# Patient-Specific Instrumentation

## Shaping the Future of Knee Arthroplasty?

Daphne Schoenmakers

# Patient-Specific Instrumentation

Shaping the Future of Knee Arthroplasty?

Daphne Schoenmakers

**Author:** Daphne Schoenmakers
**Art, cover design & layout:** Daphne Schoenmakers
**ISBN:** 978-94-6361-969-1
**Printed by:** Optima Grafische Communicatie

**Financial support for this thesis was provided by:**
Annafonds, ChiroMotion, Hanssen Footcare, Livit Ottobock Care, Nederlandse Orthopaedische Vereniging (NOV), Penders Voetzorg, Spronken Orthopedie, Q-concepts

# Patient-Specific Instrumentation

## Shaping the Future of Knee Arthroplasty?

PROEFSCHRIFT

Ter verkrijging van de graad van doctor
aan de Universiteit Maastricht,
onder gezag van Rector Magnificus, Prof. dr. Pamela Habibović,
overeenkomstig met het besluit van het college van Decanen,
te verdedigen in het openbaar
op woensdag 19 juni 2024 om 13:00 uur

door

Daphne Anne Laura Schoenmakers

**Promotor**

| | |
|---|---|
| Prof. dr. L.W. van Rhijn | *Universiteit Maastricht / Universiteit Utrecht* |

**Copromotores**

| | |
|---|---|
| Dr. N.P. Kort | *CortoClinics* |
| Dr. M.G.M. Schotanus | *Zuyderland Medisch Centrum* |

**Beoordelingscommissie**

| | |
|---|---|
| Em. Prof. dr. I.C. Heyligers | *Universiteit Maastricht (voorzitter)* |
| Prof. dr. J.J.C. Arts | *Universiteit Maastricht / Technische Universiteit Eindhoven* |
| Prof. dr. L.H. Bouwman | *Universiteit Maastricht / Zuyderland Medisch Centrum* |
| Em. Prof. dr. S.K. Bulstra | *Universitair Medisch Centrum Groningen* |
| Dr. R.C.I. van Geenen | *Amphia* |

# CONTENT

**Chapter 1** General introduction and thesis outline 9

**Part I - Weight-bearing and non-weight-bearing leg alignment**

**Chapter 2** Measurement of Lower Limb Alignment: There are within-person differences between Weight-Bearing and Non-Weight-Bearing Measurement Modalities 27
*Knee Surg Sports Traumatol Arthrosc, 2017, 25, 3569-3575.*

**Part II - Planning in Patient-Specific Instrumentation**

**Chapter 3** High intra- and interobserver reliability of planning implant size in MRI-based patient-specific instrumentation for total knee arthroplasty 47
*Knee Surg Sports Traumatol Arthrosc, 2021, 29, 573-578.*

**Chapter 4** Patient-specific instruments for total knee arthroplasty can accurately predict the component size as used peroperative 63
*Knee Surg Sports Traumatol Arthrosc, 2017, 25, 3844-3848.*

**Chapter 5** Consistency in patient-reported outcome measures after total knee arthroplasty using patient-specific instrumentation: a 5-year follow-up of 200 consecutive cases 77
*Knee Surg Sports Traumatol Arthrosc, 2018, 26, 1800–1804.*

**Part III - Innovations in digital pre- and intraoperative planning modalities for TKA**

**Chapter 6** Preoperative planning with X-PSI™ compared to MRI-based patient-specific instrumentation in total knee arthroplasty 93
*In review at J Clin Orthop Trauma, submitted August 2022.*

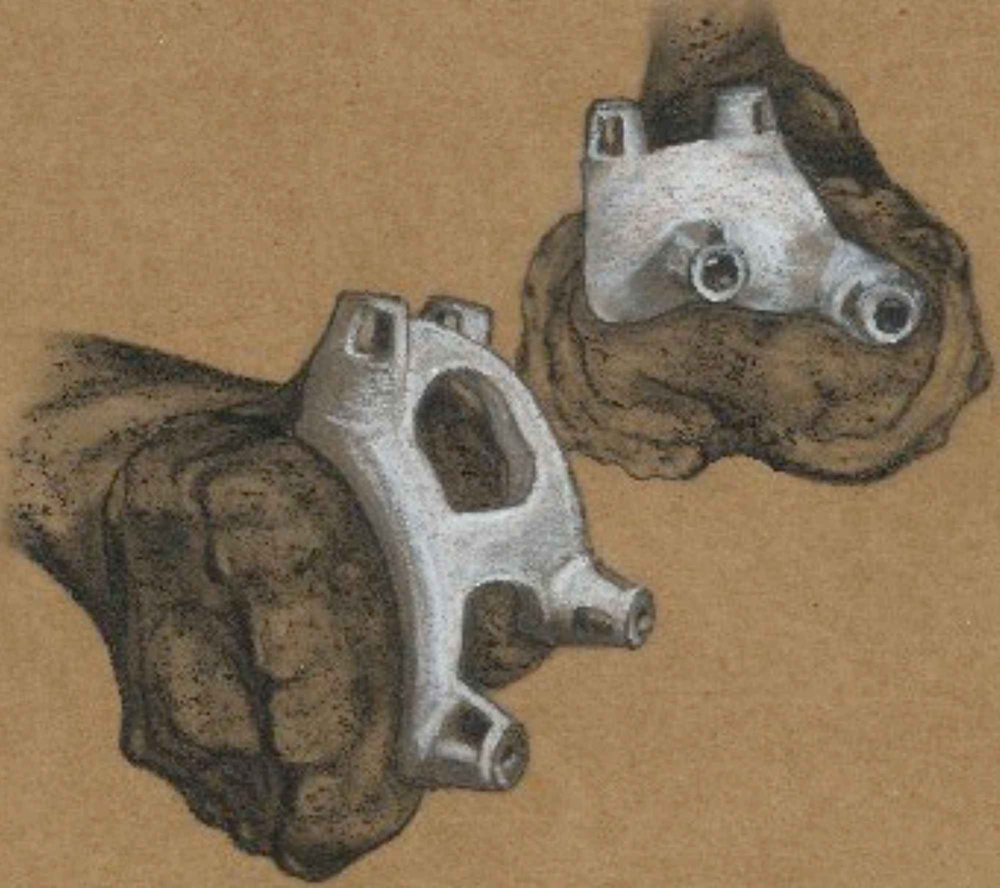
**Chapter 7** Computer-based pre- and intraoperative planning modalities for Total Knee Arthroplasty: A comprehensive review 111
*J Orthop Exp Innov, accepted November 2023.*

**Chapter 8** General discussion 139

**Chapter 9** Impact paragraph 161

**Chapter 10** Summary 171
Samenvatting 175
Résumé 179

**Appendices** Abbreviations 187
Publications 191
Dankwoord 195
Curriculum vitae 201



# 1

## General introduction

## Thesis outline

## GENERAL INTRODUCTION

### *Knee osteoarthritis: Epidemiology*

Osteoarthritis (OA) is a degenerative condition characterised by progressive breakdown and eventual loss of articular cartilage. Knee OA is of frequent occurrence and a leading cause of disability worldwide [1]. The incidence and prevalence of knee OA increase with age and are higher in women than in men [2,3].

In 2019, approximately 528 million individuals were affected by OA worldwide, representing a rise of 113% since 1990. Notably, individuals aged above 55 years constituted around 73% of the global OA population, with women accounting for 60% of OA patients [4,5,6].

The global prevalence of knee OA was 163 million individuals in 1990 and 365 million in 2019 (Figure 1) [7,8]. Given the demographic transition towards an ageing population and the increasing rates of obesity, the prevalence of OA is expected to continue to increase globally [1].

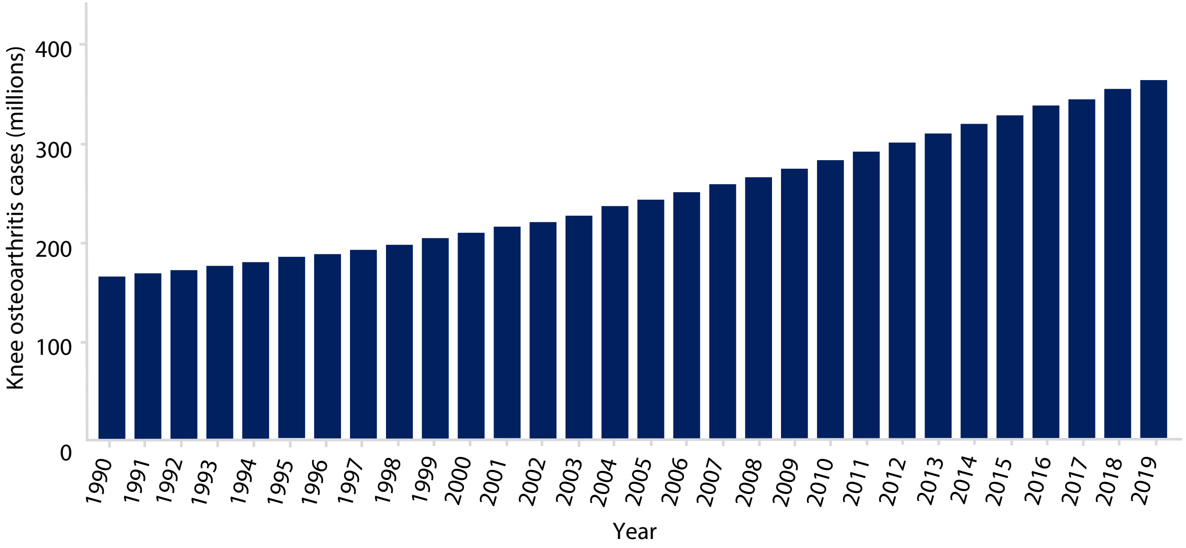


**Figure 1 Global prevalence of knee osteoarthritis from 1990 to 2019**

*Reproduced and adjusted from 'Prevalence trends of site-specific osteoarthritis from 1990 to 2019: Findings from the Global Burden of Disease Study 2019', 2022, by Long et al., doi: 10.1002/art.42089.*

In the Netherlands, knee OA is a health concern of considerable magnitude as well. In 2021, as many as 1,589,600 patients were reported to have OA by their primary care providers. Among these, knee OA affected an estimated 762,700 individuals [9]. During the same year, general practitioners diagnosed 43,700 new cases of knee OA. The gender distribution of these new cases was 16,800 males and 26,900 females, contributing to 50% of all OA diagnoses across various joints. Thus, knee OA emerges as the most prevalent subtype of OA in the Netherlands [9].

### ***Knee osteoarthritis: A whole joint disease***

Historically, OA was viewed as a degenerative condition exclusively of the articular cartilage. Today it is known that other tissues are affected too and even play a role in the progression of the disease. These other tissues are the subchondral bone, joint capsule, synovium, menisci, infrapatellar fat pad, ligaments, and peri-articular muscles [10,11]. This led to the concept of OA as a whole joint disease.

A combination of local, systemic, and external factors influence the progression of OA. With advancement of the condition, notable changes take place such as bone-remodelling, osteophyte formation, weakening of periarticular muscles, laxity of ligaments, and synovial effusion [10,11,12,13]. Articular cartilage wears down, resulting in joint space narrowing, consequently modifying the alignment of the leg. This, in combination with slackening of the knee joint ligaments, leads to increased joint laxity [13]. To counteract this, patients with knee OA often adopt a stereotypical knee-stiffening gait pattern, reinforcing dynamic knee joint stability by increased antagonist muscle co-contractions and reduced knee joint motion [13,14].

When considering total knee arthroplasty (TKA), surgeons need to recognise these OA-induced changes during the planning and operative phases of TKA.

### ***Total Knee Arthroplasty: Epidemiology***

Total knee arthroplasty (TKA) is a surgical option for patients with end-stage knee OA. The main goal of TKA is to relieve pain and restore function. TKA is globally acknowledged as a cost-effective intervention for end-stage knee OA [15].

The first TKA procedures were conducted in the late 1960s and 1970s. This was followed by substantial progress in prosthetic design, techniques, and materials [16,17]. These advancements resulted in a significantly improved survival of TKA implants. Previous literature found a 15-year prosthesis survival rate of 93% and a 25-year survival rate of 82% [18].

Along with the rising incidence of knee OA, the number of TKA procedures has been increasing too. Changes in population demographics and obesity cause an increasing demand for TKA, which will only rise in the future [19,20].

In the United States, projections suggest a drastic increase in demand for primary TKAs. By 2030, it is estimated that the number of procedures will grow by 673% to 3.48 million procedures annually [20]. Similar trends are observable in the Netherlands, where the annual number of TKAs has also been rising steadily (except for the 'Covid-19-years'). In the year 2022, a total of 26,708 TKA surgeries were registered compared to 18,507 TKA's in 2010 (Figure 2). The average age of the operated patients was 69.3 years. Ninety-seven percent of patients were diagnosed with primary knee OA. Posttraumatic conditions were identified in 2% of the patients, and rheumatoid arthritis accounted for 1% of the diagnoses [21,22].

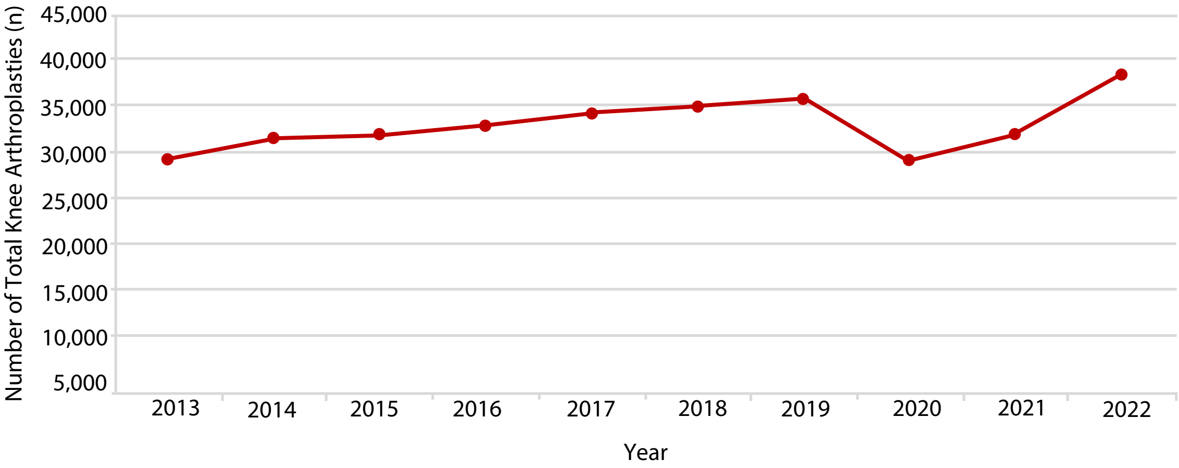


**Figure 2 Number of primary TKA in the Netherlands in 2013 to 2022**

*Data collected by the LROI (Landelijke Registratie Orthopedische Interventies).*

### ***Total Knee Arthroplasty: Surgical techniques***

The longevity of the total knee prosthesis is influenced by several factors, with alignment recognised as a crucial determinant [23,24]. Over time, different surgical techniques were introduced to achieve the desired alignment in TKA. TKA involves the removal of the femoral and tibial joint surfaces to fit the prosthesis implants. With the conventional surgical technique to place a total knee prosthesis, the orthopaedic surgeon uses intramedullary or extramedullary guides to align a cutting block to perform the bone cuts. This has been and continues to be the most used surgical technique for TKA globally.

However, this conventional technique relies on the surgeon's ability to accurately identify anatomical landmarks and the appropriate placement of the guides. As a result, there is a risk of malaligning the implants. Especially in patients with femoral or tibial deformity, the placement of intramedullary guides can be challenging. Additionally, patient dissatisfaction is reported to be high; 15% to 30% of patients report dissatisfaction after TKA [25]. The incidence of residual symptoms is also high, with only 66% of patients stating their knee to feel 'normal' after more than one-year after surgery [26]. This emphasises the opportunity for further refinement.

With innovations in computer technology, new developments took place to achieve the desired alignment. With the aim to increase long-term implant survival and enhanced clinical outcomes after TKA.

### ***Computer-Assisted Surgery***

In Computer-Assisted Surgery (CAS) computer technology is utilised for surgical planning. CAS originates from the late 1980s and early 1990s, and has changed tools and techniques for planning and executing surgeries in several medical disciplines. CAS for TKA can be classified into three types: CAS navigation, patient-specific instrumentation (PSI), and robotic devices [27,28].

### ***CAS navigation***

CAS navigation provides a real-time anatomical view and instrument tracking intraoperatively. The first TKA using CAS navigation was executed in 1997 by Frederic Picard in Grenoble, France [29,30].

While several types of CAS navigation exist, the image-free technique with infrared light-based trackers is most commonly used. With this technique, an infrared light-based optoelectronic tracker guides the positioning of cutting guides by measuring the 3D coordinates of embedded sensors [27,29,30].

At the start of the surgery, trackers are positioned in the femur and tibia, establishing reference frames. Various mechanical angles and the hip rotation centre are deducted by manipulating the hip, knee, and ankle joints. After that, a handheld device records bone morphing data, like the femoral condyles and tibial plateau. This data is then integrated into a digital 3D surface model reflecting the patient’s unique anatomy. After placing the bone-cutting guides with sensors, the localiser determines the 3D coordinates of all sensors and visualises this on a monitor. The computer system calculates the bone-cutting angles based on the position of the guides. Once the cutting guide is in the desired position, it is secured in place by the surgeon. Thereafter, the surgeon proceeds with the bone cuts and continues with the placement of the femoral and tibial implants [27,29,30].

Previous literature demonstrates that CAS navigation systems improve the accuracy and precision of component alignment in TKA [31-33]. Nevertheless, clinical superiority in functional outcomes, improved patient-reported outcome measures (PROMs), and decreased revision rates are not demonstrated [31-33]. Disadvantages of CAS navigation include increased operative time, higher costs, and exquisite specialist training for the surgical team [31,33]. Furthermore, pin track-related complications, such as infection and fractures, have been described [31]. These factors have limited the widespread use of CAS navigation.

### ***Patient-specific instrumentation***

The second type of CAS, PSI, enables surgeons to create a preoperative 3D plan. These plans are subsequently used to produce 3D moulds that guide the surgeon during TKA. The first described case of TKA using this technique was in 2007 [34].

For PSI, a CT- or MRI-scan is used to create a preoperative plan. Specialised software systems transform 2D CT- or MRI images into 3D templates of the knee joint, accompanied by a preoperative default plan made by a technician. The position and sizes of the implants in this preoperative plan can be modified to the surgeon's preferences. Following approval of the plan, the manufacturer produces 3D-printed plastic moulds with rapid prototype techniques. Subsequently, these moulds will be used intraoperatively to fit the patient's anatomy [35-37]. Figure 3 shows the moulds from the PSI system investigated in this thesis.

MRI-based PSI necessitates surgeons to avoid removing osteophytes or cartilage as the moulds account for both cartilage and bone. In contrast, CT-based PSI mandates the removal of cartilage and soft tissues to ensure an accurate fit of the moulds [35]. The moulds can either be produced as pin guides for the placement of conventional cutting guides or be equipped with integrated cutting slots [38]. After achieving the desired bony resections, the usual TKA procedure follows.

