR three-Dimension* OR personalized* OR personalised*) NEAR/6 (guide* OR model* OR template* OR instrument* OR alignment*)) OR cutting-guide* OR ((patient-specific* OR personalized* OR personalised*) AND ((3D OR 3-D) NEAR/3 print*))):ab,ti OR patient-specific*:ti) NOT ('unicompartmental knee arthroplasty'/mj OR 'unicompartmental knee prosthesis'/mj OR 'robot assisted surgery'/mj OR (unicompart* OR uni-compart* OR robot*):ti) NOT [conference abstract]/lim AND [english]/lim NOT ([animals]/lim NOT [humans]/lim)*

Web of Science Core Collection
TS=((((total NEAR/2 knee NEAR/2 (arthroplast OR replacement* OR prosthe*)) OR tka OR tkr)) AND ((((patient-specific* OR 3D OR 3-D OR 3Dimension* OR 3-Dimension* OR three-Dimension* OR personalized* OR personalised*) NEAR/5 (guide* OR model* OR template* OR instrument* OR alignment*)) OR cutting-guide* OR ((patient-specific* OR personalized* OR personalised*) AND ((3D OR 3-D) NEAR/2 print*))))) NOT TI=((unicompart* OR uni-compart* OR robot*)) NOT DT=(Meeting Abstract OR Meeting Summary) AND LA=(english)*

Cochrane Central Register of Controlled Trials
(((total NEAR/3 knee NEAR/3 (arthroplast OR replacement* OR prosthe*)) OR tka OR tkr):ab,ti OR (knee NEAR/3 (arthroplast* OR replacement* OR prosthe*)):ti) AND ((((patient NEXT specific* OR 3D OR 3 NEXT D OR 3Dimension* OR 3 NEXT Dimension* OR three NEXT Dimension* OR personalized* OR personalised*) NEAR/6 (guide* OR model* OR template* OR instrument* OR alignment*)) OR cutting NEXT guide* OR ((patient NEXT specific* OR personalized* OR personalised*) AND ((3D OR 3 NEXT D) NEAR/3 print*))):ab,ti OR patient NEXT specific*:ti) NOT ((unicompart* OR uni NEXT compart* OR robot*):ti)*

These search strings were drafted with help of the Erasmus MC Medical Library.

Study selection
After the first selection procedure, the title and abstract of the studies was scanned to make an adequate selection of the remaining articles. In this selection, non-comparative studies, reviews, non-English articles, articles without a full text available and articles that did not focus on the 3D planning of the TKA procedure, with or without PSI were excluded. When there was doubt that a study did or did not meet the exclusion criteria, extra information was extracted from the full text of the article before a final decision was made.

After the first selection procedure, the full text of the remaining articles was read. During this selection the articles were assessed on eligibility. The eligibility of the articles was evaluated by means of the following inclusion criteria: firstly, the article should focus on the 3D planning of TKA using PSI's. Secondly the article should compare the 3D planning of the TKA using PSI, with either the accuracy of the PSI (pre-operative planning vs. post-operative results on CT scan/X-ray), or compare it with other modalities including but not limited to standard surgery, navigation surgery, or robotic surgery. Besides these inclusion criteria, if the article consists of results of 3D planning and PSI during revision TKA, the article is also included.

Quality assessment
The quality of the remaining studies after the second selection was assessed using the QUADAS-2 tool **[17]**. This tool has seven criteria, each worth one "point", that are used to rate the quality of the study, mainly focusing on the risk of bias. Points were rewarded to criteria that relate to the four key domains of the QUADAS-2 tool: Patient Selection, Index Test, Reference Standard and Flow and Timing. If studies scored more than three points, they were qualified as "high quality" and articles that scored 3 point or lower were qualified as " bad quality" articles and were excluded from this review. All the articles that were awarded four or more points were included in the data analysis

5. Results

Study Selection

Articles were selected using the previously stated combination of search terms. This search string resulted in 1336 articles. A total of 1242 articles were excluded for a variety of reasons. Some of these reasons are: no full text available, articles that were non-comparative, articles containing no full text in English and studies that compared the modality with neither itself (pre-operative 3D planning vs. post-operative CT-scan/X-ray) or other modalities. After this first selection 94 articles remained and were assessed based on the full article. During this assessment the articles were evaluated on the eligibility of the study. The eligibility of the articles was scored by using several exclusion criteria.

37 articles were excluded because they looked at a different field of interest as was aimed by this article. 20 articles were excluded because they did not compare either, the used modality with another modality, or compared pre-operative planning with post-operative scans. 15 articles were excluded because the article did not contain results about TKA using PSI's. Lastly six articles were excluded because the details in the articles were insufficient and valid conclusions could not be drawn from the results, leaving 16 articles.

After the eligibility, a quality assessment was performed on the remaining articles to exterminate poorly conducted research from the review. The quality of the remaining 16 articles was reviewed based on the QUADAS-2 tool **[17]**. The scores of three articles was lower or equal to the predefined score of 3, leading to exclusion of these articles. The QUADAS-2 scores of

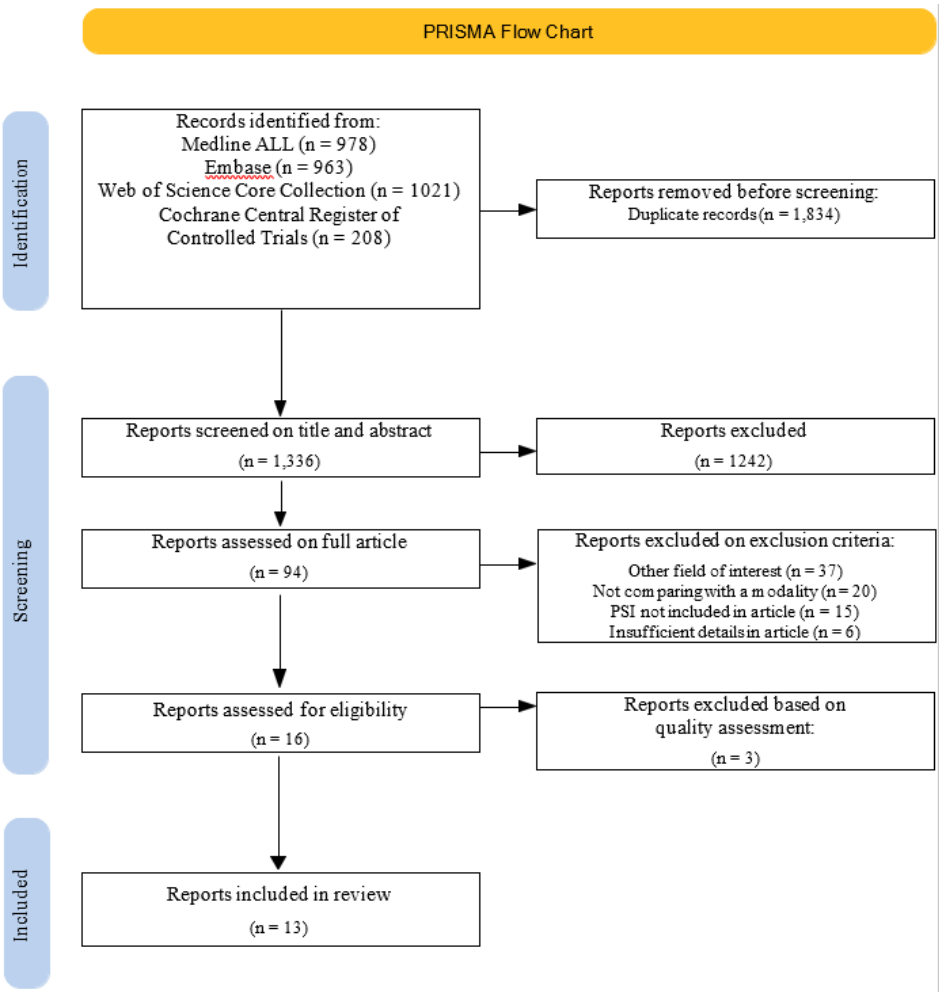

Figure 1. PRISMA flow diagram, subdivide in articles identified, screened and included in this review.

each articles is displayed in the Appendix I, *Table 1*. The remaining 13 articles were included in this review and used for the data analysis. The full PRISMA Flow Diagram is visualized in *Figure 1*. The main results of the articles are presented in *Table 2 and 3* (Appendix I).