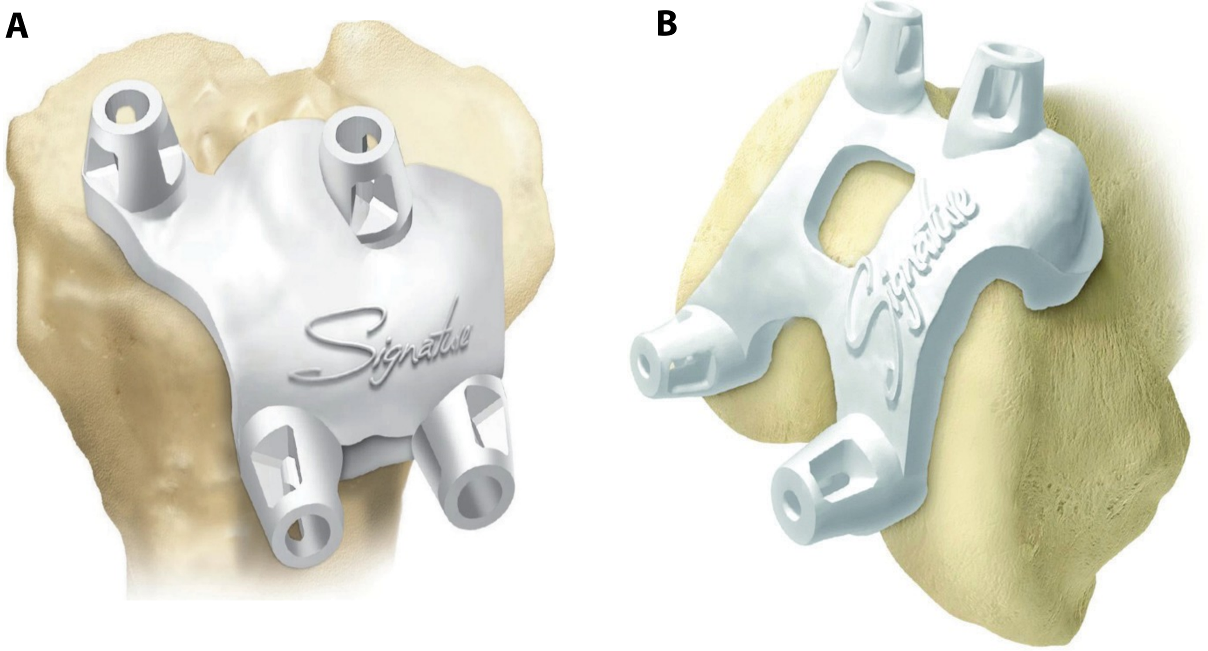


**Figure 3 Illustrations of the PSI system analysed in this thesis**
*A) Anterior view of the tibial guide, B) Anteromedial view of the femoral guide.*

PSI aimed to improve surgical precision and to eliminate variability among surgeons. Theoretically, it enhances implant positioning, notably in patients with abnormal anatomy. Finally, a part of the decision-making process is transitioned to the preoperative phase, which should ensure efficiency, reduction of surgical time, and a reduced amount of instrument trays.

Despite these theoretical advantages, studies have shown mixed results. Some studies reported no significant differences in alignment or clinical outcomes between PSI and conventional instrumentation [39]. Some authors found an improved accuracy of femoral component alignment [40,41], but more outliers for the tibial component alignment when using PSI [40]. Schotanus et al. demonstrated at least as good as, if not better, alignment with MRI-based PSI than CT-based PSI [42]. Efficiency was improved by reducing the number of instrumentation trays, fewer instruments requiring sterilisation, and potentially less in-hospital stock. However, no reduction in operation time occurred [39]. Other studies identified (marginal) benefits in terms of blood loss and operative time favouring PSI [40,41].

The potential advantages of PSI still need to be demonstrated in clinical outcomes and implant survival.

### *Robotic devices*

Robot-assisted surgery is the third type of CAS for TKA. Three robotic systems are used: passive, active, and semi-active (synergistic) robots [43-45]. The semi-active systems are the most widely used.

Passive robots do not perform surgical actions but assist the surgeon in surgical simulation, preoperative planning, or intraoperative navigation [43-45]. Active robots autonomously perform specific tasks like bone resections, although the surgeon can intervene when necessary. First-generation robotic systems for TKA were active robots introduced during the early 2000s [43-45]. Semi-active robotic systems collaborate with the surgeon to combine their capabilities to perform specific surgical steps. For instance, the semi-active robot provides the surgeon with direct feedback while the bone resections are carried out [43-45].

Several possibilities for orientation and visualisation in robotics exist. Image-based systems rely on preoperative CT, MRI, or X-rays to digitally reconstruct the knee joint. They offer therefore the possibility of preoperative planning. Imageless systems record bony landmarks intraoperatively and form a virtual construction of the knee joint from the obtained data. Specific robotic systems combine both [43-45].

Several studies showed improved alignment accuracy with robotics compared to PSI or conventional instrumentation in TKA. However, no distinct superiority in outcomes or implant survival was shown [46-48].

The abundance of developments in CAS represent the ongoing aim for improvement in TKA. Robotic systems evolved from the foundational principles of CAS navigation and PSI. It is therefore of utmost importance to understand the concepts of previous CAS in order to have the ability to apply this knowledge to newer technological developments.

## THESIS OUTLINE

Planning in TKA is a fast-evolving field where developments take place faster than ever. This thesis aims to contribute valuable insights on measuring knee alignment, the planning of PSI in TKA, and the mid-term follow-up results of PSI. It also presents preliminary experiences with a novel planning modality in PSI and offers a comprehensive overview of computer-based planning modalities in TKA.
By driving forward the understanding of these topics, this thesis aims to enhance the knowledge to empower clinical decision-making in computer-based TKA planning.

This thesis is divided into three sections.
**Part I** comprises the differences between weight-bearing and non-weight-bearing measurements in the mechanical leg axis (MLA) measurement. Accurate lower limb alignment in TKA is essential to improve clinical outcomes and prosthesis survival [23-24]. Full-length weight-bearing anteroposterior radiographs (FLR) are the gold standard for assessing knee joint alignment [49]. However, several CAS systems utilise different, mostly non-weight-bearing imaging modalities. As FLR are executed under a weight-bearing circumstance while the other modalities are conducted with the patient in a supine position, knee alignment can exhibit variability based on the patient's weight-bearing status [50].
In **Chapter 2,** within-person agreement of MLA measurements between weight-bearing FLR and non-weight-bearing measurement modalities (CAS navigation or MRI-based PSI) was assessed.

**Part II** focuses on the planning aspect of PSI for TKA and presents the mid-term follow-up of patients operated with PSI.
PSI in TKA uses individually produced disposable moulds to determine intraoperative bone cuts. The manufacturer provides the surgeon with a default planning, which the surgeon can modify before the guides are produced. **Chapter 3** evaluates the intra- and interobserver reliability among preoperative PSI planning by orthopaedic surgeons.
After modification and approval of the default plan by the surgeon, the information within the software system is sent to the manufacturer to produce the moulds for intraoperative use. If the surgeon does not modify and approve the plan, the default plan is used to produce the mould. **Chapter 4** investigates the impact of approval of the preoperative default plan on the implant size used intraoperatively. The frequency and reason for

intraoperative changes of the planned implant size will also be analysed. **Chapter 5** presents the 5-year follow-up results of the first 200 TKAs performed with PSI, focusing on implant survival rate, (serious) adverse events, and PROMs.

New technological developments occur constantly in the current fast-paced and research-driven medical environment. In the field of TKA, innovations in CAS develop faster than ever. Multiple CAS options have become available over the last years. With all available computer-based pre- and intraoperative planning modalities for TKA, physicians are challenged to implement the most suitable modality into their daily practice.

**Part III** presents the preliminary experiences of a new PSI-method for preoperative planning. Furthermore, it gives a comprehensive overview of computer-based planning modalities for TKA.
**Chapter 6** introduces the X-ray-based PSI (X-PSI), a new method for preoperative planning using weight-bearing FLR. This chapter presents the preliminary experiences of preoperative planning with X-PSI compared to MRI-based PSI planning.
With all available computer-based pre- and intraoperative planning modalities for TKA, physicians are posed with the challenge of which type to implement into their daily practice. **Chapter 7** offers a comprehensive overview of historical and currently used digital pre- and intraoperative planning modalities for TKA. Furthermore, it aims to describe key elements of each surgical planning modality and their method of use.

**General discussion**

Finally, **Chapter 8** and **Chapter 9** comprise a discussion of the findings of the previous chapters, recommendations for future studies, and valorisation.

## REFERENCES

1. Hunter DJ, Bierma-Zeinstra S (2019). Osteoarthritis. Lancet, 393, 1745-1759.
2. Lawrence RC, Felson DT, Helmick CG, Arnold LM, Choi H, Deyo RA, Gabriel S, Hirsch R, Hochberg MC, Hunder GG, Jordan JM, Katz JN, Kremers HM, Wolfe F (2008). Estimates of the prevalence of arthritis and other rheumatic conditions in the United States. Part II. Arthritis Rheum, 58(1), 26-35.
3. Silverwood V, Blagojevic-Bucknall M, Jinks C, Jordan JL, Protheroe J, Jordan KP (2015). Current evidence on risk factors for knee osteoarthritis in older adults: a systematic review and meta-analysis. Osteoarthritis Cartilage, 23(4), 507-515.
4. World Health Organization. (n.d.). Osteoarthritis. Retrieved August 1, 2023, from https://www.who.int/news-room/fact-sheets/detail/osteoarthritis.
5. GBD 2019 Diseases and Injuries Collaborators (2020). Global burden of 369 diseases and injuries in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet, 396, 1204-1222.
6. Neogi T (2013). The epidemiology and impact of pain in osteoarthritis. Osteoarthritis Cartilage, 21(9), 1145-1153.
7. Vos T, Flaxman AD, Naghavi M, Lozano R, Michaud C, Ezzati M, Shibuya K, Salomon JA, Abdalla S, Aboyans V et al. (2012). Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet, 380, 2163-2196.
8. Long H, Liu Q, Yin H, Wang K, Diao N, Zhang Y, Lin J, Guo A (2022). Prevalence Trends of Site-Specific Osteoarthritis From 1990 to 2019: Findings From the Global Burden of Disease Study 2019. Arthritis Rheumatol, 74(7), 1172-1183.
9. Nivel Zorgregistraties eerste lijn (n.d.). Artrose: Leeftijd en geslacht. Retrieved August 1, 2023, from https://www.vzinfo.nl/artrose/leeftijd-en-geslacht.
10. Loeser RF, Goldring SR, Scanzello CR, Goldring MB (2012). Osteoarthritis: a disease of the joint as an organ. Arthritis Rheum, 64(6), 1697-707.
11. Primorac D, Molnar V, Rod E, Jeleč Ž, Čukelj F, Matišić V, Vrdoljak T, Hudetz D, Hajsok H, Borić I (2020). Knee Osteoarthritis: A Review of Pathogenesis and State-Of-The-Art Non-Operative Therapeutic Considerations. Genes, 11(8), 854-888.
12. Freisinger GM, Schmitt LC, Wanamaker AB, Siston RA, Chaudhari AMW (2017). Tibiofemoral Osteoarthritis and Varus-Valgus Laxity. J Knee Surg, 30(5), 440-451.
13. Lewek MD, Rudolph KS, Snyder-Mackler L (2004). Control of frontal plane knee laxity during gait in patients with medial compartment knee osteoarthritis. Osteoarthritis Cartilage, 12, 745–751.
14. Zeni JA Jr, Higginson JS (2009). Dynamic knee joint stiffness in subjects with a progressive increase in severity of knee osteoarthritis. Clin Biomech, 24(4), 366-371.

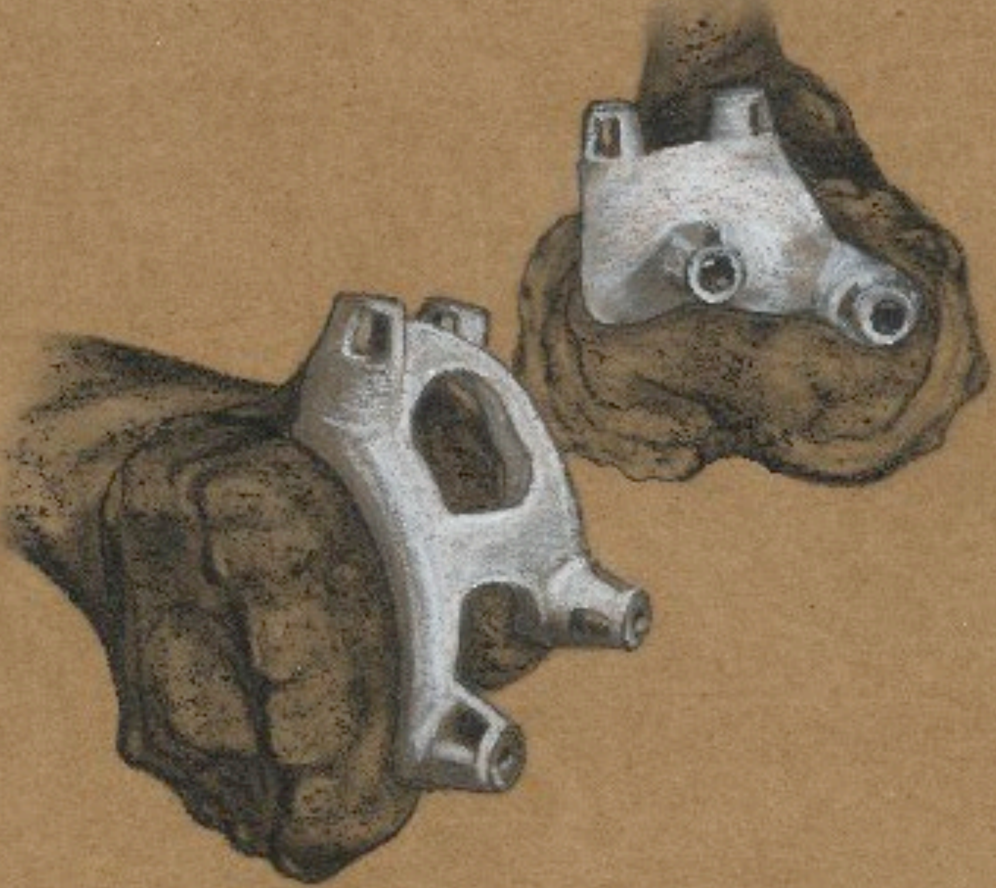
15. Losina E, Walensky RP, Kessler CL, Emrani PS, Reichmann WM, Wright EA, Holt HL, Solomon DH, Yelin E, Paltiel AD, Katz JN (2009). Cost-effectiveness of total knee arthroplasty in the United States: patient risk and hospital volume. Arch Intern Med, 169(12), 1113-1121.
16. Dall'Oca C, Ricci M, Vecchini E, Giannini N, Lamberti D, Tromponi C, Magnan B (2017). Evolution of TKA design. Acta Biomedica, 88(Suppl 2), 17-31.
17. Robinson RP (2005). The Early Innovators of Today's Resurfacing Condylar Knees. J Arthroplasty, 20(1, Suppl 1), 2-26.
18. Evans JT, Walker RW, Evans JP, Blom AW, Sayers A, Whitehouse MR (2019). How long does a knee replacement last? A systematic review and meta-analysis of case series and national registry reports with more than 15 years of follow-up. Lancet, 393(10172), 655-663.
19. Culliford D, Maskell J, Judge A, Cooper C, Prieto-Alhambra D, Arden NK (2015). Future projections of total hip and knee arthroplasty in the UK: results from the UK Clinical Practice Research Datalink. Osteoarthritis Cartilage, 23(4), 594-600.
20. Kurtz S, Ong K, Lau E, Mowat F, Halpern M (2007). Projections of primary and revision hip and knee arthroplasty in the United States from 2005 to 2030. J Bone Joint Surg Am, 89, 780-785.
21. Landelijke registratie orthopedische interventies (LROI) (2022). Jaarreportage 2022. Retrieved August 1, 2023, from https://nov.foleon.com/nov-lroi/lroi-magazine-2022/
22. Landelijke registratie orthopedische interventies (LROI) (2022). Annual report 2023. Retrieved November 6, 2023, from https://www.lroi-report.nl/app/uploads/2023/10/PDF-LROI-annual-report-2023-1.pdf
23. Werner FW, Ayers DC, Maletsky LP, Rullkoetter PJ. (2005). The effect of valgus/varus malalignment on load distribution in total knee replacements. J Biomech, 38, 349-355.
24. Kim YH, Park JW, Kim JS, Park SD (2014). The relationship between the survival of total knee arthroplasty and postoperative coronal, sagittal and rotational alignment of knee prosthesis. Int Orthop, 38(2), 379-385.
25. Bourne RB, Chesworth BM, Davis AM, Mahomed NN, Charron KDJ (2010). Patient Satisfaction after Total Knee Arthroplasty: Who is Satisfied and Who is Not? Clin Orthop Relat Res, 468(1), 57-63.
26. Nam D, Nunley RM, Barrack RL (2014). Patient dissatisfaction following total knee replacement: a growing concern? Bone Joint Journal, 96-B(11 Suppl A), 96-100.
27. Delp SL, Stulberg SD, Davies B, Picard F, Leitner F (1998). Computer Assisted Knee Replacement. Clin Orthop Relat Res, 354, 49-56.
28. Joskowicz L (2017). Computer-aided surgery meets predictive, preventive, and personalized medicine. EPMA Journal, 8, 1–4.
29. Cievet-Bonfils M, Batailler C, Lording T, Servien E, Lustig S (2020). Performing Patient-Specific Knee Replacement with Intra-Operative Planning and Assistive Device (CAS, Robotics). In: Personalized Hip and Knee Joint Replacement. Cham (CH): Springer, Chapter 26.

30. Desai AS, Dramis A, Kendoff D, Board TN (2011). Critical review of the current practice for computer-assisted navigation in total knee replacement surgery: cost-effectiveness and clinical outcome. Curr Rev Musculoskelet Med, 4(1), 11-15.
31. Jones CW, Jerabek SA (2018). Current Role of Computer Navigation in Total Knee Arthroplasty. J Arthroplasty, 33(7), 1989-1993.
32. Shatrov J, Parker D (2020). Computer and robotic-assisted total knee arthroplasty: A review of outcomes. J Exp Orthop, 7(1), 70.
33. Bauwens K, Matthes G, Wich M, Gebhard F, Hanson B, Ekkernkamp A, Stengel D (2007). Navigated total knee replacement. A meta-analysis. J Bone Joint Surg Am, 89(2), 261-9.
34. Chow JC, Torre PKD (2016). Patient-Specific Total Knee Arthroplasty. In Scuderi G, Tria A. (Eds.), Minimally Invasive Surgery in Orthopedics. Springer, Cham, pp 1319–1332, https://doi.org/10.1007/978-3-319-34109-5_124.
35. Mattei L, Pellegrino P, Calò M, Bistolfi A, Castoldi F (2016). Patient specific instrumentation in total knee arthroplasty: a state of the art. Ann Transl Med, 4(7), 126.
36. Gauci MO (2022). Patient-specific guides in orthopedic surgery. Orthop Traumatol Surg Res, 108(1S), 103154, doi: 10.1016/j.otsr.2021.103154.
37. Ast MP, Nam D, Haas SB (2012). Patient-Specific Instrumentation for Total Knee Arthroplasty: A Review. Orthop Clin N Am, 43, 17-22.
38. Ganapathi M (2014). Patient specific guides for total knee replacements – A review. Orthop Trauma, 28(5), 315-321.
39. Huijbregts HJTAM, Khan RJK, Sorensen E, Fick DPF, Haebich S (2016). Patient-specific instrumentation does not improve radiographic alignment or clinical outcomes after total knee arthroplasty: A meta-analysis. Acta Orthop, 87(4), 386–394.
40. Thienpont E, Schwab PE, Fennema P (2017). Efficacy of Patient-Specific Instruments in Total Knee Arthroplasty: A Systematic Review and Meta-Analysis. J Bone Joint Surg Am, 99(6), 521-530.
41. Gong S, Xu W, Wang R, Wang Z, Wang B, Han L, Chen G (2019). Patient-specific instrumentation improved axial alignment of the femoral component, operative time and perioperative blood loss after total knee arthroplasty. Knee Surg Sports Traumatol Arthrosc, 27, 1083–1095.
42. Schotanus MGM, Thijs E, Heijmans M, Vos R, Kort NP (2018). Favourable alignment outcomes with MRI-based patient-specific instruments in total knee arthroplasty. Knee Surg Sports Traumatol Arthros, 26, 2659–2668.
43. Sousa PL, Sculco PK, Mayman DJ, Jerabek SA, Ast MP, Chalmers BP (2020). Robots in the Operating Room During Hip and Knee Arthroplasty. Curr Rev Musculoskelet Med, 13, 309–317.
44. St Mart JP, Goh EL (2021). The current state of robotics in total knee arthroplasty. EFORT Open Rev, 6, 270-279.
45. Jacofsky DJ, Allen M (2016). Robotics in Arthroplasty: A Comprehensive Review. J Arthroplasty, 31, 2353-2363.

46. Lei K, Liu L, Chen X, Feng Q, Yang L, Guo L (2022). Navigation and robotics improved alignment compared with PSI and conventional instrument, while clinical outcomes were similar in TKA: a network meta-analysis. Knee Surg Sports Traumatol Arthrosc, 30, 721–733.
47. Kort N, Stirling P, Pilot P, Müller JH (2022). Robot-assisted knee arthroplasty improves component positioning and alignment, but results are inconclusive on whether it improves clinical scores or reduces complications and revisions: a systematic overview of meta-analyses. Knee Surg Sports Traumatol Arthrosc, 30, 2639–2653.
48. Mancino F, Cacciola G, Malahias MA, De Filippis R, De Marco D, Di Matteo V, Gu A, Sculco PK, Maccauro G, De Martino I (2020). What are the benefits of robotic-assisted total knee arthroplasty over conventional manual total knee arthroplasty? A systematic review of comparative studies. Orthop Rev, 12(s1), 8657.
49. Langenbach MR, Dohle J, Zirngibl H (2002) Determination of the axis after totalendoprosthesis of the knee: functional X-ray photography as golden standard. Z Orthop Ihre Grenzgeb, 140(1), 32-36.
50. Specogna AV, Birmingham TB, Hunt MA, Jones IC, Jenkyn TR, Fowler PJ, Giffin JR (2007). Radiographic measures of knee alignment in patients with varus gonarthrosis: effect of weightbearing status and associations with dynamic joint load. Am J Sports Med, 35(1), 65-70.

# PART I

## Weight-bearing and non-weight-bearing leg alignment



# 2

# Measurement of Lower Limb Alignment: There are within-person differences between Weight-Bearing and Non-Weight-Bearing Measurement Modalities

Schoenmakers DAL, Feczko PZ, Boonen B, Schotanus MGM, Kort NP, Emans PJ

*Knee Surg Sports Traumatol Arthrosc, 2017, 25(11), 3569-3575.*

## ABSTRACT

**Purpose:** Previous studies have compared weight-bearing mechanical leg axis (MLA) measurements to non-weight-bearing measurement modalities. Most of these studies compared mean or median values and did not analyse within-person differences between measurements. This study evaluates the within-person agreement of MLA measurements between weight-bearing full-length radiographs (FLR) and non-weight-bearing measurement modalities (computer-assisted surgery (CAS) navigation or magnetic resonance imaging (MRI)).

**Methods:** Two independent observers measured the MLA on pre- and postoperative weight-bearing FLR in 168 patients. These measurements were compared to non-weight-bearing measurements obtained by CAS navigation or MRI. Absolute differences in individual subjects were calculated to determine the agreement between measurement modalities. Linear regression was used to evaluate the possibility that other independent variables impact the differences in measurements.

**Results:** A difference was found in preoperative measurements between FLR and CAS navigation (mean of 2.5° with limit of agreement (1.96SD) of 6.4°), as well as between FLR and MRI measurements (mean of 2.4° with limit of agreement (1.96SD) of 6.9°). Postoperatively, the mean difference between MLA measured on FLR compared to CAS navigation was 1.5° (limit of agreement (1.96SD) of 4.6°). Linear regression analysis showed that weight-bearing MLA measurements vary significantly from non-weight-bearing MLA measurements. Differences were more severe in patients with mediolateral instability ($p = 0.010$), age ($p = 0.049$) and ≥3° varus- or valgus alignment ($p = 0.008$).

**Conclusion:** The clinical importance of this study lies in the finding that there are within-person differences between weight-bearing and non-weight-bearing measurement modalities. This has implications for preoperative planning, performing Total Knee Arthroplasty (TKA), and clinical follow-up after TKA surgery using CAS navigation or Patient-Specific Instrumentation (PSI).

## INTRODUCTION

Accurate lower limb alignment in Total Knee Arthroplasty (TKA) is important to improve clinical results and prosthesis survival [8,18,20]. Full-length weight-bearing anteroposterior radiographs (FLR) are regarded as the gold standard for determining knee joint alignment [19].

Other modalities that measure mechanical leg axis (MLA) include intraoperative computer navigation in Computer-Assisted Surgery (CAS) and magnetic resonance imaging (MRI) in Patient-Specific Instrumentation (PSI). Several studies have found differences between these measurement modalities [1,6,11,13,24,28,30-32]. However, most of these studies compared mean or median values of the measurement modalities and did not analyse within-person measurement differences. Comparing different measurements within individuals might be of greater value, as this shows the agreement between measurement modalities themselves. Neither correlation coefficients nor regression analysis are appropriate in the analysis of measurement method comparison data [2].

The discrepancy between measurement modalities may arise from a real difference in alignment between supine and weight-bearing status of the patient [5,29]. In addition to weight-bearing conditions previous literature has been inconsistent in which variables influence the differences between measurement modalities [7,17,26,30,32].

In this study, the authors evaluate the within-person agreement in MLA between weight-bearing measurements (FLR) and non-weight-bearing measurements (CAS navigation or MRI). In addition, independent variables that may contribute to measurement differences across modalities are examined.

## METHODS

This dual-centre matched cohort study was performed in two neighbouring hospitals located in the same geographical area in The Netherlands (Maastricht University Medical Centre (A) and Zuyderland Medical Centre (B)). A total cohort of 168 patients was analysed. Approval of the Zuyderland Institutional Review Board was obtained for this study (16-N-66).

### *Study group*

Patients operated for total knee arthroplasty, who were able to undergo weight-bearing FLR, were included.

The CAS-cohort consisted of 84 patients. All of whom had undergone TKA surgery by two experienced knee surgeons (PF and PE) at centre A, between 2010 and 2013). These patients were matched on age and gender to 84 patients from a consecutive cohort (n=200) who were operated from 2009 to 2011 with PSI by one experienced knee surgeon (NK) in hospital B. The first 10 patients operated with PSI were excluded from matching, as they were considered to potentially influence the outcomes due to the surgeon's learning curve. Therefore, the total cohort consisted of 168 patients. Demographic data were comparable in both groups (Table 1).

From five patients in the CAS-group the preoperative navigation measurements were not documented. Moreover, the proximal part of the preoperative FLR of 1 patient in the PSI-group was missing, thus, the MLA could not be measured. From 1 patient in the CAS-group, the postoperative CAS navigation measurements were not documented due to an intraoperative malfunctioning of the CAS navigation. Therefore, in total six patients were excluded from preoperative analysis and 1 patient from the postoperative analysis.

**Table 1 Demographic data**

| Characteristic | Values CAS-group (n=84)<br>Mean ±SD (range) or n (%) | Values PSI-group (n=84)<br>Mean ±SD (range) or n (%) |
|---|---|---|
| Gender | | |
| Male | 47 (56%) | 47 (56%) |
| Female | 37 (44%) | 37 (44%) |
| Age | 65.8 ±8.1<br>(42.6-79.3) | 64.3 ±7.3<br>(48.3-77.5) |
| Side | | |
| Right | 52 (61.9%) | 52 (61.9%) |
| Left | 32 (38.1%) | 32 (38.1%) |
| Weight, kg | 84.6 ±13.9<br>(55-119) | 87.9 ±13.3<br>(63-116) |
| Height, cm | 171.3 ±8.1<br>(155-190) | 171.8 ±8.8<br>(150-189) |
| Body Mass Index (BMI), kg/m$^2$ | 28.7 ±3.3<br>(20.6-34.8) | 29.9 ±4.5<br>(21.8-45.0) |

### *Imaging technique*

Operations with CAS navigation were performed with an identical surgical technique using a Stryker knee navigation system (Stryker Precision Knee Navigation Software, Stryker Corp. Kalamazoo, Michigan USA). According to the manufacturer's protocol, specific landmarks of the lower limb were digitised using a navigation pointer, with which the preoperative MLA was measured (non-weight-bearing). After implanting the definitive prosthesis components, the postoperative MLA was measured again (non-weight-bearing).

Before PSI surgery, all patients underwent an MRI-scan of the lower limb following the protocol of the manufacturer. This MRI-scan was used to create personalised positioning guides for aligning the TKA. The preoperative MLA was measured with software (Signature Personalised Patient Care Biomet, Warsaw, IN, USA) on non-weight-bearing MRI-scan.

### *Radiographic analysis*

All patients underwent weight-bearing FLR preoperatively. These measurements were then compared to the preoperative measurements obtained by either CAS navigation or MRI. In the CAS-group, postoperative FLR (12-weeks postoperatively) were also compared to the CAS navigation measurements after insertion of the total knee prosthesis. Absolute differences between measurement modalities were calculated and analysed.

For FLR, protocols were identical in both centres. All patients were bare footed and instructed to stand upright with heels and toes touching the ground. Lower limbs were fully extended and the patella directed anteriorly. A digital ruler was projected onto the images and 3 radiographs were taken. These individual radiographs were automatically merged using the digital ruler. MLA was determined using the method described by Moreland et al [22], which is the angle formed by the intersection of a line from the centre of the femoral head to the centre of the knee and a second line from the centre of the knee to the centre of the ankle. On postoperative FLR, the centres of the femoral and tibial prosthesis components were used instead of the bony landmarks of the knee.

Measurements in the CAS-group were determined in whole numbers with the iSite Enterpise software (Philips Healthcare, Foster City, California, USA). In the PSI-group, measurements were determined to within 0.1° with Pacs software (Siemens Healthcare, Munich, Federal Republic of Germany), and rounded to the nearest whole number.

In order to ensure the reliability of the FLR measurements, all FLR were analysed by two independent observers in each group (DS and PF in the CAS-group, and DS and BB in the PSI-group). The observers were blinded for each other's measurements as well as the measurements performed with CAS navigation or MRI. For intraobserver reliability analysis, the same researcher measured 10 pre- and 10 postoperative FLR in the CAS-group and 10 preoperative FLR in the PSI-group. This was done six weeks after the initial measurements were taken.

### *Statistical analysis*

Statistical analysis was performed using SPSS software (SPSS 21 Inc., Chicago, IL, USA).

Intra- and interobserver reliability of radiographic MLA measurements were determined by Intraclass Correlation Coefficients (ICCs) using a two-way random effects model for an absolute agreement definition.

To determine the agreement between measurement modalities (FLR and CAS navigation or MRI) absolute differences in individual persons were evaluated. The absolute differences between the two modalities were plotted against the average of these two measurements. The limits of agreement were used to measure the agreement between the variables and estimate the range in which 95% of the differences lie [2].

Linear regression was used to evaluate independent variables (degree of alignment deformity, body mass index (BMI), mediolateral stability during physical examination, gender, and age) that could potentially affect the differences in measurements. Statistical significance was set at $p \leq 0.05$.

## RESULTS

### *Inter- and intraobserver reliability of radiographic measurements*

All measurements of MLA on FLR demonstrated high precision with ICCs for both intra- and interobserver reliability within a range of 0.942 and 0.989.

### *Agreement between measurement modalities*

MLA measured on FLR versus measurements by CAS navigation showed differences >3° in 27.9% of the patients preoperatively and in 8.4% of patients postoperatively. MLA on preoperative FLR compared to preoperative measurements obtained by MRI showed differences >3° in 22.9% of the persons. There was a difference of ≥5° in nine patients in the CAS-group and in eight patients in the PSI-group. In 5 patients from the total cohort, a difference between 7° and 13° was observed (Figure 1).

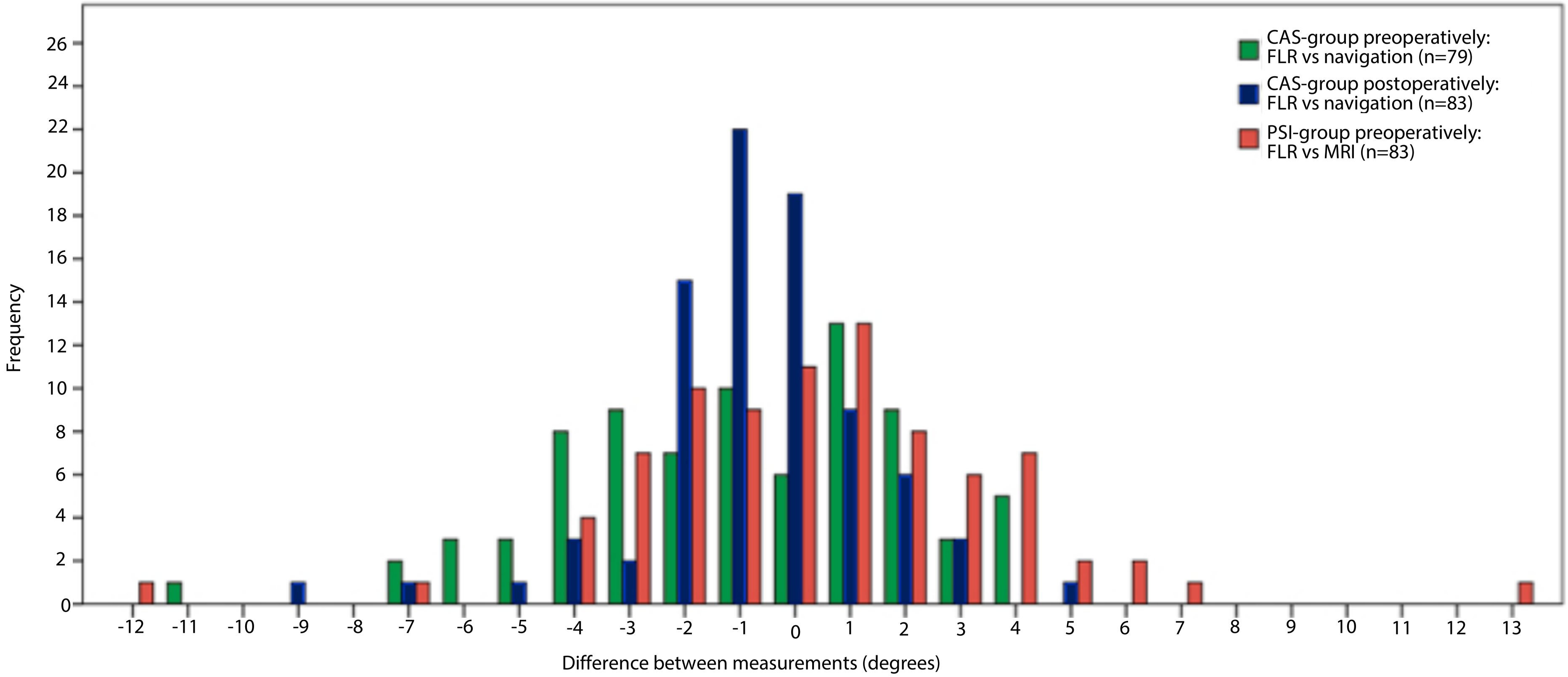


**Figure 1 Frequency of differences in individual measurements of MLA for different measurement modalities**

*MLA, mechanical leg axis; CAS, computer-assisted surgery; FLR, full-length radiograph; MRI, magnetic resonance imaging.*

*Difference represents the value measured on FLR minus the value measured by CAS navigation or MRI.*

When analysing the plots based on the Bland-Altman method [2], one can observe that CAS navigation and MRI measurements differ from FLR with mean values of 2.5° and 2.4° respectively. Postoperatively, the mean difference between MLA measured on FLR compared to CAS navigation was 1.5°. When comparing FLR with CAS navigation or MRI, the limits of agreement (1.96SD) showed values of up to 6.4° and 6.9° respectively for preoperative values, and 4.6° for postoperative comparison of FLR to CAS navigation (Figure 2A-C).

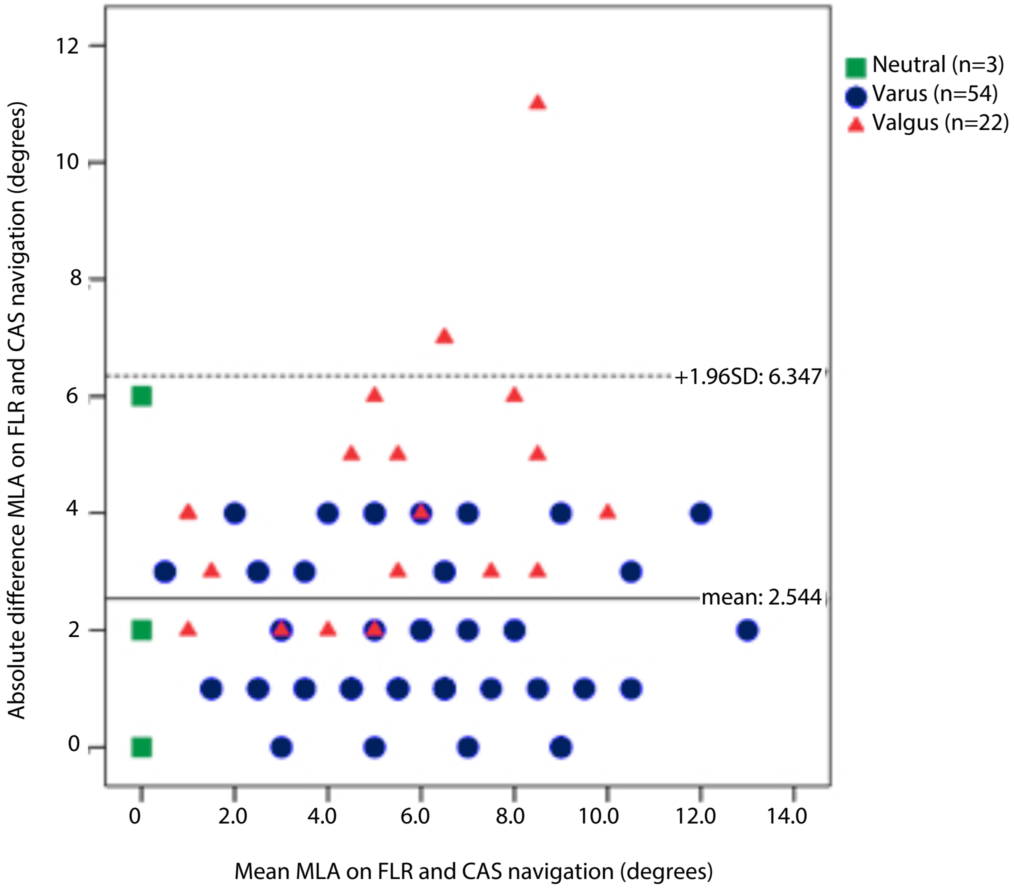


**Figure 2A Plot with agreement of MLA measurements on FLR versus CAS navigation preoperatively**

*Solid black line gives the mean difference in measurements and the dotted line gives the limit of agreement (mean difference +1.96 x SD of the differences).*

*MLA, mechanical leg axis; FLR, full-length radiograph; CAS, computer-assisted surgery.*

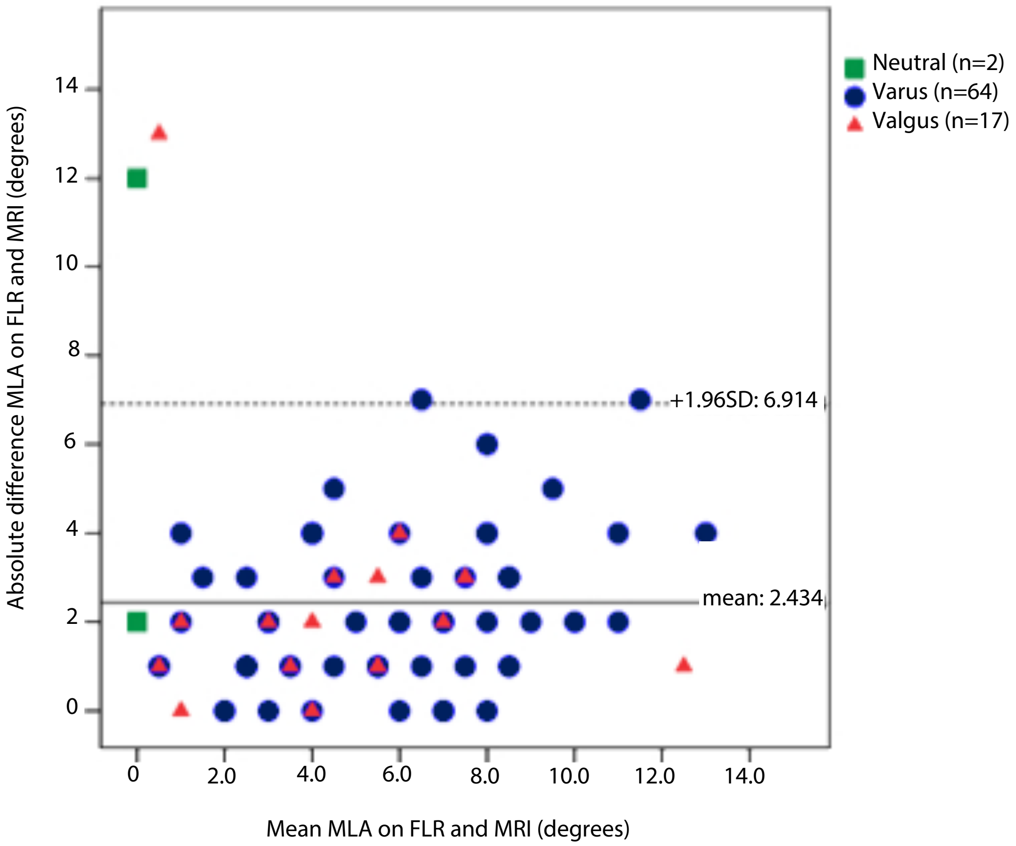


**Figure 2B Plot with agreement of MLA measurements on FLR versus MRI preoperatively**

*Solid black line gives the mean difference in measurements and the dotted line gives the limit of agreement (mean difference +1.96 x SD of the differences).*