Pre-operative versus post-operative
Different articles viewed the results of the PSI pre-operative plan versus the post-operative results. The pre-operative 3D plans were compared with the post-operative CT scans of the patients.

Femoral component
The results gathered by Franceschi et al. **[3]** conclude that the planned size of the femoral component can be accurately predicted in 100% of the cases. This claim is supported by Müller et al. **[9]**, that found the prediction accuracy of the femoral component to be 91.2%. Schotanus et al. **[15]** also investigated the femoral component prediction and found this accuracy to be 93.9% when predicted by the surgeon, however if the technician predicted the size of the femoral component, the accuracy dropped significantly to 79.8%.

Leeuwen et al. **[6]** examined the femoral rotation angle and the mechanical lateral distal femur angle, which were both found to be significantly different from the pre-operative planning. The difference in femoral rotation angle is found to be 1.2 ± 1.5 °, while the difference for the mechanical lateral distal femur angle was 90.5 ± 1.4 ° respectively ($P<0.001$). This is the only article that found a significant difference between the pre-operative plan and the post-operative results of the CT-scan. Franceschi et al., Moopanar et al., Nabavi et al., Paratte et al. and Sotozawa et al., **[3,8,11,13,16]** examined the femoral rotation angle, but found no significant difference between planned and post-op results. In addition, Franceschi et al., Gaukel et al. and Müller et al. **[3,4,9]** looked at the mechanical lateral distal femoral angle, but these articles also found no significant difference between the pre-operative planning and the post-operative results.

Besides the femoral rotation angle and the mechanical lateral distal femoral angle, the femoral flexion angle is also examined. Although various studies investigated the difference in pre and post-operative results of this angle, none of the articles reported any significant difference between the pre and post-operative alignment angles. The difference between the pre-operative plan and post-operative results of the femoral flexion angle varied from: 1.0 to 2.6 ± 1.8 mm.**[4,10,12,14]**

Lastly, most articles found a consensus for the maximal variation from the predefined 3D planning. As stated by Nabavi et al.,**[10]** the planning is acceptable if the outcome lies within the following margins: ± 3 ° of the planned angles. Based on these margins, the following results are gathered. As reported by Parratte et al.,**[12]** 100% of the femoral rotation angles was in range of the ± 3 ° variation between the pre and post-operative plan. This is supported by Moopanar et al.,**[8]** who found a similar result: 96.2%. However the variation for the femoral rotation angle in Sotozawa et al.,**[16]** was reported lower than 82%, however these results were not deemed significant. For the ± 3 ° margin of the femoral flexion angle, the results varied from 87.5% to 98% according to Gaukel et al.,**[4]** and Nabavi et al.,**[10]** respectively. The percentage of the mechanical femoral angle planned within the ± 3 ° margin was deemed between the 94% and 99%, as claimed by Franceschi et al.,**[3]** and Moopanar et al.**[8]** Lastly the mechanical lateral distal femoral angle was correctly planned within the ± 3 ° interval varied between 85.3% and 89.6% as determined by Müller et al.,**[9]** and Gaukel et al.**[4]**

Tibial component

Secondly, several articles not only studied the femoral component alignment pre and post-operatively, but also the tibial component alignment. Franceschi et al. **[3]** for example, also studied the accuracy of the tibial component, which was found to be 96%. Although the tibial accuracy was slightly lower than the femoral component, it was not found to be significantly different. However when investigating the difference between the predicted pre-operative plan made by the surgeon, 91.1% compared to the plan made by the technician, 82.6%, a significant difference can be found between these pre and post-operative results.

Several articles also reported outcomes of three different results, the mechanical tibial angle, the posterior tibial slope and the medial proximal tibial angle. For all these angles the pre-operative plans were compared with the post-operative images, constructing the difference in the TKA prosthesis placement. The mechanical tibial angle varied between 90.1 ± 2.4 ° and 91.0 °, indicating little difference between the pre and post-operative results.**[3,6,8,10,14,16]** None of these articles reported a significant difference for the outcome of the mechanical tibial angle. No significant results were also reported for the posterior tibial slope, even though these results varied more: from 2.2 ± 1.5 ° to 4.9 ± 2.7 °, although it was no defined what the pursued angle was.**[3,4,8,10,12]** Lastly the results medial proximal tibial angle were described in three articles, varying between 87 ± 1.7 ° and 96.0 °, but these also yielded no significant difference between the pre-operative and post-operative outcomes.

Some results were not reported by many of the selected articles. The coronal tibial alignment is only reported once, by Nabavi et al.,**[10]** described as an insignificant difference of 1.0 °. Two other articles reported tibial rotation as one of the outcomes, which varies from -2.6 ± 6.3 ° to 6.8 ± 4.1 °, indicating a big difference in outcome between these articles. Even though the big difference between the articles, the articles itself reported no significant difference in tibial rotation between pre-operative and post-operative angles.

HKA

Lastly, some articles regarded the HKA a valid outcome to determine the accuracy of the placed prosthesis. The HKA varied between the different articles from 178.0 ° to 184.1 ± 3.1 ° **[3,4,8-10,12,14]**, yet none of these findings found a significant difference between the planned placement and the actual placement of the prosthesis. Most articles only reported a difference of one degree, leading to a stable prediction of the HKA during the planning of the placement of TKA.

Patient-Specific Instrument versus Conventional Intervention

Besides the difference between the pre-operative plan versus the post-operative results, some articles also investigated the difference in outcome between surgeries performed with a Patient-Specific Instrument versus Conventional Intervention. In this case the Conventional Interventions is defined as TKA surgery, performed with the use of standardized equipment and instrumentation. During this surgery a four-in-one cutting block is used for the placement of the femoral component and for the tibial component a tibia cutting block is used. Both cutting blocks are provided by Smith & Nephew. The outcome of the PSI and CI was divided in different categories: femoral component, tibial component HKA, outliers and other.

Femoral Component

The first results for the femoral component focusses on the Femoral Component Rotation angle, which was studied by Ferrerra et al., who found the delta rotation angle of the PSI to be 0.3 ± 0.8 ° and of the CI to be -0.9 ± 2.0 °**[2]**. The difference in rotation angle between the PSI and the CI is reported to be significantly different in favor of the TKA perfomed by PSI, which can reach a higher accuracy in femoral component rotation. However these significant results are not supported by the remaining articles. Kosse er al., found the femoral component rotation to be 1.6 ± 2.1 ° for the PSI and 1.2 ± 2.7 ° for the CI. **[5]** Besides the results of Kosse et al., Sotozawa et al., reported similar results regarding the femoral component rotation, with a delta of -1.5 ± 2.5 ° and -0.4 ± 3.4 ° for the PSI and CI respectively. **[16]** Neither of these results found a significant difference between the PSI and the conventional intervention.

Another result investigated in several articles was frontal femoral alignment of the prosthesis. Besides several articles looking at this outcome, none of the articles presented a significant difference between the frontal femoral alignment achieved by the PSI or by the CI. The results varied between 88.8 ± 2.0 ° and 95.1 ± 4.4 ° for the PSI and 89.2 ± 2.1 ° and 94.5 ± 4.2 ° for the CI. **[2,5,12,14,16]** These results are very similar between the groups, leading to no significant difference.

Lastly for the femoral component, several articles looked at the sagittal femoral angle, where two articles found a significant difference between the PSI and the CI. AlShammari et al., investigated the sagittal femoral angle and found that the delta difference between the planned sagittal angle and the achieved sagittal angle was significantly better in the CI group: 3.2 ± 2.5 °, compared to the PSI group: 5.8 ± 3.7 °.**[14]** This statement is supported by Ferrera et al., who yielded similar results with a delta difference of 1.5 ± 2.0 ° for CI compared to 3.6 ± 1.0 ° for the PSI, leading to an advantage of conventional intervention over patient-specific instrumentation for the sagittal femoral angle.**[2]**

Tibial component

Ferrera et al., and Kosse et al., investigated not only the sagittal alignment of the femoral component, but also the sagittal alignment of the tibial component. Both articles found a significant difference between the sagittal tibial alignment of the TKA placed with PSI or with CI. Ferrera et al., found the variation in sagittal alignment of the PSI to be 5.9 ± 0.7 ° compared to the 7.0 ± 1.6 ° for the CI.**[2]** Kosse et al., supported these findings and reported the variation in sagittal alignment of the tibia to be 2.6 ± 3.2 ° for PSI and 7.8 ± 2.8 ° for CI, leading to a significant difference in favour of the placement using PSI.**[5]**

Aside from the sagittal tibial alignment, two other outcomes were investigated by several articles: the tibial component rotation angle and the frontal tibial alignment. However, unlike the outcome of the sagittal alignment, with both these other outcomes no significant difference is found between the PSI and the CI. The variation in tibial component rotation ranged between -11.8 ± 3.2 ° and 15.7 ± 7.6 ° for the PSI, whereas the results of the CI ranged between -8.7 ± 3.6 ° and 19.0 ± 8.3 °. **[2,5,12,16]**

HKA

In addition to the femoral component and the tibial component, various articles also investigated the outcome of the TKA placement on the hip-knee angle. The delta difference between the planned HKA and the placed HKA is measured in several articles leading to the following results. The HKA varied from 0.1 ° to 4.1 ± 3.1 ° for the PSI compared to the CI, which varied from 0.5 ° to 4.0 ± 2.7 °, leading to no significant difference between both groups. This is supported by Kosse et al. and AlShammari et al.**[5,14]**

Outliers

Besides the three previously mentioned categories, when comparing the PSI to the CI, some articles added other categories to determine a difference between these two methods. One of the added categories is the comparison of the number of outliers between the two groups. Gaukel et al. and Sotozawa et al. looked at different outliers for important angles in the placement of the prosthesis. Both articles found several outliers for the mechanical lateral distal femoral angle and the medial proximal tibial angle. The difference in planned alignment versus post-op alignment for the mLDFA varied from 10.4% to 18% for the PSI compared to 6.6% to 12% for the CI. **[4,16]** The difference in planned alignment versus post-op alignment for the MPTA varied from 3.0% to 12% for PSI compared to 3.0% to 20% for the CI. However neither of these outliers provided a significant difference. Yet one outlier found by Gaukel et al. was found to be significantly different between the PSI and the CI group. Gaukel et al., found the outliers of the HKA were significantly lower for the PSI group: 3.0% compared to the CI group: 11.3%, leading to a higher percentage of outliers for the HKA angle during the conventional intervention. Even though the same surgical technique was used, significantly less cases were outside of the postoperative ± 3° range when using single-use PSI instrumentation as compared to standard instruments. **[4]**

Others

Lastly there are other results some articles investigated that could indicate a better performance from either methods. Ferrera et al. investigated the influence of both methods on the average blood loss during the surgery. They found that the average blood loss during PSI was 140 ± 56.7 ml, while the average blood loss during CI was 290 ± 112.5 ml.**[2]** This is supported by AlShammari et al. who found the average blood loss to be 162.1 ± 84.4 ml for PSI and 150 ± 85.8 ml for CI.**[14]** However there is no significant difference between the two methods. In addition to the average blood loss, mean operation time was another outcome that was investigated by two other articles. The mean operation time varied from 40.4 ± 5.6 min to 66 ± 15 min for PSI compared to 68 ± 10 min for the CI, indicating no significant difference in operation time between the two methods.**[5,9,11]**

6. Discussion

The aim of this review was to provide an overview of the potential of Patient-Specific Instruments and the accuracy of this method in comparison to Conventional Intervention in TKA surgery. When evaluating the results gathered from all the different articles studied in this review it can be generally concluded that 3D planning and PSI has an easily achieved accuracy that does not vary substantial from the pre-operative plan, leading to a similar reliability compared to CI. In addition, 3D planning and PSI can be used to achieve a higher post-operative accuracy during revision TKA, especially in cases where the anatomical landmarks are hard to identify.

Looking at the results of the pre-operative plan versus the post-operative results, it can be seen that there are only a few results that are significantly different between the pre and post-operative results for the femoral component. These findings apply to the femoral rotation angle and mechanical lateral distal femur angle. This could lead to the conclusion that the pre-operative plan differs from the post-operative result in these angles and therefore cannot accurately be translated from planning to post-op result.
However if we look more closely to these results we can see that the difference only varies from the pre-operative plan with 1.2 ± 1.5 ° and 90.5 ± 1.4 ° for the femoral rotation and for the LDFA respectively.**[6]** Even though these variations are small, it still provides possible shortcomings of the

implementation of pre-operative 3D planning during surgery. Yet, because these variations are so small and do not lead to large malpositioning of the prosthesis, they are deemed clinically irrelevant.
Besides these differences, no other articles found a significant difference between the pre and post-operative results**.** In addition some articles looked at the planned size of the prosthesis before the surgery and comparing this with the post-operative size of the prosthesis. Franceschi et al. found that in 100% of the cases the prosthesis can be accurately predicted based on the 3D plan, which could significantly improve operation time and require less surgery trays to be used during surgery.**[4]** Combining these findings, it can be assumed that pre-operative planning can accurately predict the placement and the size of the femoral component in TKA surgery.**[3,4,8-10,12,14]**

For the tibial component roughly the same outcomes were used to describe the comparison between the pre-operative planning and the post-operative results. However for the tibial component, none of the articles reported a significant difference between the pre and post-operative results. This leads to the assumption that for the tibial component the pre-operative plan can successfully predict the placement and size of the tibial component in TKA surgery.
Although none of the results are significant, a large variation between the planned and achieved results can be seen as reported by Parratte et al. who found a 6.8 ± 4.1 ° variation in tibial rotation.**[6,12]** compared to the . Even though these results are not deemed significantly different from the pre-operative plan, a large variation in these results, as is demonstrated above, should still be taken into account in future research.
Lastly Schotanus et al. reported a significant difference in the planned size of the prosthesis and the post-operatively placed size between a surgeon and technician: 93.9% vs 79.8% for the femoral component and 91.% vs 82.6% for the tibial component respectively.**[15]** However these results may be biased, because during surgery, the surgeon is the decisive factor and must decide which size prosthesis is placed. Therefore a surgeon is more likely to choose his predicted size over the size of the technician, leading to an increased prediction by the surgeon. Yet, this still provides valuable information for the rest of the thesis. Therefore the 3D plannings that are made during this thesis will always be submitted to a surgeon for approval, eliminating this inconsistency.

Besides the comparison of the pre-operative plan with the post-operative results, some articles compared the PSI technique with conventional intervention. As previously mentioned the conventional intervention is defined as TKA surgery, performed with the use of standardized equipment and instrumentation. In total six articles looked at the difference in performance of the PSI compared to the CI.

For the femoral component two significant results are found by Ferrera et al. They reported a significant difference in femoral component rotation and in sagittal femoral alignment. Firstly the femoral component rotation was significantly better in the PSI group compared to the CI group, meaning the femoral rotation could be more accurately achieved with the use of PSI.**[2]** During CI the rotation of the femoral component is based on the surgical epicondylar axis. This axis is based on the medial and lateral epicondyle. However finding these anatomical landmarks is dependent on the experience of the surgeon. This is negligible in PSI surgery, as the PSI is used to determine the femoral rotation, leading to a better outcome in femoral rotation.
Secondly Ferrera et al. found a significant difference in the sagittal femoral alignment

of the prosthesis, which was better in the CI group compared to the PSI group.**[2]** This claim is supported by AlShammari et al.**[14]** These authors claim these results are justified by both the difficulty of defining the correct landmarks on the surgical anatomical axis and the fact that the flexion of the component is less predictable in the pre-operative planning software.**[2]** In addition, the sagittal alignment is strongly determined by the intramedullar fixation, where a longer intramedullary rod increases the extension of the component due to the curvature of the femur.**[2,14]**

Besides, the femoral component, Ferrera et al. also investigated the tibial component and found one significant result. According to Ferrera et al. the sagittal tibial alignment is significantly better for the PSI group compared to the CI group.**[4]** This is supported by Kosse et al, who found similar results, concluding a better sagittal tibial alignment for patients treated with PSI instead of CI.**[5]** Besides the significant difference in the sagittal tibial alignment, no other outcomes are deemed statistically different. However in difficult cases, where anatomical landmarks are difficult to identify, Sotozawa et al. described an added benefit of using PSI, specifically the 3D planning, which can give a better overview pre-operative which could help with decision making.**[16]** Therefore, for each revision TKA during this thesis, a 3D planning is made to aid the surgeon during important decisions.