*MLA, mechanical leg axis; FLR, full-length radiograph; MRI, magnetic resonance imaging.*

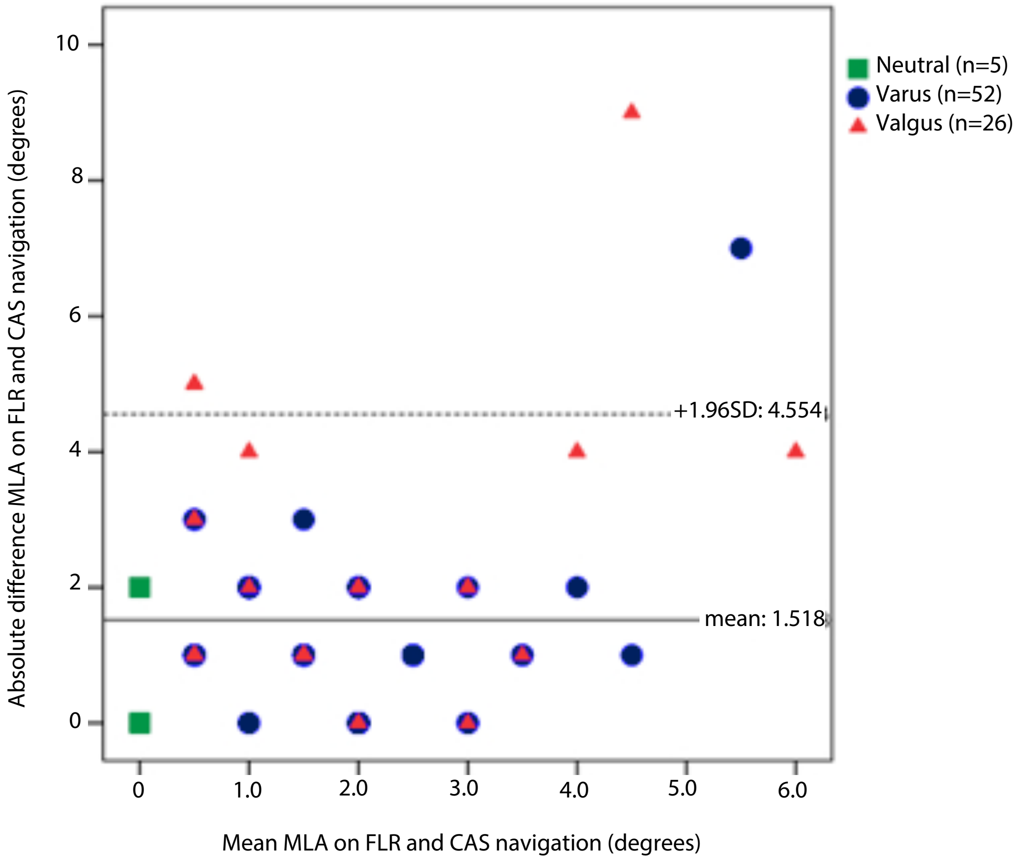


**Figure 2C Plot with agreement of MLA measurements on FLR versus CAS navigation postoperatively**

*Solid black line gives the mean difference in measurements and the dotted line gives the limit of agreement (mean difference +1.96 x SD of the differences).*

*MLA, mechanical leg axis; FLR, full-length radiograph; CAS, computer-assisted surgery.*

### *Factors influencing differences in measurement of MLA*

Multiple linear regression analysis revealed low coefficients of determination in the CAS-group ($R^2$ of 0.132 preoperatively and 0.122 postoperatively). Differences between measurements on FLR and CAS navigation were significantly higher in preoperative measurements when mediolateral instability (during physical examination) was present ($p = 0.010$) as well as with increasing age ($p = 0.049$). For postoperative measurements, differences became significantly higher when the MLA deviated ≥ 3° from neutral MLA ($p = 0.008$).

Regression analysis showed no significant differences (n.s.) between measurements of FLR and MRI for any of the independent variables entered in the analysis.

## DISCUSSION

The most important finding of the present study was that within-person MLA measurements were found to be different when comparing weight-bearing FLR to non-weight-bearing measurement modalities (CAS navigation or MRI).
This study shows high ICC, which is in line with previous literature (intraobserver reliability ICC range 0.91-1.00[4,30], interobserver reliability ICC range 0.72-0.99[4,30]).

The discrepancy between measurement modalities may arise from a real difference in alignment between supine and the weight-bearing status of the patient, which has been recognised in prior research. Weight-bearing radiographs can differ up to 2.0° from radiographs in supine position [5,29]. Willcox et al [30] assessed the agreement between FLR and CAS navigation measurements of MLA, and showed wider limits of agreement of -9.4° and 8.6° preoperatively, and -5.0° to 5.4° postoperatively. This is line with the findings of the current work.
Winter et al [31] assessed the relationship between preoperative FLR and MRI measurements of MLA and showed a correlation between the two techniques (Pearson's correlation coefficient (r) = 0.88) and a large absolute variability in measurements in the same patient, with differences up to 8°. As previously noticed, correlation does not equate to agreement [2]. Based on the absolute differences described by Winter et al [31], a mean difference of 2.6° could be calculated from their data, which is similar to the mean difference found in the present study (2.4°). Paternostre et al [24] also assessed the differences in MLA measurements between FLR and MRI and found no significant difference (evaluation by Student's t test). They found differences >3° in 23% of patients, which was similar to the current study (differences higher than 3° in 22.9% of the persons). Moreover, they stated that the difference seems to be related to higher Kellgren-Lawrence stages where deformity increased under load-bearing conditions.

In the present study, it was found that discrepancies were higher in preoperative measurements compared to postoperative measurements. Other authors have also concluded that preoperative measurements involve a higher degree of ligamentous imbalance, which may lead to greater alignment deformity while weight-bearing [23]. Knees are balanced after TKA and therefore the postoperative difference between weight-bearing and non-weight-bearing gets smaller [23].

In 5 patients, an outlying difference between 7° and 13° was observed. This could be the result of several factors such as fixed flexion deformity, incorrect placement or loosening of navigation trackers, ligamentous imbalance, and measurement or administration errors. The complete analysis was repeated without these 5 outliers. The results from this analysis did not differ from our previous results including outliers. Only the mean difference decreased marginally within a range of 0.1°-0.3°, as expected.

It has been noted in previous literature that the risk of inaccuracy of MLA is more likely in the presence of flexion of the knee or rotation of the leg [17,26]. Measurements of MLA with CAS navigation or with MRI are independent from rotation or flexion since they are three-dimensional. Previous studies demonstrated that CAS navigation measurements are precise [12,33]. The system-determined error has been described within 1° in the coronal plane [10,25,33]. Nonetheless, there is a potential for error since the registration process of CAS navigation is subject to inter- or intrasurgeon variations when demarcating correct landmark registration, or potential loosening of the tracker [27,33]. For PSI, measurements are also subject to movements of the patient during scanning in MRI.

Previous literature is non-concurrent on indicating independent factors that influence MLA measurements [6,7,24,28,30-32]. In addition to weight-bearing status, variable factors may influence the measurements resulting in increased discrepancy. Our findings show that mediolateral instability and age had a significant influence on the differences between preoperative FLR and CAS navigation measurements. A ≥3° alignment deformity from neutral MLA resulted in significantly higher differences in postoperative CAS-group measurements. However, these differences were only of very small clinical relevance with $R^2$ ranging from 0.122 to 0.284.

The present study contains some limitations. The afore-mentioned potential errors were not investigated in either the CAS navigation's registration process or the MRI-scan. A further shortcoming of this study is the lacking determination of flexion and rotation data. As a result, they could not be analysed as confounding variables. Another limitation of the present study results from the fact that two patient samples were used. Obtaining all 3 modalities (FLR, CAS navigation, and MRI) in the same patient sample would be desirable to reduce bias. Finally, other measurement modalities (e.g. computed tomography (CT), single-photon emission computed tomography (SPECT/CT) or 3D reconstructions using SterEOS software) have been evaluated in previous literature[3,9,14-16,21], but were not included in the present study. Comparison of more measurement modalities in individual persons might be of added value in future research.

## CONCLUSION

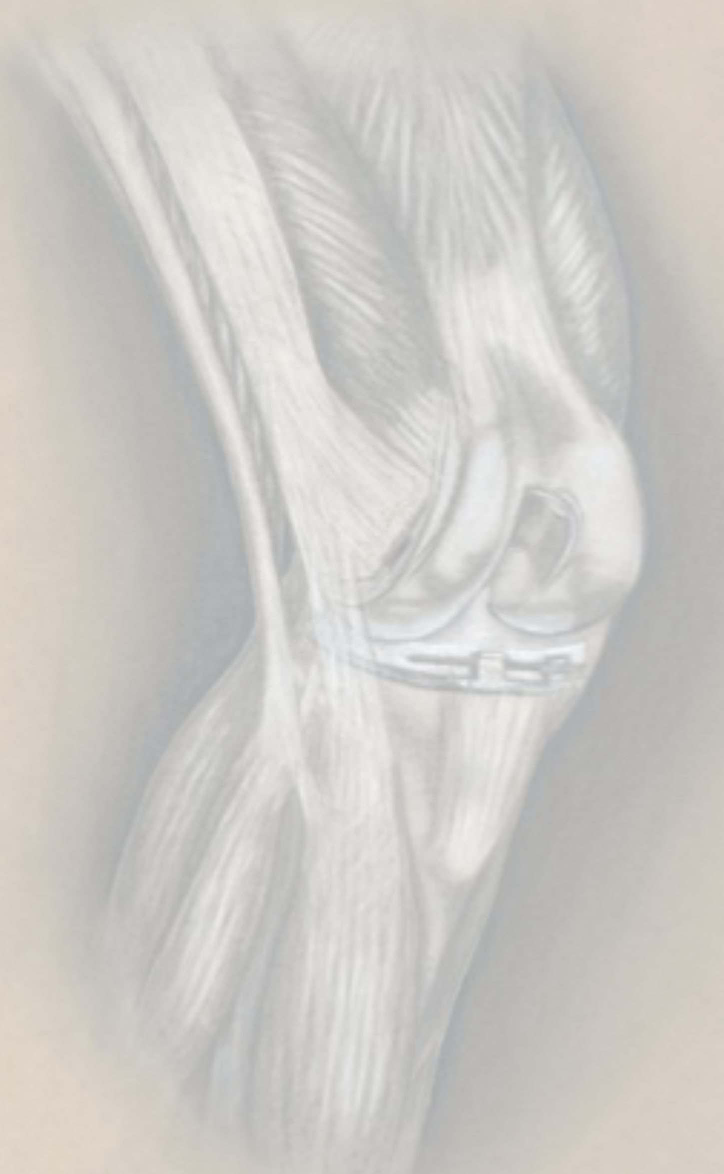
The clinical importance of this study lies in the finding that differences were observed in within-person MLA measurements. A mean difference of up to 2.5 degrees between weight-bearing and non-weight-bearing MLA measurements has implications for preoperative planning, performing TKA, and clinical follow-up after TKA surgery using CAS navigation or PSI.

## REFERENCES

1. Babazadeh S, Dowsey MM, Bingham RJ, Ek ET, Stoney JD, Choong PF (2013). The long leg radiograph is a reliable method of assessing alignment when compared to computer-assisted navigation and computer tomography. Knee, 20(4), 242-249.
2. Bland JM, Altman DG (1986). Statistical methods for assessing agreement between two methods of clinical measurement. Lancet, 1(8476), 307-310.
3. Boonen B, Kerens B, Schotanus MG, Emans P, Jong B, Kort NP (2016). Inter-observer reliability of measurements performed on digital long-leg standing radiographs and assessment of validity compared to 3D CT-scan. Knee, 23(1), 20-24.
4. Bowman A, Shunmugam M, Watts AR, Bramwell DC, Wilson C, Krishnan J (2016). Inter-observer and intra-observer reliability of mechanical axis alignment before and after total knee arthroplasty using long leg radiographs. Knee, 23(2), 203-208.
5. Brouwer RW, Jakma TS, Bierma-Zeinstra SM, Ginai AZ, Verhaar JA (2003). The whole leg radiograph: standing versus supine for determining axial alignment. Acta Orthop Scand 74(5), 565-568.
6. Choi WC, Lee S, An JH, Kim D, Seong SC, Lee MC (2011). Plain radiograph fails to reflect the alignment and advantages of navigation in total knee arthroplasty. J Arthroplasty, 26(5), 756-764.
7. Dexel J, Kirschner S, Gunther KP, Lutzner J (2014). Agreement between radiological and computer navigation measurement of lower limb alignment. Knee Surg Sports Traumatol Arthrosc, 22(11), 2721-2727.
8. Fang DM, Ritter MA, Davis KE (2009). Coronal alignment in total knee arthroplasty: just how important is it? J Arthroplasty, 24(6), 39-43.
9. Gbejuade HO, White P, Hassaballa M, Porteous AJ, Robinson JR, Murray JR (2014). Do long leg supine CT scanograms correlate with weight-bearing full-length radiographs to measure lower limb coronal alignment? Knee, 21(2), 549-552.
10. Graydon AJ, Malak S, Anderson IA, Pitto RP (2009). Evaluation of accuracy of an electromagnetic computer-assisted navigation system in total knee arthroplasty. Int Orthop, 33(4), 975-979.
11. Hauschild O, Konstantinidis L, Baumann T, Niemeyer P, Suedkamp NP, Helwig P (2010). Correlation of radiographic and navigated measurements of TKA limb alignment: a matter of time? Knee Surg Sports Traumatol Arthrosc, 18(10), 1317-1322.
12. Hauschild O, Konstantinidis L, Strohm PC, Niemeyer P, Suedkamp NP, Helwig P (2009). Reliability of leg alignment using the OrthoPilot system depends on knee position: a cadaveric study. Knee Surg Sports Traumatol Arthrosc, 17(10), 1143-1151.
13. Hinterwimmer S, Graichen H, Vogl TJ, Abolmaali N (2008). An MRI-based technique for assessment of lower extremity deformities - reproducibility, accuracy, and clinical application. Eur Radiol, 18(7), 1497-1505.

14. Hirschmann MT, Konala P, Amsler F, Iranpour F, Friederich NF, Cobb JP (2011). The position and orientation of total knee replacement components: a comparison of conventional radiographs, transverse 2D-CT slices and 3D-CT reconstruction. J Bone Joint Surg Br, 93(5), 629-633.
15. Holme TJ, Henckel J, Hartshorn K, Cobb JP, Hart AJ (2015). Computed tomography scanogram compared to long leg radiograph for determining axial knee alignment. Acta Orthop, 86(4), 440-443.
16. Huellner MW, Strobel K (2014). Clinical applications of SPECT/CT in imaging the extremities. Eur J Nucl Med Mol Imaging, 41(1), S50-58.
17. Kannan A, Hawdon G, McMahon SJ (2012). Effect of flexion and rotation on measures of coronal alignment after TKA. J Knee Surg, 25(5), 407-410.
18. Kim YH, Park JW, Kim JS, Park SD (2014). The relationship between the survival of total knee arthroplasty and postoperative coronal, sagittal and rotational alignment of knee prosthesis. Int Orthop, 38(2), 379-385.
19. Langenbach MR, Dohle J, Zirngibl H (2002). Determination of the axis after totalendoprosthesis of the knee: functional X-ray photography as golden standard. Z Orthop Ihre Grenzgeb, 140(1), 32-36.
20. Lotke PA, Ecker ML (1977). Influence of positioning of prosthesis in total knee replacement. J Bone Joint Surg Am, 59(1), 77-79.
21. Meijer MF, Boerboom AL, Bulstra SK, Reininga IH, Stevens M (2017). Do CAS measurements correlate with EOS 3D alignment measurements in primary TKA? Knee Surg Sports Traumatol Arthrosc, 25(9), 2894-2903.
22. Moreland JR, Bassett LW, Hanker GJ (1987). Radiographic analysis of the axial alignment of the lower extremity. J Bone Joint Surg Am, 69-A(5), 745-749.
23. Panzica M, Kenawey M, Liodakis E, Brandes J, Krettek C, Hankemeier S (2014). Effect of intraoperative weight-bearing simulation on the mechanical axis in total knee arthroplasty. Arch Orthop Trauma Surg, 134(5), 673-677.
24. Paternostre F, Schwab PE, Thienpont E (2014). The difference between weight-bearing and non-weight-bearing alignment in patient-specific instrumentation planning. Knee Surg Sports Traumatol Arthrosc, 22(3), 674-679.
25. Pitto RP, Graydon AJ, Bradley L, Malak SF, Walker CG, Anderson IA (2006). Accuracy of a computer-assisted navigation system for total knee replacement. J Bone Joint Surg Br, 88-B(5), 601-605.
26. Radtke K, Becher C, Noll Y, Ostermeier S (2010). Effect of limb rotation on radiographic alignment in total knee arthroplasties. Arch Orthop Trauma Surg, 130(4), 451-457.
27. Robinson M, Eckhoff DG, Reinig KD, Bagur MM, Bach JM (2006). Variability of landmark identification in total knee arthroplasty. Clin Orthop Relat Res, 442, 57-62.
28. Seo SS, Seo JH, Sohn MW, Kim YJ (2012). Differences in measurement of lower limb alignment among different registration methods of navigation and radiographs in TKA using the OrthoPilot system. Orthopedics, 35(10), 50-55.

29. Specogna AV, Birmingham TB, Hunt MA, Jones IC, Jenkyn TR, Fowler PJ, Giffin JR (2007). Radiographic measures of knee alignment in patients with varus gonarthrosis: effect of weightbearing status and associations with dynamic joint load. Am J Sports Med, 35(1), 65-70.
30. Willcox NM, Clarke JV, Smith BR, Deakin AH, Deep K (2012). A comparison of radiological and computer navigation measurements of lower limb coronal alignment before and after total knee replacement. J Bone Joint Surg Br, 94(9), 1234-1240.
31. Winter A, Ferguson K, Syme B, McMillan J, Holt G (2014). Pre-operative analysis of lower limb coronal alignment - A comparison of supine MRI versus standing full-length alignment radiographs. Knee, 21(6), 1084-1087.
32. Yaffe MA, Koo SS, Stulberg SD (2008). Radiographic and navigation measurements of TKA limb alignment do not correlate. Clin Orthop Relat Res, 466(11), 2736-2744.
33. Yau WP, Leung A, Liu KG, Yan CH, Wong LL, Chiu KY (2007). Interobserver and intra-observer errors in obtaining visually selected anatomical landmarks during registration process in non-image-based navigation-assisted total knee arthroplasty. J Arthroplasty, 22(8), 1150-1161.



# PART II

## Planning in Patient-Specific Instrumentation

# 3

# High intra- and interobserver reliability of planning implant size in MRI-based patient-specific instrumentation for total knee arthroplasty

Schoenmakers DAL, Theeuwen DMJ, Schotanus MGM, Jansen EJP, van Haaren EH, Hendrickx RPM, Kort NP

*Knee Surg Sports Traumatol Arthrosc, 2021, 29(2), 573-578.*

## ABSTRACT

**Purpose:** Patient-specific instrumentation (PSI) in total knee arthroplasty (TKA) uses individually designed disposable guides to determine intraoperative bone cuts. The manufacturer provides the surgeon with proposed planning which can be modified and should be approved by the surgeon before the guides are produced. This study aims to assess the intra- and interobserver reliability among preoperative planning by orthopaedic surgeons using PSI. The authors hypothesise a high intra- and interobserver reliability in planning TKA using PSI.

**Methods:** Four orthopaedic surgeons modified and approved 40 preoperative MRI-based PSI plannings three times. The surgeons were blinded to their own and each other's results. Intra- and interobserver reliability was obtained for planned implant size, resection, and position of the implant.

**Results:** Intraobserver reliability Intraclass Correlation Coefficients (ICC) were excellent for femoral and tibial implant size with a range of 0.948–0.995 and 0.919–0.988, respectively. Interobserver reliability for femoral and tibial implant size showed an ICC range of 0.953–0.982 and 0.839-0.951, respectively. Next to implant size, intra- and interobserver reliability demonstrated good to an excellent agreement (ICC > 0.75) for 7 out of 12 remaining parameters and 6 out of 12 remaining parameters, respectively.

**Conclusion:** Preoperative planning of TKA implant size using MRI-based PSI showed excellent intra- and interobserver reliability. Further research on the comparison of predicted implant size preoperatively to intraoperative results is needed.

## INTRODUCTION

Patient-specific instrumentation (PSI) in total knee arthroplasty (TKA) uses individually designed, disposable guides, to determine intraoperative bone cuts. Patient-specific preoperative 3D models for the femur and the tibia can be generated either from preoperative magnetic resonance imaging (MRI) or computed tomography scans (CT). A technician is able to make a default plan for the implant size and position using this data. The surgeon can make adjustments to all settings of the femur and tibia component, taking in mind each patient's anatomical variations. After the case is approved, the manufacturer produces disposable guides for intraoperative use. Previous literature has shown that the plan provided by the technician can differ from the approved plan by the surgeon [4, 10, 12]. Consequently, differences between the suggested and appropriate component size may occur. Therefore, the expertise of the surgeon is essential for evaluating and approving the planning provided by the manufacturer. Nonetheless, none of these studies evaluated the intra- or interobserver reliability of the planning made by the surgeon.

Multiple other studies have been conducted to assess radiographic and clinical outcome of conventional TKA compared to PSI [6, 7, 14]. Other studies compared CT- to MRI-based PSI for TKA [1, 13, 16]. However, no literature exists on evaluating the reliability of the planning method itself by comparing repetitive preoperative planning within or between orthopaedic surgeons. This comparison is of added value since it demonstrates whether TKA-planning using PSI is itself reliable. Therefore, the present study is designed to assess the intra- and interobserver reliability among preoperative planning by orthopaedic surgeons using PSI. The authors hypothesise that there is a high intra- and interobserver reliability in planning TKA using PSI.

## METHODS

The study group consists of all patients who underwent TKA in 2015 using PSI (Signature$^{TM}$ system, Zimmer-Biomet Inc., Warsaw, IN) based on a preoperative MRI in the Zuyderland Medical Centre (Sittard-Geleen, the Netherlands). A total of 309 patients were included. From this cohort, 40 patients were randomly selected and anonymised by Materialise NV (Leuven, Belgium). The preoperative plan, in the default setting as suggested by Materialise NV, had to be evaluated, adjusted where necessary, and approved by the surgeon.

Institutional review board (METC Z, Heerlen, the Netherlands) approval was obtained for this study (trial number 13-N-117).

### *Measurements*

Four orthopaedic surgeons were each given three folders, within every folder the selected 40 cases in a random order. As a result, each surgeon performed standard preoperative planning three times per case within two weeks. All surgeons were senior surgeons and had a minimum experience of three years with PSI for TKA.

Only the manufacturer had information regarding matching case numbers until the evaluation of all approved plannings. For each case the following 14 parameters were planned: femoral size, femoral posterior medial resection, femoral mediolateral displacement, femoral distal medial resection, femoral flexion-extension, femoral varus-valgus, femoral rotation from epicondylar axis, tibial size, tibial anteroposterior displacement, tibial mediolateral displacement, tibial resection from highest point, tibial posterior slope, tibial varus-valgus, and tibial rotation.

### *Outcome measurements*

The primary outcome measurements were intra- and interobserver reliability of planned size component for the femur and tibia. The secondary outcome measurements were intra- and interobserver reliability of all remaining planned measurements as described above.

### *Statistical analysis*

All statistical analyses were performed using SPSS software version 25 (SPSS Inc., Chicago, Illinois).

The Intra- and interobserver reliability of all measurements were determined by Intraclass Correlation Coefficients (ICCs), using an absolute-agreement two-way mixed effects model for intraobserver reliability, and an absolute-agreement two-way random effects model for interobserver reliability.

ICC values less than 0.5 are indicative of poor reliability, values between 0.5 and 0.75 indicate moderate reliability, values between 0.75 and 0.9 indicate good reliability, and values greater than 0.90 indicate excellent reliability [9].

## RESULTS

Determination of femoral- and tibial implant size showed excellent agreement with ICCs for intraobserver reliability within a range of 0.948 - 0.995 and 0.919 - 0.988 respectively, as well as excellent ICCs for interobserver reliability within a range of 0.953-0.982 and 0.839-0.951 respectively (Table 1).

**Table 1. Intra- and inter-observer Intraclass Correlation Coefficients of surgical parameters in patient-specific TKA**

| | Intra ICC Surgeon 1 | Intra ICC Surgeon 2 | Intra ICC Surgeon 3 | Intra ICC Surgeon 4 | Inter ICC |
|---|---|---|---|---|---|
| Femoral distal medial resection | 0.902 (0.842-0.943) | 1.000 | 1.000 | 0.923 (0.874-0.956) | 0.919 (0.881-0.950) |
| Femoral flexion extension | 0.595 (0.423-0.742) | 0.620 (0.451-0.760) | 1.000 | 0.823 (0.724-0.895) | 0.487 (0.369-0.624) |
| Femoral mediolateral displacement | 1.000 | 0.987 (0.979-0.993) | 1.000 | 1.000 | 0.997 (0.995-0.998) |
| Femoral posteromedial resection | 1.000 | 1.000 | 1.000 | 1.000 | 0.998 (0.997-0.999) |
| Femoral rotation from epicondylar axis | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 |
| Femoral size | 0.987 (0.979-0.993) | 0.990(0.983-0.994) | 0.977(0.959-0.987) | 0.966 (0.942-0.981) | 0.970 (0.953-0.982) |
| Femoral varus/valgus | 1.000 | 0.737 (0.604-0.840) | 1.000 | 1.000 | 0.129 (0.065-0.231) |
| Tibial anteroposterior displacement | 0.737 (0.604-0.839) | 0.816 (0.715-0.891) | 0.972 (0.954-0.984) | 0.942 (0.905-0.967) | 0.250 (0.160-0.379) |
| Tibial mediolateral displacement | 0.900 (0.839-0.942) | 0.754 (0.626-0.851) | 1.000 | 0.384 (0.186-0.579) | 0.177 (0.101-0.294) |
| Tibial posterior slope | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 |
| Tibial resection from highest point | 0.946 (0.911-0.969) | 0.939 (0.901-0.965) | 0.997 (0.994-0.998) | 0.932 (0.889-0.961) | 0.743 (0.584-0.851) |
| Tibial rotation | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 |
| Tibial size | 0.973 (0.955-0.985) | 0.976 (0.959-0.987) | 0.977(0.962-0.987) | 0.935(0.867-0.967) | 0.910 (0.839-0.951) |
| Tibial varus/valgus | 1.000 | 0.560 (0.383-0.715) | 1.000 | 1.000 | 0.081 (0.032-0.164) |

*Intraclass Correlation Coefficients (95%Confidence interval).*

*Intra ICC, Intra-observer Intraclass Correlation Coefficients; Inter ICC, Inter-observer Intraclass Correlation Coefficients.*

The maximum size change when an implant size was changed, when compared to other plannings within the same case, was 1 size for the femoral component and 2 sizes for the tibia component. The amount of adjusted implant sizes and differences between the implant sizes within the same case per surgeon are shown in Table 2.

**Table 2 Amount of adjusted cases and differences between adjusted plans within same case per surgeon**

| | Surgeon 1 | | Surgeon 2 | | Surgeon 3 | | Surgeon 4 | |
|---|---|---|---|---|---|---|---|---|
| | n (%) | Difference | n (%) | Difference | n (%) | Difference | n (%) | Difference |
| Femoral distal medial resection | 7 (17.5%) | 1 mm: 4<br>1.5 mm: 1<br>2 mm: 2 | 0 (0%) | N/A | 0 (0%) | N/A | 9 (22.5%) | 0 mm: 1<br>1 mm: 3<br>1.5 mm: 2<br>2 mm: 3 |
| Femoral flexion extension | 18 (45%) | 0 dg: 2<br>1 dg: 10<br>2 dg: 4<br>2.2 dg: 1<br>2.5 dg: 1 | 38 (95%) | 0 dg: 20<br>0.5 dg: 15<br>1 dg: 3 | 0 (0%) | N/A | 4 (10%) | 0.7 dg: 1<br>0.8 dg: 1<br>1 dg: 1<br>1.5 dg:1 |
| Femoral mediolateral displacement | 0 (0%) | N/A | 1 (2.5%) | 2.3 mm: 1 | 0 (0%) | N/A | 0 | N/A |
| Femoral posteromedial resection | 0 (0%) | N/A | 1 (2.5%) | 0 mm: 1 | 0 (0%) | N/A | 0 | N/A |
| Femoral rotation from epicondylar axis | 0 (0%) | N/A | 0 (0%) | N/A | 0 (0%) | N/A | 0 | N/A |
| Femoral size | 8 (20%) | 0 size: 2<br>1 size: 6 | 5 (12.5%) | 1 size: 5 | 14 (35%) | 0 size: 3<br>1 size: 11 | 25 (62.5%) | 0 size: 8<br>1 size: 17 |
| Femoral varus/valgus | 0 (0%) | N/A | 4 (10%) | 0 dg: 2<br>0.5 dg: 2 | 0 (0%) | N/A | 0 (0%) | N/A |

**Table 2 Continued**

| | Surgeon 1 | | Surgeon 2 | | Surgeon 3 | | Surgeon 4 | |
|---|---|---|---|---|---|---|---|---|
| | n (%) | Difference | n (%) | Difference | n (%) | Difference | n (%) | Difference |
| Tibial anteroposterior displacement | 35 (87.5%) | 0 mm: 1<br>0.1-0.5 mm: 14<br>0.6-1.0 mm: 16<br>1.1-1.5 mm: 3<br>3.2 mm: 1 | 33 (82.5%) | 0 mm: 1<br>0.1-0.5 mm: 14<br>0.6-1.0 mm: 15<br>1.1-1.5 mm: 3 | 1 (2.5%) | 1.7 mm: 1 | 4 (10%) | 0.7 mm: 2<br>0.8 mm: 1<br>1.5 mm: 1 |
| Tibial mediolateral displacement | 37 (92.5%) | 0 mm: 2<br>0.1-0.5 mm: 8<br>0.6-1.0 mm: 14<br>1.1-1.5 mm: 4<br>1.6-2.0 mm: 7<br>2.1 mm: 1<br>2.6 mm: 1 | 36 (90%) | 0.1-0.5 mm: 15<br>0.6-1.0 mm: 13<br>1.1-1.5 mm: 6<br>1.6-2.0 mm: 2 | 0 (0%) | N/A | 4 (10%) | 2.5 mm: 1<br>2.6 mm: 1<br>6.2 mm: 1<br>7.3 mm: 1 |
| Tibial posterior slope | 0 (0%) | N/A | 0 (0%) | N/A | 0 (0%) | N/A | 0 (0%) | N/A |
| Tibial resection from highest point | 36 (90%) | 0 mm: 27<br>2 mm: 9 | 40 (100%) | 0 mm: 19<br>0.5 mm: 6<br>1 mm: 12<br>1.5 mm: 1<br>2 mm: 2 | 1 (2.5%) | 1 mm: 1 | 19 (47.5%) | 0 mm: 8<br>1 mm: 3<br>2 mm: 8 |
| Tibial rotation | 0 (0%) | N/A | 0 (0%) | N/A | 0 (0%) | N/A | 0 (0%) | N/A |

*n, number of adjusted cases; N/A, not applicable; dg, degree(s).*

Furthermore, intra- and interobserver reliability demonstrated excellent to good agreement (ICC>0.75) for 7 out of 12 remaining parameters, and 6 out of 12 remaining parameters respectively. A different agreement per surgeon, with an intraobserver reliability range from moderate to excellent (ICC range >0.5 - >0.9) was found in 2 out of 12 parameters, as well as in the range from poor to excellent (ICC range <0.5 - >0.9) (Figure 1 and Figure 2).

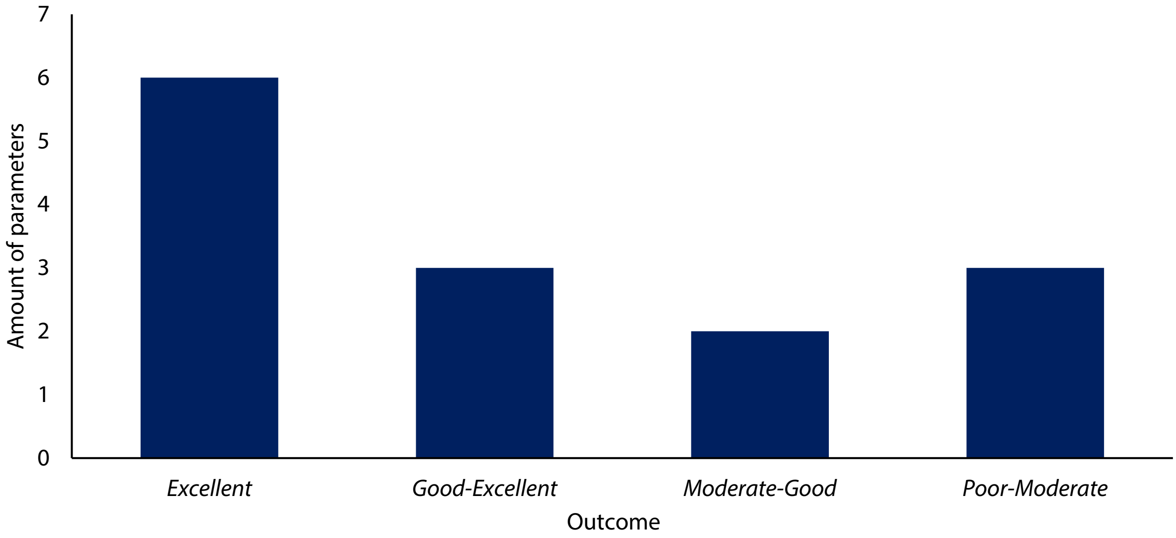


**Figure 1 Number of parameters in each intraobserver reliability range**

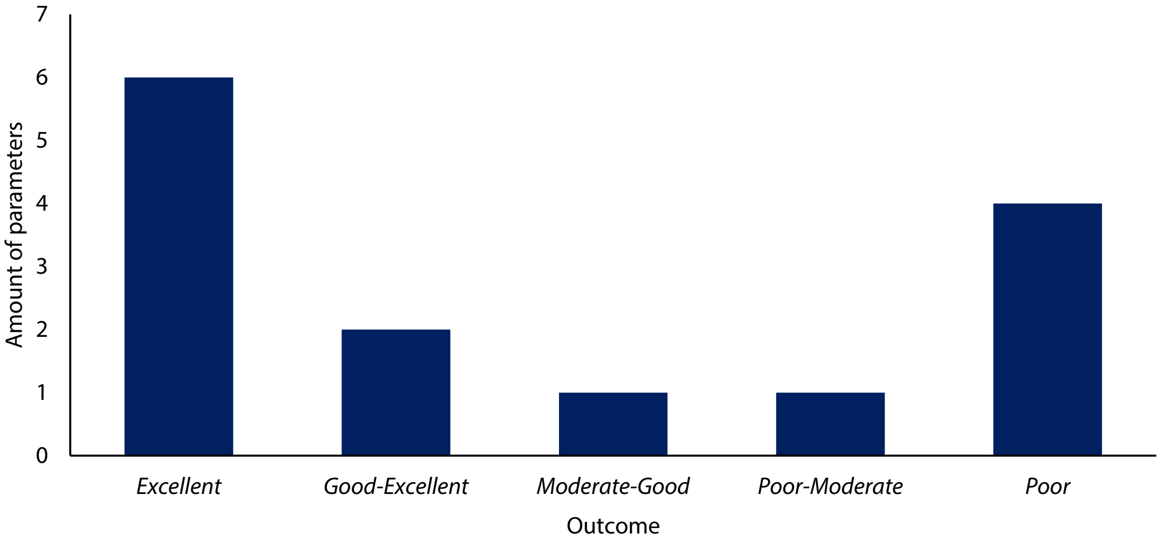


**Figure 2 Number of parameters in each interobserver reliability range**

For 3 parameters (femoral rotation from the epicondylar axis, posterior tibial slope, tibial rotation) no changes to the proposed planning were made by any of the surgeons, resulting in an intra- and interobserver reliability ICC of 1.00.

Table 3 shows an overview per case of changes from proposed planning, and alterations within adjusted plannings. All modifications per surgeon are listed in Table 2.

**Table 3 Amount of adjusted cases combined for all surgeons**

| | Total number of cases adjusted from default plan *n (%)* | Adjusted plans within same case identical *n* |
|---|---|---|
| Femoral distal medial resection | 16 (10%) | 1 |
| Femoral flexion extension | 60 (37.5%) | 22 |
| Femoral mediolateral displacement | 1 (0.6%) | N/A |
| Femoral posteromedial resection | 1 (0.6%) | 1 |
| Femoral rotation from epicondylar axis | 0 (0%) | N/A |
| Femoral size | 52 (32.5%) | 13 |
| Femoral varus/valgus | 4 (2.5%) | 2 |
| Tibial anteroposterior displacement | 73 (45.6%) | 2 |
| Tibial mediolateral displacement | 77 (48.1%) | 2 |
| Tibial posterior slope | 0 (0%) | N/A |
| Tibial resection from highest point | 96 (60%) | 54 |
| Tibial rotation | 0 (0%) | N/A |
| Tibial size | 63 (39.4%) | 28 |
| Tibial varus/valgus | 19 (11.9%) | 6 |

*n, number of adjusted cases, or number of identical adjusted plans within same case; N/A, not applicable.*

## DISCUSSION

This study shows that planning of TKA using PSI by different surgeons results in an excellent agreement for implant sizes between surgeons as well as in repeated planning by the same surgeon. Next to implant size, intra- and interobserver reliability demonstrated good to excellent agreement (ICC>0.75) for 7 out of 12 remaining settings and 6 out of 12 parameters respectively. Hence, it may be stated that PSI is a reliable method for planning of a TKA.

Previous studies have shown that PSI planning accurately predicts the implant size used intraoperatively [5, 8, 12]. The current study shows that planning of the implant size, within and between orthopaedic surgeons, is reliable. The maximum size difference was 1 implant size for the femur, and 2 implant sizes for the tibia, compared to the other plannings of the same patient.

Changes to the default plan can result in different implant sizes. Overall, more changes were made to the tibia than the femur. This may explain the greater difference in default and approved implant size for the femur and tibia: 1 size versus 2 sizes, respectively. TKA surgery can be planned more effectively by understanding the size change frequency of implants, in combination with intraoperative concordance to the preoperative plan. Consequently, when implant sizes can be accurately predicted, and planning implant sizes itself is reliable, the operating team will be able to minimize intraoperative implant size errors in advance. This may lead to improved operating room efficiency due to a decreased number of required operative trays (eq. reliable patient specific trays), less inventory planning, and possibly lowering hospital costs per TKA procedure. This may be of interest for future research.