Lastly, several other outcomes are investigated, such as HKA, mean operation time, mean blood loss and outliers. Only Gaukel et al. found a significant difference in outliers of the HKA between the PSI and CI groups, where the PSI group had 3% outliers, the CI group has 11% outliers.**[4]** No specific reason for the increase in outliers was given by the authors. However, it is assumed that during conventional intervention, everything is extremely dependent on the experience of the surgeon, while during PSI, the experience of the surgeon is less important, as the PSI guides the surgeon during the surgery. Therefore yielding less outliers.**[4,16]** These outcomes provides a solid foundation for the usage of PSI over CI in more difficult cases.

There were several limitations to the articles studied in this review. Firstly, some articles included in this review had a low number of participants. For example Ferrera et al. only had 15 patients included, as well as AlShamarri et al. and Leeuwen et al. who included 29 and 39 patients respectively.**[2,6,14]** This can consequently result in less representative data and could possibly lead to false (non-) significant results.
Secondly there is a large variation in results reported between studies. The range of the tibial rotation reported by the articles varies between -11.8 and +15.7, which is a variation of nearly 28 °.**[2,5]**
Lastly, some studies neglect to distinctly make a comparison between the either the pre and post-operative results or between PSI and conventional intervention, using clear, unambiguous parameters as their primary outcome.**[11]** These articles provide no further evidence during this investigation and should not have been included in this review.

Furthermore, this systematic review also has its limitations. First of all, the studies used different outcome measurements to define gathered results. Therefore the results can be difficult to interpret as they investigate a different outcome. Besides the wide variety of outcome measurements, it is also notable that although there are many results, only a few of them are deemed significant. This proves PSI is an accurate and reliable method for TKA. However is also proves that PSI is not significantly better than the conventional intervention, leading to the question whether PSI should be used. Yet, as already stated several times before, this review is providing important information on 3D planning and PSI in TKA. This information is key in the investigation in the rest of this thesis. Therefore, even though the results are not significant, it still provides insights for this thesis. In addition, due to the lack of comparable data and the difference in outcome measurements, no meta-analysis could be performed. A meta-analysis could have provided us with a scaling factor, which could eliminate the variation in the articles with a low population and would have led to less bias in this thesis.

Even though this review has its limitations, combining all these gathered results provide important knowledge for the rest of this thesis. During the thesis, multiple different 3D plannings will be made. With this literature study in mind, we now know that for planning the femoral component, the femoral rotation angle and the LDFA are of importance, because these angles are most likely to differ from the pre-operative planning. The same goes for the tibial rotation angle for the tibia component. In addition, when planning the placement of the component, the 3D planning should always be examined by an orthopaedic surgeon, since they obtain better prediction results.**[3,4,8-10,16]** 3D planning could also have an added benefit in difficult cases, in which a 3D planning can give a better overview and could help the surgeon make difficult decisions. Therefore for each revision TKA, a 3D planning will be made to aid the surgeon.
As for the designing of the PSI, the sagittal femoral alignment and femoral rotation needs to be included, to increase the accuracy of the PSI. For the tibial component the sagittal tibial alignment is of key importance and should therefore be included in the PSI design. Together with a PSI, 3D planning will assist the surgeon in revision TKA and eliminate certain difficulties during this procedure.
Therefore these outcomes provide a solid foundation for the usage of 3D planning and PSI in revision surgery.**[2,4,5,14,16]**

In conclusion, articles studied in this systematic review show that when evaluating the results, it can be concluded that PSI has an high accuracy based on the comparison of the pre and post-operative results and can therefore be used to achieve a higher post-operative accuracy during TKA surgery. However when comparing PSI with the conventional intervention, few significantly different results are found, leading to the conclusion that PSI yields the same results as CI with standard instrumentation. However, in difficult cases, where the anatomical landmarks are unidentifiable or substantial deformities are present, PSI can yield better results. This is especially the case during revision surgery, where both factors are often present. Therefore 3D planning and PSI can play an important role in revision TKA surgery.

Further research on this subject is needed, using larger study populations and standardized outcome measurements as primary outcome. To conduct data that can be used in a broader clinical area, more research needs to be done on the use of PSI during TKA revision surgery, as this surgery is even more complicated and PSI could play an important role in addressing problems with this revision surgery. This will depict a better, more reliable overview of the possibilities, advantages and disadvantages of 3D planning and PSI in this particular field

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Appendix I.

QUADAS-2 Tool

	Risk of Bias				Applicability Concerns			
Study	Patient Selection	Index Test	Reference Standard	Flow and Timing	Patient Selection	Index Test	Reference Standard	Total Score
De Santis et al., 2017 (1)	**+**	**+**	**?**	**-**	**?**	**+**	**?**	**3**
Ferrara et al., 2015 (2)	+	-	?	-	+	+	+	4
Franceschi et al., 2014 (3)	+	+	+	+	?	+	?	5
Gaukel et al., 2022 (4)	+	-	-	+	+	+	+	5
Kosse et al., 2018 (5)	+	+	+	?	+	+	+	6
Leeuwen et al., 2015 (6)	?	+	-	+	+	-	+	4
León-Muñoz et al,. 2020 (7)	**-**	**+**	**-**	**-**	**+**	**-**	**+**	**3**
Moopanar et al., 2014 (8)	+	?	+	+	+	?	+	5
Müller et al., 2022 (9)	+	+	-	+	?	+	?	4
Nabavi et al., 2017 (10)	+	?	-	+	+	+	+	5
Nizam et al., 2018 (11)	?	+	?	+	+	-	+	4
Parratte et al., 2013 (12)	+	+	+	-	+	+	+	6
Qiu et al., 2017 (13)	**+**	**?**	**+**	**-**	**?**	**+**	**?**	**3**
AlShammari et al., 2021 (14)	+	+	+	+	+	-	?	5
Schotanus et al., 2017 (15)	+	?	+	+	?	+	+	5
Sotozawa et al., 2022 (16)	-	+	+	-	+	?	+	4

Note. + = Low Risk; - = High Risk; ? = Unclear

Bold articles scored < 4 points and are therefore excluded from the data analysis of this review

Table 1. QUADAS-2 tool. All articles are awarded points based on seven criteria. Articles that scored < than 4 points are excluded from the review.

Pre-operative plan vs. post-operative alignment

	Femoral Component						**Tibial Component**							**HKA**
Study	*Planned size prosthesis (%)*	*Within planned ± 3 mm interval (%)*	*Femoral rotation angle (°)*	*Femoral flexion angle (°) (delta)*	*Mechanical femoral angle MFA (°) (delta)*	*Mechanical Lateral distal femoral angle (°)*	*Planned size prosthesis (%)*	*Within planned ± 3 mm interval (%)*	*Mechanical tibial angle (°)*	*Posterior tibial slope (°) (delta)*	*Medial proximal tibial angle (°)*	*Coronal tibial alginment (°)*	Tibial rotation (°) (delta)	
Franceschi et al., 2014 (3)	Femoral component: 100	Frontal: 94 Sagittal: 71 Transverse: 88	0.0 vs. 0.0 ± 2		90 ± 1 vs. 90 ± 2	92 ± 2 vs. 90 ± 3	Tibial component: 96	Frontal: 93 Sagittal: 70	90 ± 0 vs. 90 ± 2	4 ± 2 vs. 3 ± 4				180 ± 1 vs. 180 ± 3
Ferrara et al., 2015 (2)														
Gaukel et al., 2022 (4)		Femoral component flexion: 87.5 LDFA: 89.6		2.0 vs. 1.0 (1.0)		90.0 vs. 91.0		MTPA: 97 Tibial posterior slope: 89.9		3.0 vs. 3.0	90.0 vs. 90.0			179.0 vs. 178.0
Kosse et al., 2018 (5)														
Leeuwen et al., 2015 (6)		HKA: 75.6	0.0 vs. 1.2 ± 1.5* **P<0.001**			90.0 vs 90.5 ± 1.4* **P=0.03**			90.0 vs. 90.4 ± 2.5					
Moopanar et al., 2014 (8)		Femoral: 96.2 Mechanical axis: 99	0.8 ± 1.1		90 vs. 90 ± 3			Tibial alignment: 92.7 Varus alignment: 98.5 Valgus alignment: 94.2	90.0 vs. 90.7	? Vs. 4.9 ± 2.7				180 vs. 181.1 ± 2.4
Müller et al., 2022 (9)	91.2	HKA: 85.3 Femur LDFA: 85.3				90.0 vs. 87.9 ± 2.0		Tibial MPTA: 97.1			90.0 vs. 87.0 ± 1.7			180.0 vs. 179.0 ± 2.6