Previous studies have emphasised that changes in the initial technician's plan were necessary to get an accurate preoperative planning of the implant sizes. Intraoperative alterations in implant size were significantly lower for the plans approved by the surgeon compared to the default plans provided by the technician [4, 10, 12]. Based on this previous literature, the expertise of the surgeon is thus essential for evaluating and approving the default planning provided by the manufacturer.

Intra- and interobserver reliability ICC were 1.00 for femoral rotation from the epicondylar axis, posterior tibial slope, and tibial rotation because none of the surgeons modified these parameters. Due to general consensus on these parameters, less variation will occur, with a higher agreement as result. When there is less consensus on a certain parameter, more changes are made which will result in a lower agreement. Surgeon 3 made the fewest alterations to the proposed plannings, resulting in an excellent agreement (ICC > 0.90) for intraobserver reliability for all settings. Thus, high ICC can be caused by good agreement between adjusted plannings, or due to no alterations made to the proposed plan. Additionally, the adjustment of one parameter can derive alterations of other parameters. For example, an increase of resection might result in the need for a smaller implant size and adjustments in placement of the newly chosen implant size. Awareness of this effect is essential when interpreting the results of this article. This 'snowball effect', as well as less consensus on certain parameters with more changes to the default planning and therefore more differences within and between surgeons, may explain why parameter such as femoral flexion/extension and tibial displacement showed less agreement.

Mechanical alignment technique is considered well performed when the overall limb alignment is within three degrees of neutral. Varus- and valgus angles for both femur and tibia showed modifications with a maximum of 0.5 and 2 degrees respectively. Given that the maximum difference of varus/valgus angles is 2 degrees within the same case, it is supposed that these changes are of no clinical importance. Moreover, adjustments to varus/valgus alignment are known to be dependent on the surgeon's philosophy for an anatomical-, (adjusted) mechanical-, or (restricted) kinematic alignment technique [2, 11]. A patient's specifications, such as findings from physical examination (for example preoperative leg axis, body mass index, and laxity) and previous medical history, can be determinative in the decision for a certain alignment.

Patient-specific characteristics uncontrollable by planning software, namely, ligamentous balancing and lower limb alignment, can require intraoperative changes. Therefore, correct matching of the preoperative plan and intraoperative observations is a crucial factor in PSI-assisted TKA. In case of a mismatch, it is the surgeon's responsibility to consider a switch to conventional instrumentation. In previous literature intraoperative modifications were made to the preoperative plan in 23% up to 36% of MRI-based and CT-based PSI-assisted TKA respectively. Most of these changes occurred due to a poor match between the preoperative plan and intraoperative observations for the tibial component [3, 4, 15].

Furthermore, each surgeon has a 'personal touch' not only in planning, but also intraoperatively with his or her own preferences of additional releases, the decision whether or not recuts are needed, or the consideration to select a thicker insert in patients with a high BMI. Nonetheless, excellent agreement for implant sizes between surgeons and within surgeons was found in this study. Also, the agreement of implant size did not differ between the surgeons who made multiple changes to the proposed plans compared to the surgeon who made very little changes to the proposed plan.

This study has some limitations. Firstly, no power analysis for the number of surgeons, the number of patient cases, and repetitive measurements have been conducted. However, Koo et al. suggested as rule of thumb that researchers should obtain at least 30 heterogeneous samples and involve at least 3 observers whenever possible when conducting a reliability study [9]. Therefore, in the present study 40 patients were included and planned by 4 different orthopaedic surgeons. Secondly, only one type of PSI was evaluated in this study. Other PSI planning systems may perform differently. Thus, these results may not be representative of all PSI technologies available. No comparison to the intraoperative results was made during this study; this study focused on the agreement of repeated planning by different surgeons - the correlation between the planned and placed implant has already been addressed in previous studies.

This study represents the first assessment of intra- and interobserver reliability in PSI TKA. The study showed an excellent intra- and interobserver reliability, among which implant sizes. This may contribute to more optimal and potentially effective preoperative planning of TKA surgery in the future. Therefore, this topic can be of interest for further research. Future research, with larger dataset measurements and different types of both MRI- and CT-based PSI, is necessary to further evaluate these results.

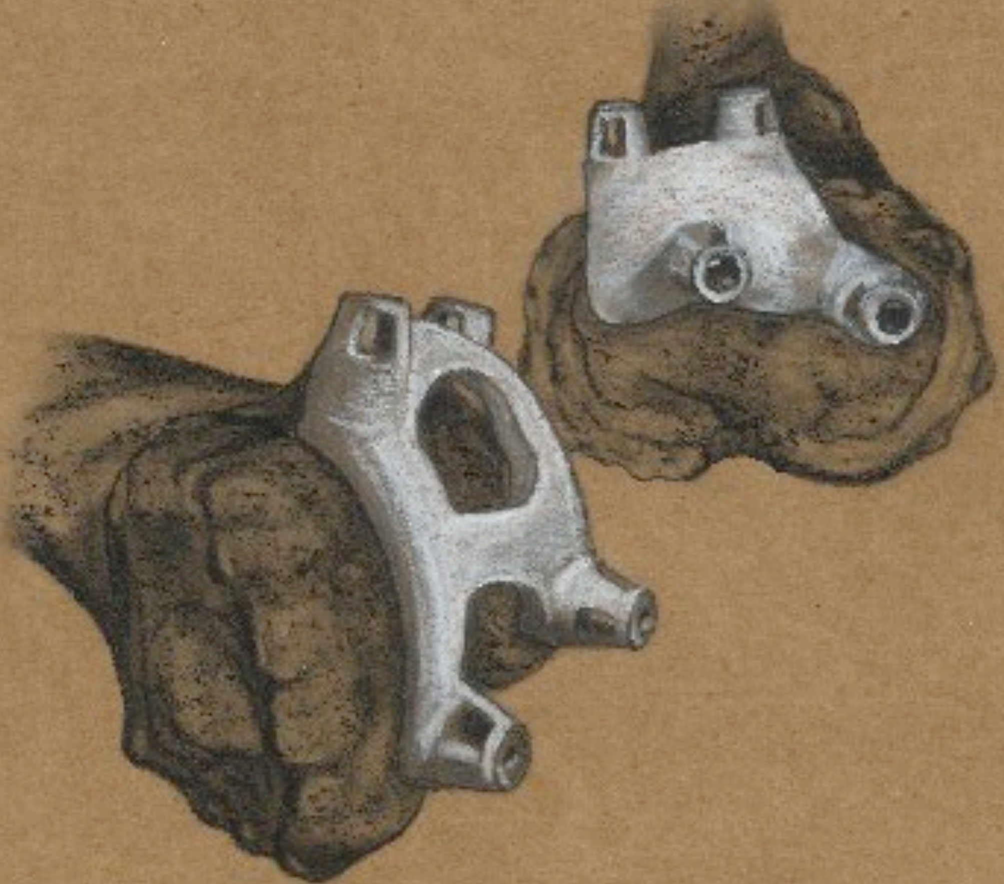
## CONCLUSION

Preoperative planning of TKA implant size using MRI-based PSI showed excellent intra- and interobserver reliability. Future research on comparison of predicted implant size preoperatively to intraoperative results is needed.

## References

1. An VGV, Sivakumar BS, Phan K, Levy YD, Bruce WJM (2017). Accuracy of MRI-based vs. CT-based patient-specific instrumentation in total knee arthroplasty: A meta-analysis. J Orthop Sci, 22(1), 116-120.
2. An VVG, Twiggs J, Leie M, Fritsch BA (2019). Kinematic alignment is bone and soft tissue preserving compared to mechanical alignment in total knee arthroplasty. Knee, 26(2), 466-476.
3. Cavaignac E, Pailhé R, Laumond G, Murgier J, Reina N, Laffosse JM, Bérard E, Chiron P (2015). Evaluation of the accuracy of patient-specific cutting blocks for total knee arthroplasty: a meta-analysis. Int Orthop, 39, 1541-1552.
4. Cucchi D, Menon A, Compagnoni R, Ferrua P, Fossati C, Randelli P (2018). Significant differences between manufacturer and surgeon in the accuracy of final component sizeprediction with CT-based patient-specific instrumentation for total knee arthroplasty. Knee Surg Sports Traumatol Arthrosc, 26(11), 3317-3324.
5. De Vloo R, Pellikaan P, Dhollander A, Vander Sloten J (2017). Three-dimensional analysis of accuracy of component positioning in total knee arthroplasty with patient specific and conventional instruments: A randomized controlled trial. Knee, 24(6), 1469-1477.
6. Gong S, Xu W, Wang R, Wang Z, Wang B, Han L, Chen G (2019). Patient-specific instrumentation improved axial alignmentof the femoral component, operative time and perioperative blood loss after total knee arthroplasty. Knee Surg Sports Traumatol Arthrosc, 27(4), 1083-1095.
7. Huijbregts HJTAM, Khan RJK, Sorensen E, Fick DP, Haebich S (2016). Patient-specific instrumentation does not improve radiographic alignment or clinical outcomes after total knee arthroplasty. Acta Orthop, 87(4), 386–394.
8. Issa K, Rifai A, McGrath MS, Callaghan JJ, Wright C, Malkani AL, Mont MA, McInerney VK (2013). Reliability of Templating with Patient-Specific Instrumentation in Total Knee Arthroplasty. J Knee Surg, 26, 429-434.
9. Koo TK, Li MY (2016). A Guideline of Selecting and Reporting Intraclass Correlation Coefficients for Reliability Research. J Chiropr Med, 15(2), 155-163.
10. Pietsch M, Djahani O, Hochegger M, Plattner F, Hofmann S (2013). Patient-specific total knee arthroplasty: the importance of planning by the surgeon. Knee Surg Sports Traumatol Arthrosc, 21(10), 2220-2226.
11. Rivière C, Iranpour F, Auvinet S, Howell S, Venditolli PA, Cobb J, Parratte S (2017). Alignment options for total knee arthroplasty: A systematic review. Orthop Traumatol Surg Res, 103(7), 1047-1056.
12. Schotanus MGM, Schoenmakers DAL, Sollie, R, Kort NP (2017). Patient-specific instruments for total knee arthroplasty can accurately predict the component size as used peroperative. Knee Surg Sports Traumatol Arthrosc, 25(12), 3844-3848.

13. Schotanus MGM, Thijs E, Heijmans M, Vos R, Kort NP (2018). Favourable alignment outcomes with MRI-based patient-specific instruments in total knee arthroplasty. Knee Surg Sports Traumatol Arthrosc, 26, 2659–2668.
14. Thienpont E, Schwab PE, Fennema P (2017). Efficacy of Patient-Specific Instruments in Total Knee Arthroplasty - A Systematic Review and Meta-Analysis. J Bone Joint Surg Am, 99, 521-530.
15. Woolson ST, Harris AHS, Wagner DW, Giori NJ (2014). Component alignment during total knee arthroplasty with use of standard or custom instrumentation. J Bone Joint Surg, 96(5), 366-372.
16. Wu XD, Xiang BY, Schotanus MCM, Liu ZH, Chen Y, Huang W (2017). CT- versus MRI-based patient-specific instrumentation for total knee arthroplasty: A systematic review and meta-analysis. Surgeon, 15(6), 336-348.



# 4

# Patient-specific instruments for total knee arthroplasty can accurately predict the component size as used peroperative

Schotanus MGM, Schoenmakers DAL, Sollie R, Kort NP

*Knee Surg Sports Traumatol Arthrosc, 2017, 25(12), 3844-3848.*

## ABSTRACT

**Purpose:** Patients-specific instrumentation (PSI) for implantation of total knee arthroplasty (TKA) can be used to predict the implant size for both the femur and the tibia component. This study aims to determine the impact of approval of the PSI planning for TKA on the frequency of, and reason for intraoperative changes of implant sizes.

**Methods:** The clinical records of 293 patients operated with MRI- (90.4%) and CT-based (9.6%) PSI were reviewed for actual used implant size. Preoperative default planning from the technician and approved planning by the operating surgeon were compared with the intraoperative implanted component size for both the femur and tibia. Intraoperative reason for not following the default sizes was outdated. Furthermore, MRI- and CT-based PSI were compared for these outcomes.

**Results:** In 93.9 and 91.1% for, respectively, the femur and tibia (n.s.), the surgeon planned size was implanted during surgery. The predicted size of the femur ($p <0.00$) and the tibia ($p <0.00$) component planned by a technician differed from the implanted component sizes in 62 (21.2%) and 51 (17.4%) patients, respectively. In 17 cases, the femoral component size was adapted intraoperative based on the expert opinion of the operating surgeon. In 26 cases, the tibia component was changed during the surgery because of a mediolateral overhang, sclerotic bone, medial or lateral release, limited extension and/or fixed varus deformity. The results between the MRI- and CT-based PSI did not differ (n.s.).

**Conclusion:** PSI is a tool to help the surgeon to achieve the best possible results during TKA. The planning made by a technician should always be validated and approved by the operating surgeon who has the ultimate responsibility regarding the operation. With PSI, the operating surgeon is able to minimise intraoperative implant size errors in advance to improve operating room efficiency with possible lowering hospital costs per procedure.

## INTRODUCTION

Half a decade ago, patient-specific instrumentation (PSI) for total knee arthroplasty (TKA) were introduced. This simplified procedure eliminates the use of intramedullary guides. Published results on PSI are contradictory. None of the studies demonstrates a significant improvement of postoperative mechanical axis alignment when compared to conventional instrumentation [16, 20]. On the other hand, preoperative digital templating appears to be accurate in predicting the implant size used in TKAs with high reproducibility when used by residents and TKA surgeons [7]. The system can predict intraoperative bony resections, component sizes, alignment, and can prevent unknown constraints during surgery (e.g. extreme implant size, special implant orders) which may improve operating room efficiency [8, 10]. This may result in a reduction of the overall number of surgical instruments and may reduce associated operation expenses [1, 6, 13]. However, the used preoperative imaging techniques (e.g. MRI- or CT-scan) may influence these results.

CT-scans have limitations in visualising and outlining the intra-articular cartilage [22]. Furthermore, CT-based knee models appeared to be slightly larger than the patient's bones when compared to MRI-based 3D knee models, which were slightly smaller [21]. On the other hand, it is shown that the use of CT-based PSI can reduce costs [15]. The PSI system used in this study comes with a planning tool for which suggested planning settings should be approved by the operating surgeon. If not, the guides will be manufactured based on the templates produced by a technician.

This study aims to determine the impact of approval of PSI planning for TKA on the frequency of, and reason for intraoperative changes of the implant size. There are less data to support the accuracy of MRI- and CT-based PSI for TKA to preoperative predict the component size as used during surgery. This case series study hypothesised that both MRI- and CT-based PSI can accurately predict the component size as used perioperative.

## METHODS

A consecutive cohort (n=293) of TKA patients operated between 2012 and 2013 with MRI- or CT-based PSI (Signature, Biomet, Warsaw INC) by a single experienced knee arthroplasty surgeon was included in this study. Default planning from the manufacturer and surgeon approved digital planning were compared with the actual implant size used intraoperatively for both the femur and the tibia. A total of 28 (9.6 %) patients were not eligible for MRI scans and were operated using CT-based PSI. The CT-group consisted of patients with claustrophobia (n= 9), patients with movement artefacts during long MRI scans (n=8) and/or those with implanted electronic devices (pacemaker, neurostimulator for bladder control or cochlear implants; n=12). Baseline demographics and perioperative clinical outcomes are listed in Table 1.

**Table 1 Patient baseline demographics and perioperative clinical outcome**

| Characteristic | PSI cohort (n = 293) |
|---|---|
| Median age, years (range) | 70.1 (43.8–88.9) |
| Male, n (%) | 121 (41.2) |
| Right, n (%) | 152 (51.9) |
| Mean BMI, (range) | 29 (20–47) |
| ASA I/II/III, n | 99/177/17 |
| MRI-based guide, n (%) | 265 (90.4) |

An MRI- or CT-scan was used to generate a computerised three-dimensional (3D) joint reconstruction (default), planned by a technician. This 3D default template enables the surgeon to preoperatively plan the knee replacement using digital planning software (SOMS, Biomet, Warsaw INC) to determine the component sizes and alignment for each patient-specific case. Preoperative default templates from the technician and templates approved by operating surgeon were compared with the intraoperative implanted component size for both the femur and tibia.

The size of the actual components and polyethylene insert used intraoperatively was recorded. The number of patients for which the template size was equal to the intraoperative placed implant was calculated for the following groups: surgeon vs. operation room (OR) (identical size, deviation of 1 size, deviation of >1 size), technician vs. OR (identical size, deviation of 1 size, deviation of >1 size) and surgeon vs. technician (identical size, deviation of 1 size, deviation of >1 size).

When a component size differed, the operative record was checked for the reason not using the approved component size. Furthermore, MRI- and CT-based PSI were compared for these outcomes.

This study was validated and approved by the Independent Review Board (METC Atrium-Orbis-Zuyd Heerlen, the Netherlands; IRB-nr.14N50) and registered online at the Dutch Trial Register (www.trialregister.nl).

### ***Statistical analysis***

Statistical Package for the Social Sciences Statistics Software version 17.0 for Windows (SPSS, Inc., Chicago, Illinois) was used to test any difference of proportions (Fisher exact test).

A post hoc power analysis was done in order to check if this study had sufficient statistical power to detect a treatment effect. P value was considered to be statistically significant at $P \leq 0.05$ for all analyses.

## RESULTS

The proportion of templates approved by the surgeon correctly predicted the size of the femoral (n.s.) and tibial (n.s.) components in 276 (93.9%) and 267 (91.1%) patients, respectively. Femoral ($p < 0.00$) and tibial ($p < 0.00$) component sizes predicted by the planning made by the technician differed from the implanted component sizes in 62 (21.2%) and 51 (17.4%) patients, respectively. There were no conversions from PSI procedures to conventional instrumentation in this study.

The planned component size of the femur from both the technician and operating surgeon was different from the implanted component sizes in two patients. In 29 patients (femur, n=13 and tibia, n=16), the planned size from the technician and the operating surgeon was similar but differed from the implanted size. In 12 other patients, the size for the femur (n=2) and tibia (n=10) estimated by the technician and the implanted size were comparable.

In 17 patients, the femoral component size was adapted peroperatively, based on the expert opinion of the operating surgeon. In 12 patients, the tibial component was changed during the surgery to prevent possible irritation of the capsule and collateral ligaments because of a mediolateral overhang. In 13 other patients, the implant sizes changed, because of sclerotic bone, medial or lateral release, limited extension, fixed varus deformity, and for one patient because of minor medial overhang (<3mm). For 16 patients, the planning of the technician and surgeon were similar but different from the actual implanted size, and in 10 patients, the planning of the technician was similar to the actual implanted size.

Postoperative radiographs showed that the perioperative adjustments for implant sizes were correct and justified. The amount and percentage of differences in planned implant sizes provided by the technician and operating surgeon compared to the actual implanted sizes (OR) are summarised in Table 2.

**Table 2 Amount and percentage of identical sized in approved templates (Surgeon) and default templates (Technician) compared to the used size used peroperative (OR) and agreement between the surgeon and technician**

| | Femur (n=293) | Tibia (n=293) |
|---|---|---|
| Surgeon vs. OR, n (%) | 276 (93.9) | 267 (91.1) |
| Upsized, n (%) | 4 (1.4) | 5 (1.7) |
| Downsized, n (%) | 13 (4.4) | 21 (7.1) |
| Error of 1 size, n (%) | 15 (5.1) | 25 (8.5) |
| Error of >1 size, n (%) | 2 (0.7) | 1 (0.3) |
| Technician vs. OR, n (%) | 231 (78.8) | 242 (82.6) |
| Upsized, n (%) | 5 (1.7) | 33 (11.3) |
| Downsized, n (%) | 57 (19.5) | 18 (6.1) |
| Error of 1 size, n (%) | 56 (19.1) | 46 (15.7) |
| Error of >1 size, n (%) | 6 (2.0) | 5 (1.7) |
| Surgeon vs. technician, n (%) | 243 (82.9) | 248 (84.6) |
| Upsized, n (%) | 3 (1.0) | 38 (13.0) |
| Downsized, n (%) | 47 (16.0) | 7 (2.4) |
| Error of 1 size, n (%) | 49 (16.7) | 41 (14.0) |
| Error of >1 size, n (%) | 1 (0.3) | 4 (1.4) |

The results of the PSI group subdivided into MRI- and CT-based PSI did not differ between the planning made by the technician, operating surgeon and the actual implanted size. These results and the results of the inlay sizes are summarised in Tables 3 and 4, respectively.

A post hoc power analysis revealed that there was sufficient statistical power ($1-\beta=0.98$) to detect a treatment effect when comparing the outcomes between the surgeon and technician. The power was not sufficient regarding the comparison between MRI- and CT-based PSI for the femur ($1-\beta=0.05$) and tibia ($1-\beta=0.35$) component.

**Table 3 Amount and percentage of differences in approved templates (Surgeon) and default templates (Technician) compared to the actual used size perioperative (OR) and between the surgeon and technician when the PSI group is subdivided into MRI- and CT-based PSI for both femur and tibia size**

| | MRI (n = 265) | CT (n = 28) | P value |
|---|---|---|---|
| Identical femur size | | | |
| Surgeon vs. OR, n (%) | 252 (95.1) | 24 (85.7) | n.s. |
| Technician vs. OR, n (%) | 212 (80.0) | 19 (67.9) | n.s. |
| Surgeon vs. technician, n (%) | 219 (82.6) | 24 (85.7) | n.s. |
| Identical tibia size | | | |
| Surgeon vs. OR, n (%) | 240 (90.6) | 27 (96.4) | n.s. |
| Technician vs. OR, n (%) | 222 (83.8) | 20 (71.4) | n.s. |
| Surgeon vs. technician, n (%) | 227 (85.7) | 21 (75.0) | n.s. |

**Table 4 Amount and percentage of the used size of inlay**

| Inlay size | Amount (n = 293) |
|---|---|
| 10 | 96 (32.8 %) |
| 12 | 148 (50.5 %) |
| 14 | 42 (14.3 %) |
| 16 | 7 (2.4 %) |

## DISCUSSION

The most important finding of the present study was that the predicted femoral and tibial component size in primary TKA with PSI, preoperatively approved by the operating surgeon, results in a more accurate prediction of the actual size of the femoral and tibial components used during surgery as compared to the planning settings made by a technician.

Digital preoperative planning can accurately predict the component sizes and therefore minimise the number of surgical trays used peroperatively [5, 10, 11, 18]. However, results on this topic are inconclusive [11, 18]. Only a few papers studied the accuracy of planning component size with the use of PSI for TKA (Table 5). The results in the literature on the topic of size prediction vary with authors, reporting good accuracy of the PSI to predict component size [18] and others reporting frequent intraoperative directed changes [10, 14]. The default template for both the femur and tibia size when templated by a technician was different compared to the approved size for both femur and tibia components. Therefore, the default templates should always be validated digitally and approved by the operating

surgeon [14, 19] to minimise intraoperative implant size error. With PSI's, the operating surgeon is able to recognize abnormal implant sizes preoperatively [8, 10]. These abnormal sizes can be delivered in advance to improve operating room efficiency [10]. This may result in a reduction of the overall number of instruments and surgical trays necessary (reduction from 9 to 3 trays) and therefore decrease expenses associated with sterilization of instruments, storage, staff time and setup time for the operating room [1, 6, 13]. In addition, less instrumentation could help to improve tray and operating room turnover which allows more cases to be completed and thereby lowering hospital costs per procedure [10].
Potential differences in component sizes could not be explained by the use of different imaging techniques, i.e. MRI- vs. CT-based templates [8]. Both MRI- and CT-based PSI's showed comparable percentages of correctly predicted intraoperative implant sizes. Early experiences with MRI-based PSI's for TKA showed outcomes similar to this study [3, 4]. However, this study was not in line with a case-controlled study showing that the actual femoral and tibial component sizes were statistically significantly different from the default size [2]. More recently, a RCT comparing MRI- with CT-based PSI's for TKA, both from the same manufacturer, found no significant differences regarding the perioperative changes for both implant components [17].
The results of this study are in line with other studies using PSI (Table 5) and superior compared to conventional two-dimensional (2D) templating (Table 5). When using conventional 2D templates, the implant size and component alignment are templated in two planes: anterior-posterior and lateral [7, 9, 10, 12]. With PSI's, the surgeon is able to plan from multiple views in a virtual 3D design of the knee joint. PSI also includes more visual options: planning of bony resection, implant alignment (e.g. rotation, varus–valgus, slope and flexion–extension) and an overall view of the planned biomechanical axis. Despite the fact that all the default settings from the technician were approved, Stronach et al. [19] found worse outcome regarding the planned femoral and tibial component size (Table 5).

This study found excellent results in predicting the exact implant size when a surgeon approves the preoperative planning with minimal intraoperative changes. Although well designed, this study does have some limitations. First, this study shows planning data only. Patient reported outcome measures and functional and radiological outcomes are not described. Second, the present study was not randomised to compare conventional TKA with PSI TKA. Third, only one PSI system was from one manufacturer was used which might have affected the outcome. Therefore, our results could be inapplicable for other PSI designs from other manufacturers. Fourthly, because of the small number of patients in the

CT-group, a type II error cannot be ruled out. Finally, in the current study, all patients were operated by one experienced knee surgeon who probably has less to learn from such an assisting tool than low-volume surgeons or residents [6]. This could raise questions about the general applicability.

This study showed that PSI is able to minimise intraoperative implant size errors in advance to improve operating room efficiency with possible lowering hospital costs per procedure [1, 6, 8, 10], while none of the previous studies using PSI demonstrates a significant improvement of postoperative mechanical axis alignment when comparing PSI with conventional instrumentation [16, 20].

**Table 5 Literature overview on templating total knee arthroplasty. Approved templates (Surgeon) and default templates (Technician) compared to the actual used size perioperative (OR) for both femur and tibia size**

| Author(s) | N | Template | Surgeon-OR correct femur/tibia component | Technician-OR correct femur/tibia component |
|---|---|---|---|---|
| Boonen et al. [2] | 40 | PSI, Signature (MRI) | 95%/90% | 80.0%/72.5% |
| Boonen et al. [4] | 200 | PSI, Signature (MRI) | 88.0%/70.5% | 78.5%/59.0% |
| Hsu et al. [7] | 48 | 2D Digital templating software[a] | TKA 54 % | NA |
| Issa et al. [8] | 89 | PSI, shapematch[b] (MRI) | 95.5%/93.0% | NA |
| Kniesel et al. [9] | 94 | 2D digital templating software[c] | With reference ball 52%<br>Without reference ball 33% | NA |
| Levine et al. [10] | 176 | 2D digital templating software[d] | 66%/58.5% | NA |
| Miller and Purtill [12] | 50 | 2D digital templating software | 64%/60% | NA |
| Pietsch et al. [14] | 50 | PSI[e] (MRI) | 100%/84% | 84%/38% |
| Stronach et al. [19] | 66 | PSI, Signature (MRI) | 23%/47% | NA |
| Current study | 293 | PSI, Signature (MRI and CT) | 93.9%/91.1% | 78.8%/82.6% |

[a] *OrthoView LLC Jacksonville, Florida.*

[b] *Stryker Orthopaedics, Mahwah, NJ.*

[c] *Medi-Cad AP-X-rays, Hectec GmbH; Niederviehbach, Germany.*

[d] *Advanced Case Plan, Stryker Imaging, Flower Mound, Texas.*

[e] *Patient-Specific Instrumentation, Zimmer, Warsaw, USA.*

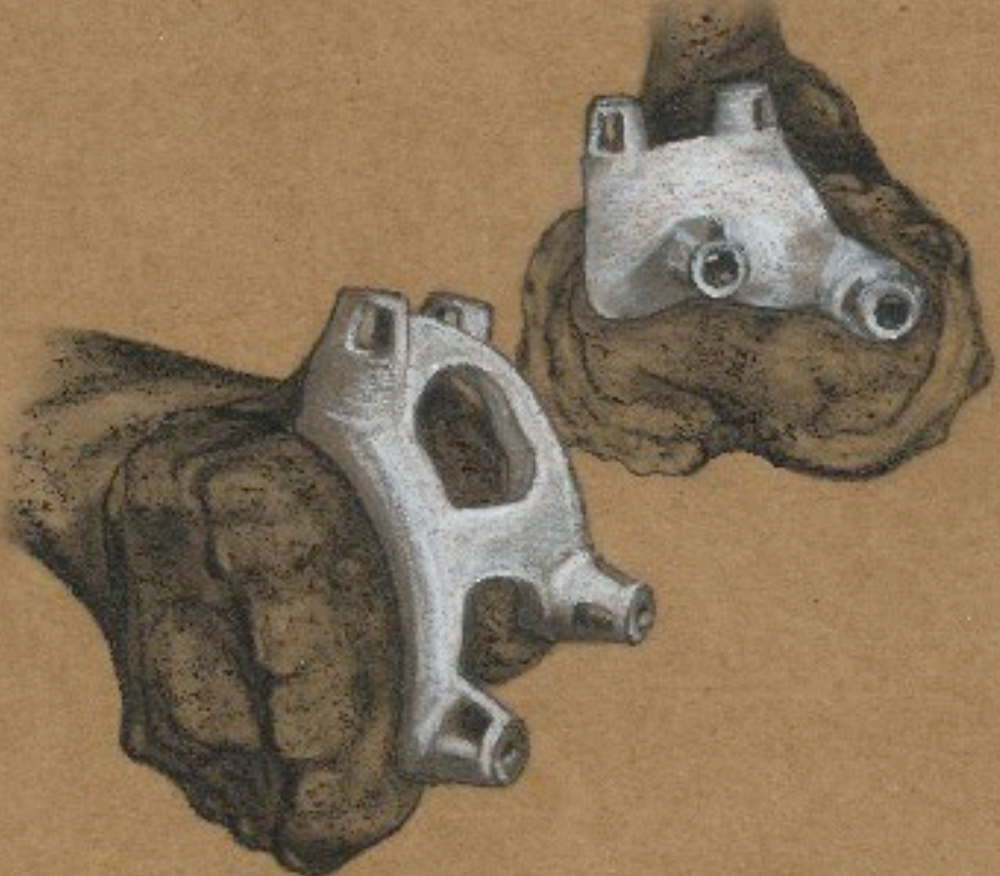
## CONCLUSION

Despite the retrospective nature of this study, this study provided valuable information regarding the potential ability to preoperatively predict the perioperative component sizes. PSI is a tool to help the surgeon to achieve the best possible results during TKA. The planning made by a technician should always be validated and approved by the operating surgeon who has ultimate responsibility regarding the operation.

## REFERENCES

1. Barrack RL, Ruh EL, Williams BM et al (2012). Patient specific cutting blocks are currently of no proven value. J Bone Joint Surg, 94(Suppl A), 95–99.
2. Boonen B, Schotanus MG, Kort NP (2012). Preliminary experience with the patient-specific templating total knee arthroplasty. Acta Orthop, 83(4), 387–393.
3. Boonen B, Schotanus MG, Kerens B et al (2013). Intra-operative results and radiological outcome of conventional and patientspecific surgery in total knee arthroplasty: a multicenter randomised controlled trial. Knee Surg Sports Traumatol Arthrosc, 21(10), 2206–2212.
4. Boonen B, Schrander DE, Schotanus MGM et al (2015). Patient Specific Guides in total Knee Arthroplasty: A two year Follow up of the first two hundred consecutive cases performed By a single Surgeon. J Clin Rheumatol Muscoloskelet Med, 1, 1–10.
5. Del Gaizo D, Soileau ES, Lachiewicz PF (2009). Value of preoperative templating for primary total knee arthroplasty. J Knee Surg, 22(4), 284–293.
6. Hamilton WG, Parks NL, Saxena A (2013). Patient-specific instrumentation does not shorten surgical time: a prospective, randomized trial. J Arthroplasty, 28(8 Suppl), 96–100.
7. Hsu AR, Kim JD, Bhatia S, Levine BR (2012). Effect of training level on accuracy of digital templating in primary total hip and knee arthroplasty. Orthopedics, 35(2), e179–e183.
8. Issa K, Rifai A, McGrath MS et al (2013). Reliability of templating with patient-specific instrumentation in total knee arthroplasty. J Knee Surg, 26, 429–434.
9. Kniesel B, Konstantinidis L, Hirschmüller A et al (2014). Digital templating in total knee and hip replacement: an analysis of planning accuracy. Int Orthop, 38(4), 733–739.
10. Levine B, Fabi D, Deirmengian C (2010). Digital templating in primary total hip and knee arthroplasty. Orthopedics, 33(11), 797.
11. Lorio R, Siegel J, Specht LM et al (2009). A comparison of acetate vs digital templating for preoperative planning of total hip arthroplasty: is digital templating accurate and safe? J Arthroplasty, 24(2), 175–179.
12. Miller AG, Purtill JJ (2012). Accuracy of digital templating in total knee arthroplasty. Am J Orthop (Belle Mead NJ), 41(11), 510–512.
13. Nunley RM, Ellison BS, Ruh EL et al (2012). Are patient-specific cutting blocks cost-effective for total knee arthroplasty? Orthop Relat Res, 470(3), 889–894.
14. Pietsch M, Djahani O, Hochegger M et al (2013). Patient-specific total knee arthroplasty: the importance of planning by the surgeon. Knee Surg Sports Traumatol Arthrosc, 21(10), 2220–2226.
15. Rubin LE, Murgo KT (2013). Brief report: total knee arthroplasty performed with patient-specific, pre-operative CT-guided navigation. R I Med J, 96(3), 34–37.

16. Sassoon A, Nam D, Nunley R, Barrack R (2015). Systematic review of patient-specific instrumentation in total knee arthroplasty: new but not improved. Clin Orthop Relat Res, 473, 151–158.
17. Schotanus MGM, Sollie R, van Haaren EH et al (2016). Radiological discrepancy between MRI- and CT-based patientspecific matched guides for total knee arthroplasty from the same manufacturer: a randomised controlled trial. Bone Joint J, 98-B(6), 786–792.
18. Specht LM, Levitz S, Iorio R et al (2007). A comparison of acetate and digital templating for total knee arthroplasty. Clin Orthop Relat Res, 464, 179–183.
19. Stronach BM, Pelt CE, Erickson J, Peters CL (2013). Patient-specific total knee arthroplasty required frequent surgeon-directed changes. Clin Orthop Relat Res, 471(1), 169–174.
20. Thienpont E, Schwab PE, Fennema P (2014). A systematic review and meta-analysis of patient-specific instrumentation for improving alignment of the components in total knee replacement. Bone Joint J, 96-B(8), 1052–1061.
21. White D, Chelule KL, Seedhom BB (2008). Accuracy of MRI vs CT imaging with particular reference to patient specific templates for total knee replacement surgery. Int J Med Robot, 4(3), 224–231.
22. Winder J, Bibb R (2005). Medical rapid prototyping technologies: state of the art and current limitations for application in oral and maxillofacial surgery. J Oral Maxillofac Surg, 63, 1006–1015.



# 5

# Consistency in patient-reported outcome measures after total knee arthroplasty using patient-specific instrumentation: a 5-year follow-up of 200 consecutive cases

Schoenmakers DAL, Schotanus MGM, Boonen B, Kort NP

*Knee Surg Sports Traumatol Arthrosc, 2018, 26(6), 1800-1804.*

## ABSTRACT

**Purpose:** The purpose of this study was to evaluate the 5-year follow-up results of the first 200 total knee arthroplasties (TKA) performed by one high-volume surgeon, using patient-specific instrumentation (PSI). To date, there has been no other research into the mid-term follow-up of TKA performed using PSI.

**Methods:** A total of 184 consecutive patients (200 TKA) were evaluated. Outcome measures included implant survival rate, adverse events, and the following patient-reported outcome measures (PROMs); Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), Oxford Knee Score (OKS), Pain Visual Analogue Score (VAS) and EuroQol-5D Score (EQ-5D).

**Results:** Revision surgery was performed for late secondary prosthetic joint infection (n=1, total revision), aseptic loosening (n=1, tibial component revision), instability (n=1, isolated polyethylene insert exchange), and polyethylene insert breakage (n=1, isolated polyethylene insert exchange). Other adverse events were as follows: debridement, antibiotics and implant retention for early prosthetic joint infection (n=1), surgical debridement for haemarthrosis (n=1), superficial wound infection (n=2), thromboembolic events (n=2), compartment syndrome (n=1), and nerve injury (n=2). All median outcome scores for patient reported outcome measures at 5 years improved significantly compared with the preoperative values ($p \leq 0.05$). Median outcome scores were not significantly different between 1- and 5-year moments of follow-up, except for a significant decrease of EQ-VAS ($p \leq 0.05$) between these two follow-up moments.

**Conclusion:** PROMs are consistent for 5-year follow-up of TKA using PSI. After 5 years of follow-up, revision surgery for any reason occurred in four patients (2%).

## INTRODUCTION

Positioning of knee prosthesis components and lower limb alignment after total knee arthroplasty (TKA) are important factors influencing implant survival and clinical results [17,19,25]. Surgical techniques have evolved over time, and now there are several methods used that assist in obtaining the desired alignment of TKA. One of these methods includes patient-specific instrumentation (PSI). PSI uses guides based on a preoperative MRI- or CT-scan of the patient's leg. This technology has the potential to increase cost-effectiveness due to the reduction in surgical time and the need for fewer surgical trays [24].

Many previous studies have compared alignment obtained with PSI to standard instrumentation, with mixed results [1,3-5,9,10,13,15,21]. Research on the use of PSI shows a reduction in surgical time [4,5,8,10,21,24], blood loss [4,5,9,24], and hospital stay [9,21] in comparison to conventional instrumentation. Others did not find significant differences in surgical time [1], blood loss [1,8,21], or hospital stay [1,4,8,24].

Fewer studies focused on short-term functional follow-up results, which shows similar good outcomes when compared to conventional instrumentation [1,6,20]. However, no data exists with regard to longer follow-up results of TKA performed using PSI. In continuation of the previous study by Boonen et al [6], this study presents the five-year follow-up results of the first 200 consecutive cases operated on by one single high-volume surgeon. The focus of this study is on implant survival rate, adverse events, and on patient reported outcome measures (PROMs). The authors hypothesise that results of TKA performed using PSI after five years of follow-up show similar good outcomes compared to earlier follow-up.

## METHODS

Data was collected from the first 184 patients, on whom 200 TKAs were performed using PSI. The data consisted of patient records of their preoperative appointment and routine one-, two-, and five-year follow-up appointments.

### *Cohort and surgical technique*

The Signature$^{TM}$ system (Zimmer-Biomet Inc., Warsaw, IN) was used in this cohort. The patients underwent surgery between July 2009 and March 2011. Inclusion- and exclusion criteria, as well as surgical techniques and perioperative management are described in previous reports [5,6]. Baseline characteristics are listed in Table 1.

**Table 1 Baseline characteristics**

| Characteristic | Median (interquartile range (IQR), or absolute numbers (%) |
|---|---|
| Females, n (%) | 106 (57.6%) |
| Median age at surgery date, years (IQR) | 68.1 (60.7-74.6) |
| Bilateral TKA cases, n (%) | 16 (8.7%) |
| Median follow up, years (IQR) | 5.5 (5.2-5.9) |

### *Outcome measurements*

Implant survival rate was defined as revision surgery for any reason. All revision surgeries and adverse events were recorded during the five-year follow-up.

Preoperatively, patients completed the following questionnaires: the Western Ontario and McMaster osteoarthritis index (WOMAC; scored from 0 to 100, 0 being the worst outcome and 100 being the best possible outcome) [27], the Oxford Knee Score (OKS; scored from 12 to 60, with 12 being the worst outcome and 60 being the best possible outcome) [12], the Pain Visual Analogue Score (VAS; scored from 0 to 10, 0 representing no pain and 10 representing the worst imaginable pain) and the EuroQol (The EQ-5D-3L) including the EQ-Index (scored from 1 to 3, 1 represents perfect health and no disabilities) and EQ-Visual Analog Scale (EQ-VAS; records the respondent's own assessment of their health status on a vertical VAS where the scores are anchored on 100 equal to 'Best imaginable health state' and 0 equal to 'Worst imaginable health state') [7]. The health states, defined by the EQ-5D-3L, can be converted to a single index value using the calculator provided by The EuroQol Group.

Scores on the questionnaires were compared between the different follow-up visits. The same set of questionnaires was completed by patients themselves right before their appointments preoperatively, and one, two, and five years postoperatively.