Nabavi et al., 2017 (10)		HKA: 98 Flexion/extension femoral component: 98 Femoral coronal alignment: 96 Femoral rotation: 90	0.0 vs. 0.0	0.0 vs. 1.0			Posterior tibial slope: 92 Coronal tibial component: 100	90.0 vs. 91.0	0.0 vs. 6.0	90.0 vs. 96.0	0.0 vs. 1.0		180.0 vs. 179.0
Nizam et al., 2018 (11)													
Parratte et al., 2013 (12)		Femoral rotation ± 3%: 100 HKA: 92.6	0.0 vs. 0.9	(2.6 ± 1.8)	(1.4 ± 1.1)				(2.2 ± 1.5)			(6.8 ± 4.1)	180 vs. 179
AlShammari et al., 2021 (14)				96 vs. 95.1 ± 4.4				90.0 vs. 90.2 ± 2.3					180 vs. 184.1 ± 3.1
Schotanus et al., 2017 (15)	Femoral component surgeon: 93.9 Femoral component technician: 79.8* **P<0.001**					Tibial component surgeon: 91.1 Tibial component technician: 82.6* **P<0.001**							
Sotozawa et al., 2022 (16)		Femoral rotation: 82	0.0 vs. -1.5 ± 2.5		90.0 vs. 88.8 ± 2.0		Tibial rotation: 88	90.0 vs. 90.1 ± 2.4				0.0 vs. -2.6 ± 6.3	

*Table 2. Pre-operative plan vs. post-operative results. This table is divided in placement of the femoral and tibial component and the HKA. The femoral and tibial component placement is divided in planned prosthesis size and several rotation angles. The results with an * are deemed significant.*

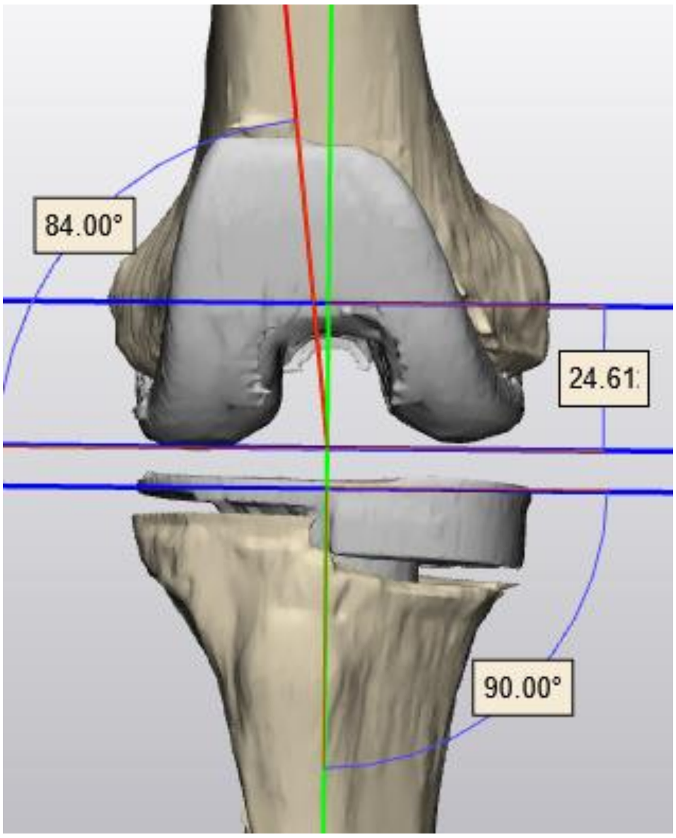
Comparison *Patient Specific Instrument vs. Conventional Intervention*

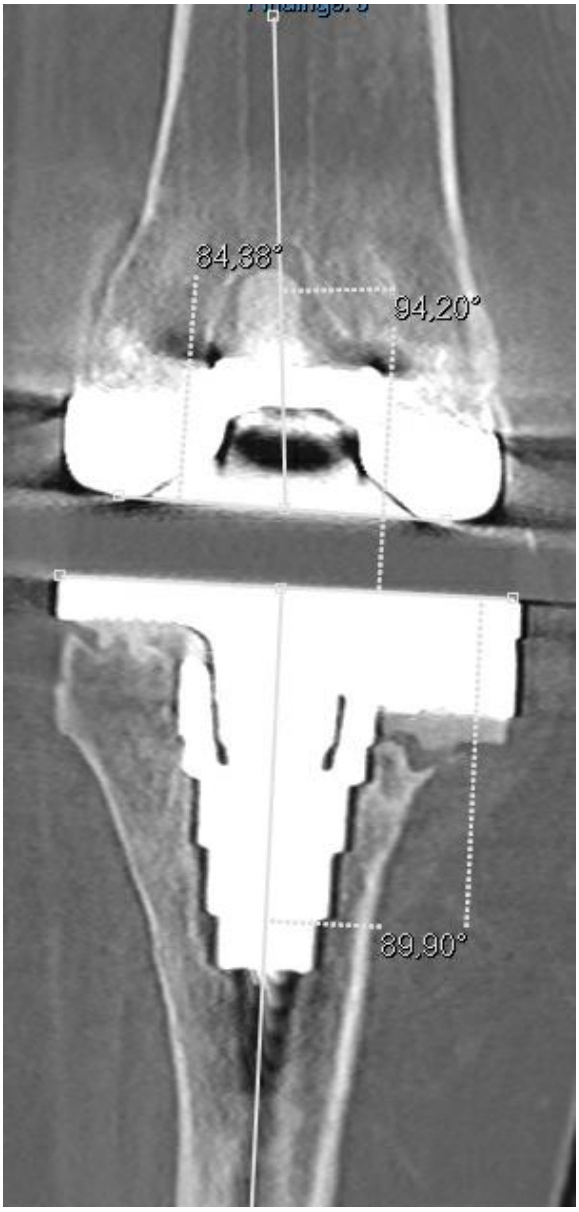
	Outliers			**Femoral component**			**Tibial component**			**HKA**	**Other**	
Study	*HKA outliers (%)*	*mLDFA outliers (%)*	*MPTA outliers (%)*	*Femoral component rotation (°)*	*Frontal femoral alignment (°)*	*Sagittal femoral alignment (°)*	*Tibial component rotation (°)*	*Frontal tibial alignment (°)*	*Sagittal tibial alignment (°)*	*HKA angle (°)*	*Mean operative time (min)*	*Blood loss (mL)*
Franceschi et al., 2014 (3)												
Ferrara et al., 2015 (2)				0.3 ± 0.8 vs. -0.9 ± 2.0* **(P<0.01)**	90.3 ± 1.6 vs. 90.2 ± 1.7	3.6 ± 1.0 vs. 1.5 ± 2.0* **(P=0.01)**	-11.8 ± 3.2 vs. -8.7 ± 3.6	0.0 ± 1.0 vs. -0.1 ± 1.3	5.9 ± 0.7 vs. 7.0 ± 1.6* **(P<0.01)**			140 ± 56.7 vs. 290 ± 112.5
Gaukel et al., 2022 (4)	3.0 vs. 11.3* **P=0.004**	10.4 vs. 6.6	3.0 vs. 2.1									
Kosse et al., 2018 (5)				1.6 ± 2.1 vs. 1.2 ± 2.7	95.6 ± 1.9 vs. 96.3 ± 1.8	3.2 ± 4.0 vs. 3.2 ± 3.5	15.7 ± 7.6 vs. 19.0 ± 8.3	88.0 ± 2.5 vs. 87.8 ± 1.8	2.6 ± 3.2 vs. 7.8 ± 2.8* **P=0.02**	0.1 vs. 0.5	66 ± 15 vs. 68 ± 10	
Leeuwen et al., 2015 (6)												
Moopanar et al., 2014 (8)												
Müller et al., 2022 (9)											***40.4 ± 5.6***	
Nabavi et al., 2017 (10)												
Nizam et al., 2018 (11)											***62***	

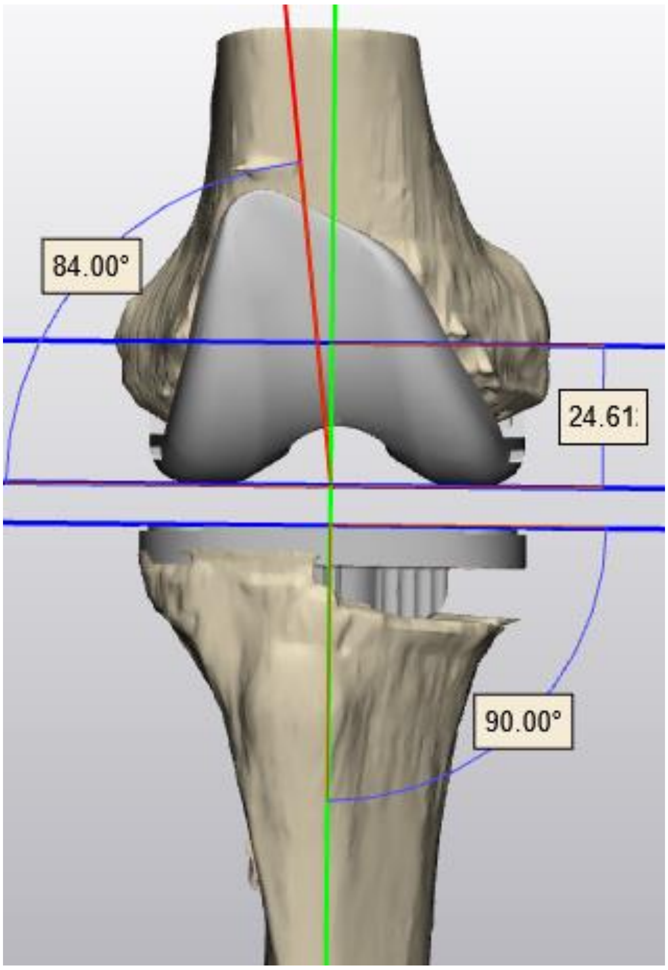
Parratte et al., 2013 (12)					89.8 vs. 90.1		5.85 vs. 5.9	89.1 vs. 88.6				
AlShammari et al., 2021 (14)					95.1 ± 4.4 vs. 94.5 ± 4.2	5.8 ± 3.7 vs. 3.2 ± 2.5* **P=0.01**		90.2 ± 2.2 vs. 89.4 ± 1.8	84.8 ± 4.5 vs. 85.4 ± 3.3	4.1 ± 3.1 vs. 4.0 ± 2.7		162.1 ± 84.4 vs. 150 ± 85.8
Schotanus et al., 2017 (15)												
Sotozawa et al., 2022 (16)		18 vs. 12	12 vs. 20	-1.5 ± 2.5 vs. -0.4 ± 3.4	88.8 ± 2.0 vs. 89.2 ± 2.1		-2.6 ± 6.3 vs. -4.7 ± 8.1	90.1 ± 2.4 vs. 88.9 ± 1.9				

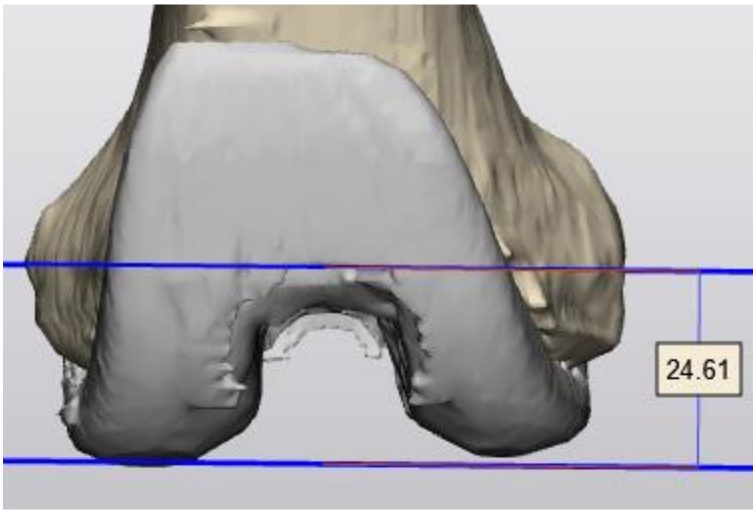
*Table 3. Comparison of PSI vs. CI. The results are divided into 5 categories, where the results with an * are deemed significant.*

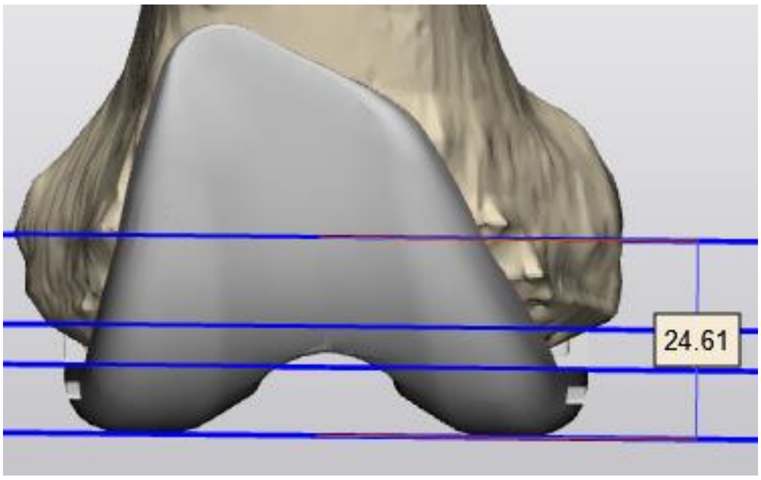
Appendix B

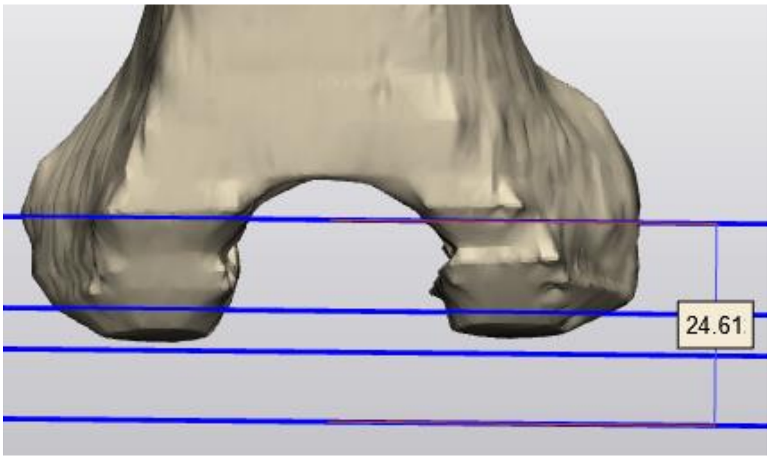












Maat: **Femur 3TS (R)**

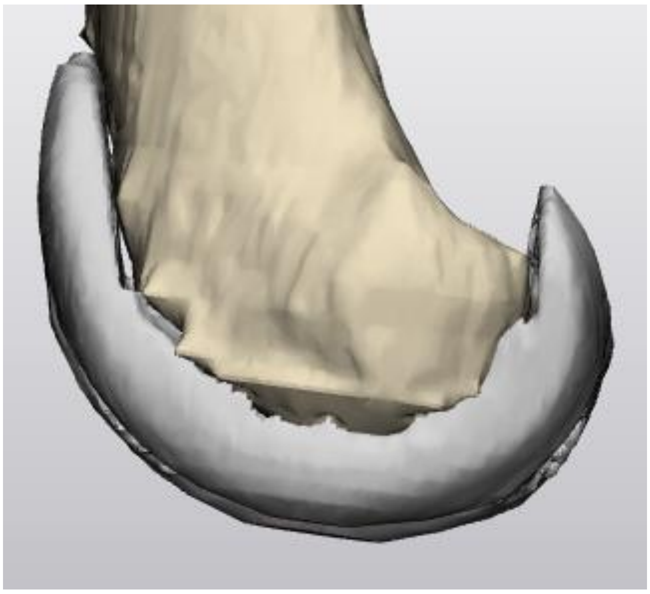
Maat 3 Femur lijkt goed aan te sluiten op de voorgaande geplaatste prothese. De vorige prothese lijkt in Varus geplaatst. Echter is er geen lange been opname, dus is dit gebaseerd op de CT.

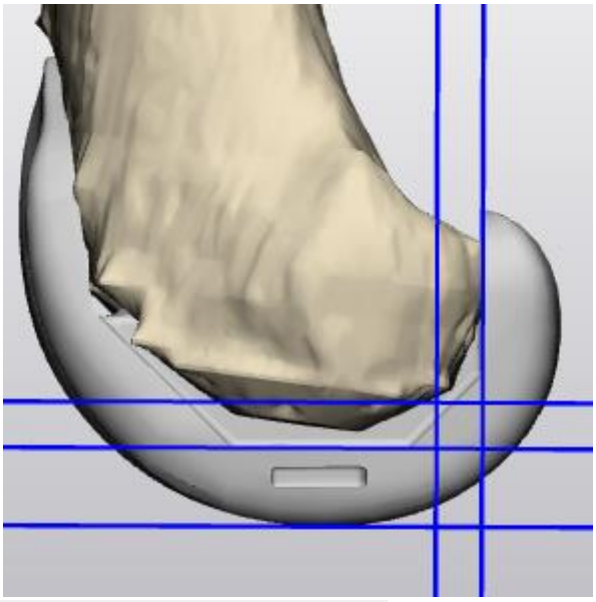
De afstand tot de mediale epicondyle is ongeveer 25mm.

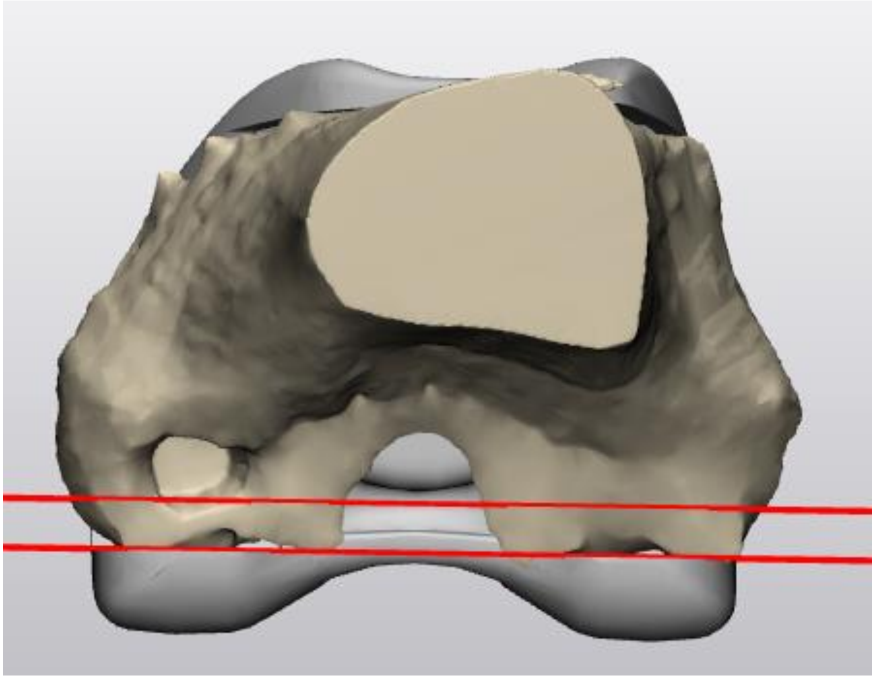
Het resultaat hiervan is beiderzijds een distale augmentatie van 5mm. Er kan ook gekozen worden om de prothese te proximaliseren op het laterale bot, waardoor alleen mediaal een 5mm augmentatie nodig is.

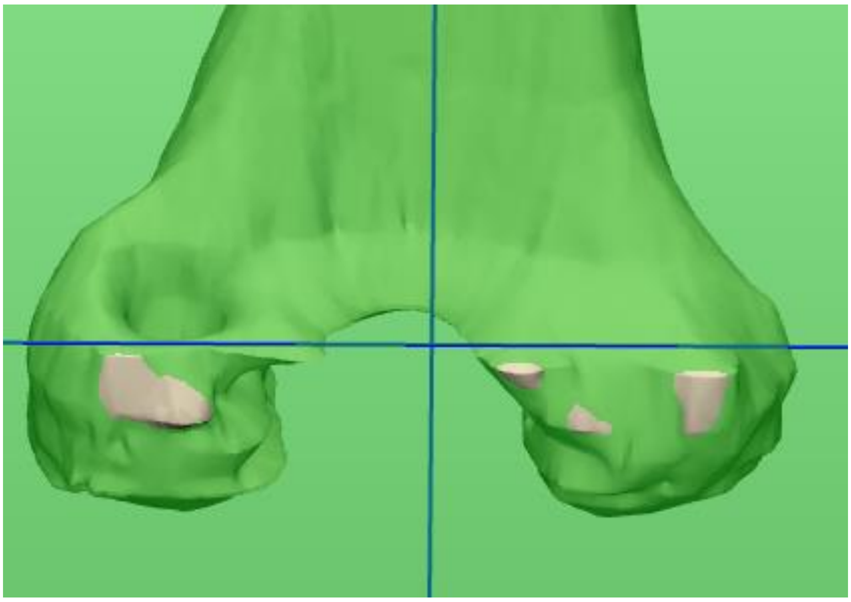
Er lijkt posterieur wat botverlies te zijn, echter is er geen augmentatie nodig, zowel lateraal als mediaal. Op de laatste afbeelding is te zien dat er precies contact is met beide oppervlakten.

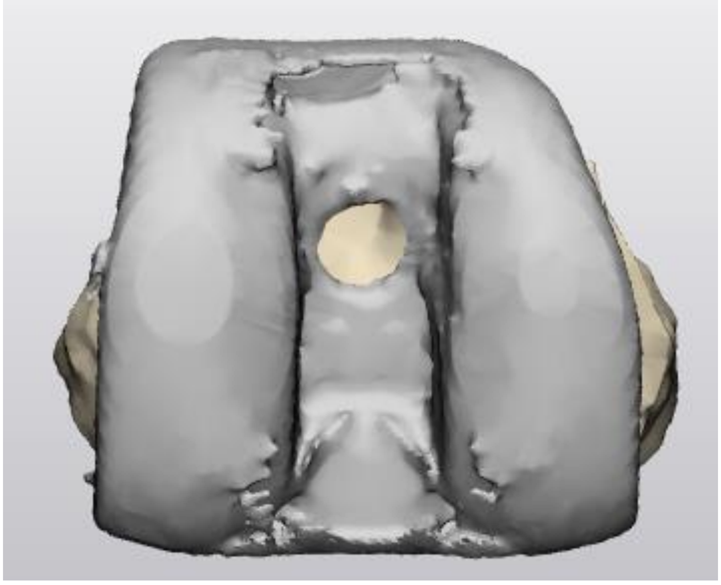
De rotatie van het originele component lijkt ongeveer 1° t.o.v. de chirugische epicondylaire as. De anterieure zaagsnede kan dus gebruikt worden voor de uitlijning van het femur component.

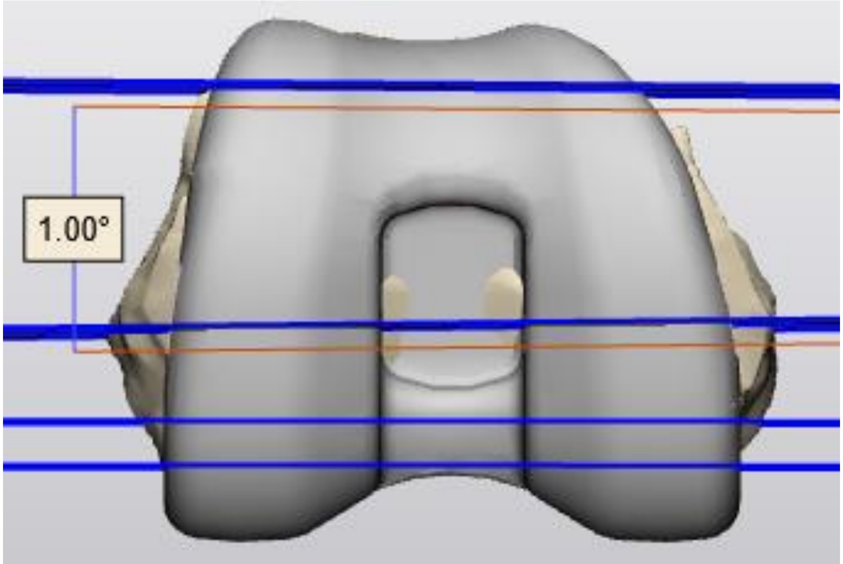




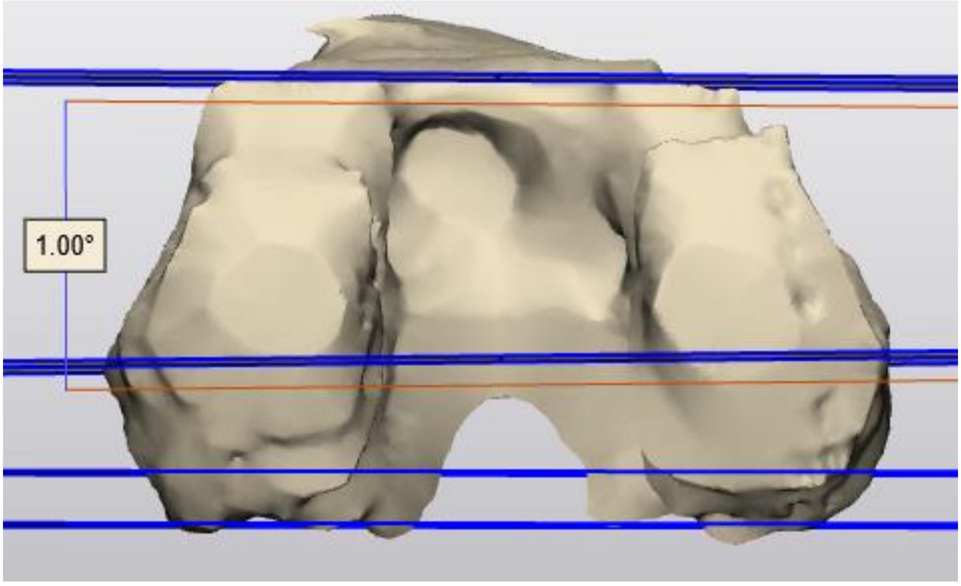




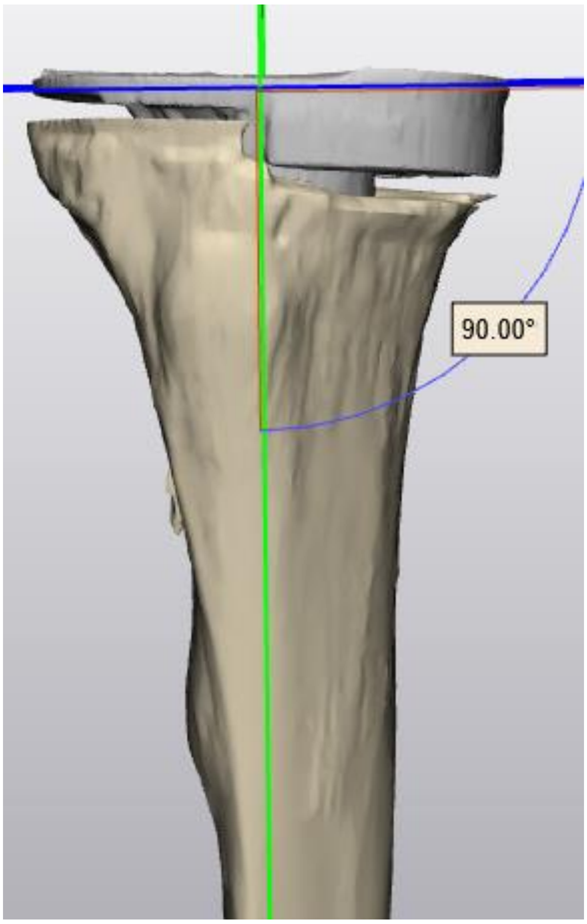


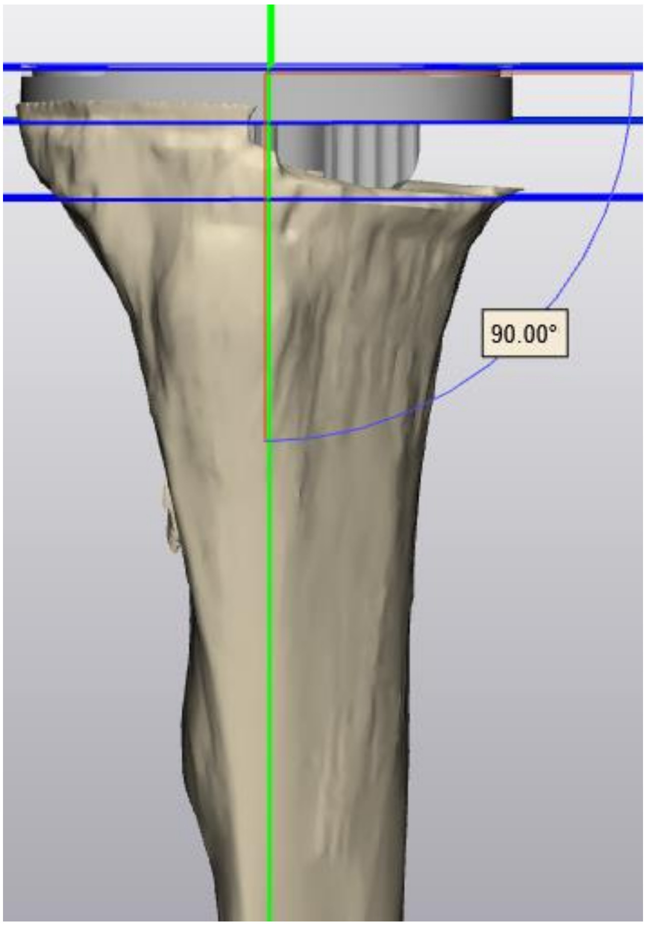


1.00°



1.00°





MaatL **2 Baseplate / 3 Baseplate**

Het tibia plateau staat volledig los van het bot. Om het defect mediaal te overbruggen moet de prothese gedistaliseerd worden, zodat mediaal het defect met een 10mm augmentatie gevuld kan worden.

Lateraal lijkt er voldoende afsteun zonder augmentaties. Mediaal is een 10mm augmentatie vereist.

De rotatie van het tibia component wordt vastgesteld op 18° endorotatie t.o.v. van het midden van het tuberositas.

Een tibia 3 Baseplate lijkt mediaal uit te steken door het grote defect, waardoor er voor een 2 Baseplate is gekozen.