At the time of five-year follow-up 11 patients (12 TKAs, 6%) were deceased of causes unrelated to TKA. Of the patients, 116 (128 TKAs, 64%) attended their five-year follow-up appointment, while 57 (60 TKAs, 30%) cancelled their follow-up appointment, and three (3 TKAs, 1.5%) did not complete the questionnaires. The aforementioned questionnaires were sent out by post to these 60 patients (63 TKAs, 31.5%); 54 patients returned their questionnaires (57 TKAs, 28.5%), two (2 TKAs, 1%) were not able to participate due to Alzheimer's disease, one (1 TKA, 0.5%) declined to participate, and three others (3 TKAs, 1.5%) did not respond, so additional information could not be obtained. These six patients (6 TKAs, 3%) were considered lost to follow-up.

Five patients (5 TKAs, 2.5%) were excluded from overall analysis of the questionnaires because of revision surgery or prosthetic joint infection. PROMs were evaluated from 162 patients (177 TKAs, 88.5%), with a median follow-up of 5.5-years (IQR 5.2-5.9 years) (Figure 1).

### *Institutional review board approval*

Institutional review board (METC Z, Heerlen, the Netherlands) approval was obtained for the study (trial number 12-N-139).

### *Statistical analysis*

All statistical analyses were performed using SPSS software version 20.0 (SPSS Inc., Chicago, Illinois). Descriptive statistics were used for baseline characteristics. The Shapiro-Wilk test showed that data was not normally distributed. Therefore, Wilcoxon Signed Ranks Tests were performed on significant interactions. A threshold for all statistical comparisons of p-value ≤ 0.05 was considered to be statistically significant. Data are presented as median with interquartile ranges (IQR) or with frequencies.

## RESULTS

After five years of follow-up, four patients (4 TKAs, 2%) had undergone revision surgery (Figure 1). One patient required total revision for a secondary haematogenic prosthetic joint infection associated with a colon ascendens tumour (26.4 months after TKA). Prior to this two-step revision, the patient underwent debridement, antibiotics, and implant retention in another medical centre. Furthermore, revision of the tibial component was required in one patient for aseptic loosening (25.7 months after TKA). Isolated polyethylene insert exchange with retention of total knee prosthesis occurred in two patients due to instability of collateral ligaments or breakage of the polyethylene insert after trauma (30.0 months and 44.4 months after TKA, respectively).

One patient received debridement, antibiotics, and implant retention for early prosthetic joint infection (16 days after TKA). Surgical (arthroscopic) debridement was done in one patient to alleviate pain due to haemarthrosis (44 days after placement of TKA). One patient required fasciotomy due to compartment syndrome five days after surgery. Two patients received oral antibiotics for superficial wound infections. Other complications were pulmonary embolism six days after surgery (n=1), minor stroke nine days after surgery (n=1), femoral nerve lesion after femoral nerve block anaesthesia (n=1), and temporarily tibial nerve neuropraxia (n=1).

PROMs measured preoperatively and at the follow-up moments are shown in Table 2. After five years of follow-up, all median outcome scores for PROMs improved significantly from preoperative values ($p \leq 0.05$). No significant differences were observed between postoperative scores one, two or five years after the operation, except for a significant decrease of EQ-VAS from one- to five-year follow-up ($p=0.002$).

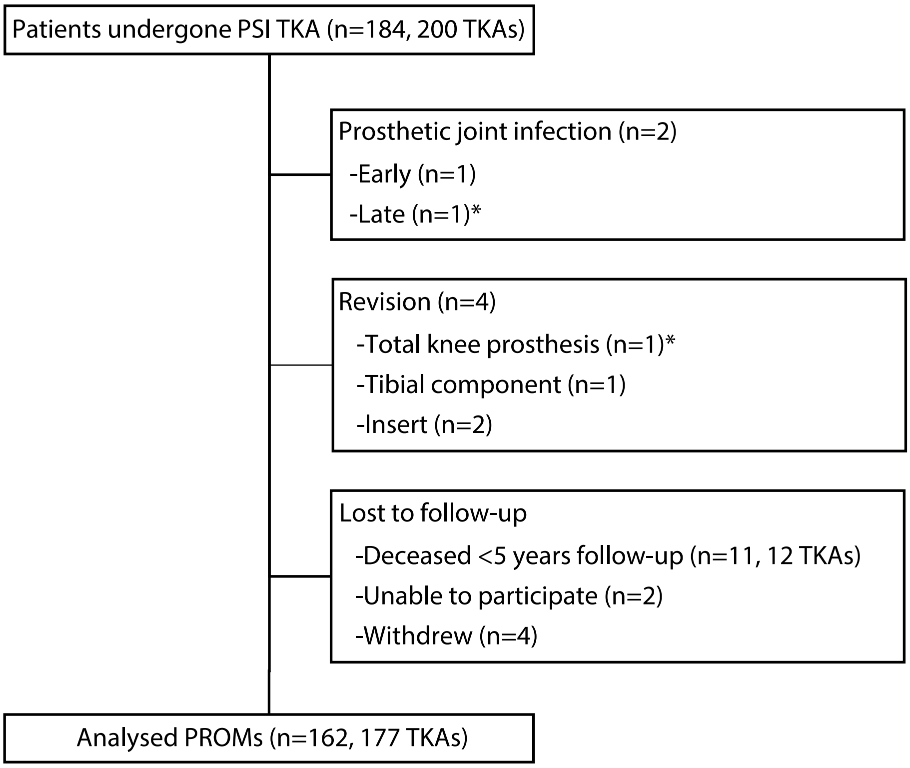


**Figure 1 Diagram of the number of patients enrolled in the study, patients with revision or prosthetic joint infection, number of patients lost to follow-up, and analysed PROMs**

**Occurred in same patient.*

**Table 2 Results at the different follow-up visits presented as median scores and interquartile range**

| | Preoperative | 1-year postoperative | 2-year postoperative | 5-year postoperative |
|---|---|---|---|---|
| WOMAC | 57 (39-79) | 91 (72-97)* | 90 (72-98)* | 90 (68-98)* |
| OKS | 21 (16-26) | 41 (36-45)* | 41 (33-45)* | 42 (33-46)* |
| VAS | 7 (6-8) | 2 (0-5)* | 2 (0-5)* | 1 (0-5)* |
| EQ-Index | 0.788 (0.719- 0.805) | 0.874 (0.805-1.00)* | 0.874 (0.805-1.00)* | 0.874 (0.805-1.00)* |
| EQ-VAS | 60 (50-80) | 80 (70-90)* | 80 (70-90)* | 80 (60-90)*# |

*WOMAC, Western Ontario McMaster Universities Osteoarthritis index; OKS, Oxford Knee score (OKS); VAS, Pain Visual Analogue Score (VAS); EQ-index and EQ-VAS, EQ-5D-3L.*
** significant difference from preoperative score (p <0.01).*
*# significant difference from 1-year postoperative score (p=0.002).*

## DISCUSSION

The most important finding of the present study is that five-year follow-up results from 200 TKAs using PSI show similar good outcomes in PROMs compared to the one-year follow-up. Also, revision for any reason occurred in four patients (2%), which is well within range of the five-year TKA survival of 93-97% as found by others [11,16]. Sadoghi et al [28] used worldwide arthroplasty registers to evaluate the reasons for revision. The authors found aseptic loosening (29.8%), septic loosening (14.8%), and pain (9.5%) as most common causes for revision. Instability and implant breakage accounted for 6.2% and 4.7%, respectively [28]. In the present study, we found aseptic- and septic loosening to account for 50% of all revisions. Furthermore, Boonen et al [3] found no significant different occurrence of adverse events between PSI and conventional instrumented TKAs. While the sample size in the current study (n=200) is too small for drawing valid conclusions on reasons for revision, the revision rates reported here are not strikingly different from the results found by the aforementioned authors.

Our data includes two patients (1%) with prosthetic joint infection; which is similar to the rates reported in literature. Kurtz et al [18] identified prosthetic joint infection incidence of 1.55% within two years and 0.46% between two and up to 10 years follow-up. Pulido et al [23] found a similar incidence of 1.1% with a mean time to diagnosis occurring 431 days after surgery. Other studies identified an infection incidence of 1.8% up to 3.6% [22,29].

PROMs are considered to represent the best objective measurement of the patients' own health perception [26]. Nonetheless, PROMs remain inherently subjective, prone to an individual's interpretation and perception of joint functioning [14,26]. The authors of the present study received several times the feedback from patients that they found it difficult to score the PROM's. Additionally, patients described having difficulties in keeping other conditions or illnesses out of consideration that might have impaired mobility, general condition or quality of life. In the present study, PROMs measuring health-related quality of life were used next to domain-specific PROMs (e.g. pain, function, satisfaction after TKA) to provide a holistic and global approach to the TKA outcome assessment, as suggested by Hossain et al [14]. Several studies proposed the use of performance-based measures as an addition to PROMs [2,14]. Especially in younger patients, this may be of added value to future prospective studies.

In this study it was shown that almost all PROMs did not significantly differ between one- and five years after TKA using PSI. Only the EQ-VAS (self-rated health score) decreased significantly at the five-year follow-up compared to one year postoperatively. Due to aging and associated health issues, decreased self-rated health scores could be a logical consequence. Yet, the self-rated health score was still significantly better than the preoperative value. This may show that problems resulting from knee arthritis alone only partially determine the overall health score.

The strength of this study is that it is the first study that presents five-year follow-up results of TKA performed using PSI. Furthermore, 200 consecutive patients, operated on by one single surgeon were evaluated. Therefore, the clinical relevance of this study lays in the confirmation of good mid-term results that can be expected from PSI TKA, in terms of implant survival, adverse events, and PROMs. A limitation of this study was the usage of only one PSI system, therefore these results may not be applicable to all existing PSI systems. Moreover, the present study did not directly compare results from TKA using PSI with results of conventional TKA or other surgical techniques. In addition, our study exclusively contains cases from a high-volume TKA surgeon whereas results may not be the same for lower volume surgeons. Consequently, future research should focus on comparing PSI with other surgical techniques and PSI usage in lower volume surgeons. Furthermore, future research should assess longer follow-up results of TKA using PSI once these data are available.

## CONCLUSION

PROMs are consistent for five-year follow-up of TKAs using PSI. After five years of follow-up, revision surgery for any reason occurred in four patients (2%). Building on the findings in this study, future research should focus on the follow-up results of PSI longer than 5 years after surgery, the usage of PSI in lower volume surgeons, and the comparison with other surgical techniques for performing TKA.

## REFERENCES

1. Abane L, Anract P, Boisgard S, Descamps S, Courpied JP, Hamadouche M (2015). A comparison of patient-specific and conventional instrumentation for total knee arthroplasty: a multicentre randomised controlled trial. Bone Joint J, 97-B, 56–63.
2. Bolink SA, Grimm B, Heyligers IC (2015). Patient-reported outcome measures versus inertial performance-based outcome measures: a prospective study in patients undergoing primary total knee arthroplasty. Knee, 22, 618–623.
3. Boonen B, Schotanus MG, Kerens B, van der Weegen W, Hoekstra HJ, Kort NP (2016). No difference in clinical outcome between patient-matched positioning guides and conventional instrumented total knee arthroplasty two years post-operatively: a multicentre, double-blind, randomised controlled trial. Bone Joint J, 98-B, 939–944.
4. Boonen B, Schotanus MG, Kerens B, van der Weegen W, van Drumpt RA, Kort NP (2013). Intra-operative results and radiological outcome of conventional and patient-specific surgery in total knee arthroplasty: a multicentre, randomised controlled trial. Knee Surg Sports Traumatol Arthrosc, 21, 2206–2212.
5. Boonen B, Schotanus MG, Kort NP (2012). Preliminary experience with the patient-specific templating total knee arthroplasty. Acta Orthop, 83, 387–393.
6. Boonen B, Schrander DE, Schotanus MGM, Hulsmans FJ, Kort NP (2016). Patient Specific Guides in total Knee Arthroplasty: a two year follow up of the first two hundred consecutive cases performed by a single Surgeon. J Clin Rheumatol Musculoskelet Med, 5, 10–15.
7. Brooks R (1996). EuroQol: the current state of play. Health Policy, 37, 53–72.
8. Chareancholvanich K, Narkbunnam R, Pornrattanamaneewong C (2013). A prospective randomised controlled study of patientspecific cutting guides compared with conventional instrumentation in total knee replacement. Bone Joint J, 95-B, 354–359.
9. Ferrara F, Cipriani A, Magarelli N, Rapisarda S, De Santis V, Burrofato A, Leone A, Bonomo L (2015). Implant positioning in TKA: comparison between conventional and patient-specific instrumentation. Orthopedics, 38, e271-280.
10. Fu H, Wang J, Zhou S, Cheng T, Zhang W, Wang Q, Zhang X (2015). No difference in mechanical alignment and femoral component placement between patient-specific instrumentation and conventional instrumentation in TKA. Knee Surg Sports Traumatol Arthrosc, 23, 3288–3295.
11. Gothesen O, Espehaug B, Havelin L, Petursson G, Lygre S, Ellison P, Hallan G, Furnes O (2013). Survival rates and causes of revision in cemented primary total knee replacement: a report from the Norwegian Arthroplasty Register 1994–2009. Bone Joint J, 95-B, 636–642.
12. Haverkamp D, Breugem SJ, Sierevelt IN, Blankevoort L, van Dijk CN (2005). Translation and validation of the Dutch version of the Oxford 12-item knee questionnaire for knee arthroplasty. Acta Orthop, 76, 347–352.

13. Heyse TJ, Tibesku CO (2014). Improved femoral component rotation in TKA using patient-specific instrumentation. Knee, 21, 268–271.
14. Hossain FS, Konan S, Patel S, Rodriguez-Merchan EC, Haddad FS (2015). The assessment of outcome after total knee arthroplasty: are we there yet? Bone Joint J, 97-B, 3–9.
15. Jiang J, Kang X, Lin Q, Teng Y, An L, Ma J, Wang J, Xia Y (2015). Accuracy of patient-specific instrumentation compared with conventional instrumentation in total knee arthroplasty. Orthopedics, 38, e305–e313.
16. Khan M, Osman K, Green G, Haddad FS (2016). The epidemiology of failure in total knee arthroplasty: avoiding your next revision. Bone Joint J, 98-B, 105–112.
17. Kim YH, Park JW, Kim JS, Park SD (2014). The relationship between the survival of total knee arthroplasty and postoperative coronal, sagittal and rotational alignment of knee prosthesis. Int Orthop, 38, 379–385.
18. Kurtz SM, Ong KL, Lau E, Bozic KJ, Berry D, Parvizi J (2010). Prosthetic joint infection risk after TKA in the Medicare population. Clin Orthop Relat Res, 468, 52–56.
19. Lotke PA, Ecker ML (1977). Influence of positioning of prosthesis in total knee replacement. J Bone Joint Surg Am, 59, 77–79.
20. Nam D, Nunley RM, Berend KR, Lombardi AV, Barrack RL (2016). The impact of custom cutting guides on patient satisfaction and residual symptoms following total knee arthroplasty. Knee, 23, 144–148.
21. Noble JW Jr, Moore CA, Liu N (2012). The value of patientmatched instrumentation in total knee arthroplasty. J Arthroplasty, 27, 153–155.
22. Peersman G, Laskin R, Davis J, Peterson M (2001). Infection in total knee replacement: a retrospective review of 6489 total knee replacements. Clin Orthop Relat Res, 392, 15–23.
23. Pulido L, Ghanem E, Joshi A, Purtill JJ, Parvizi J (2008). Periprosthetic joint infection: the incidence, timing, and predisposing factors. Clin Orthop Relat Res, 466, 1710–1715.
24. Rathod PA, Deshmukh AJ, Cushner FD (2015). Reducing blood loss in bilateral total knee arthroplasty with patient-specific instrumentation. Orthop Clin N Am, 46, 343–350.
25. Ritter MA, Faris PM, Keating EM, Meding JB (1994). Postoperative alignment of total knee replacement. Its effect on survival. Clin Orthop Relat Res, 299, 153–156.
26. Rolfson O, Malchau H (2015). The use of patient-reported outcomes after routine arthroplasty: beyond the whys and ifs. Bone Joint J, 97-B, 578–581.
27. Roorda LD, Jones CA, Waltz M, Lankhorst GJ, Bouter LM, van der Eijken JW, Willems WJ, Heyligers IC, Voaklander DC, Kelly KD, Suarez-Almazor ME (2004). Satisfactory cross cultural equivalence of the Dutch WOMAC in patients with hip osteoarthritis waiting for arthroplasty. Ann Rheum Dis, 63, 36–42.
28. Sadoghi P, Liebensteiner M, Agreiter M, Leithner A, Bohler N, Labek G (2013). Revision surgery after total joint arthroplasty: a complication-based analysis using worldwide arthroplasty registers. J Arthroplasty, 28, 1329–1332.

29. Soriano A, Bori G, Garcia-Ramiro S, Martinez-Pastor JC, Miana T, Codina C, Macule F, Basora M, Martinez JA, Riba J, Suso S, Mensa J (2008). Timing of antibiotic prophylaxis for primary total knee arthroplasty performed during ischemia. Clin Infect Dis. 46, 1009–1014.

# PART III

## Innovations in digital pre- and intraoperative planning modalities for TKA

# 6

# Preoperative planning with X-PSI compared to MRI-based patient-specific instrumentation in total knee arthroplasty

Schoenmakers DAL, Schotanus MGM, Kort NP

*In review at J Clin Orthop Trauma, submitted August 2022.*

## ABSTRACT

**Purpose:** X-ray-based patient-specific instrumentation (PSI) for total knee arthroplasty (TKA) is a new method for preoperative planning of TKA. This study presents the preliminary experiences with preoperative planning of TKA, comparing Zimmer Biomet's X-PSI with MRI-based planning for patient-specific instrumentation (PSI).

**Methods:** One high-volume experienced orthopaedic surgeon modified and approved preoperative X-PSI and MRI-based PSI planning of 20 patients. Absolute differences in individual subjects of the planning by both modalities were evaluated for the following parameters: femoral- and tibial implant size, femoral resection (medial-distal, lateral-distal, medial-posterior, and lateral-posterior), tibial resection (medial and lateral), femoral flexion-extension angle, femoral- and tibial varus/valgus angle, posterior slope tibia, tibial rotation, and femoral- and tibial rotation.

**Results:** The planned implant size was within one size difference between X-PSI and MRI-based planning of the same patient in 95% of cases for femoral implant size and 90% of the cases for tibial implant size. Furthermore, femoral resection levels were more comparable between both imaging modalities, whereas more variation was seen between planned tibial resection levels.

**Conclusion:** This study presents preliminary experiences with X-PSI planning compared to MRI-based patient-specific instrumentation (PSI) planning. Further research on X-ray-based PSI is needed.

## INTRODUCTION

Technological developments in total knee arthroplasty (TKA) have aimed to improve the accuracy of proper implant planning and placement. Accurate preoperative planning, selection of correct implant size, the optimal position of implant components, and prevention of implant-related complications has been the subject of numerous studies [6, 10, 12]. In the past, analogue and digital radiograph-based preoperative planning systems have been introduced. Later, patient-specific instrumentation (PSI) based on 3D imaging became more popular.

PSI for TKA has been the subject of various studies in the last years. Preoperative PSI planning of TKA is primarily based on preoperative magnetic resonance imaging (MRI) or computed tomography (CT) images. Several authors studied patient-specific cutting guides produced from MRI or CT imaging methods. It was found that MRI-based PSI creates a lower proportion of outliers in coronal alignment compared to CT-based planning [1, 11, 15, 16, 19]. Studies investigating the accuracy of digital templating showed an accurate prediction of implant size compared to implanted component sizes [5, 14]. Furthermore, it has been suggested that template-directed instrumentation is a cost-effective approach in primary TKA and might improve operating room time management [4, 9]. Nonetheless, one of the significant barriers of implementation of PSI technology is the need for a CT- or MRI scan.

A new development in this field is the introduction of X-PSI planning. This surgical planning system utilises X-ray technology to generate three-dimensional anatomic models for patient-specific implant positioning. This constructed model allows the surgeon to review, edit and approve the surgical placement of the implant components, identical to previous PSI methods. The approved planning is then used to manufacture 3D-printed guides intended for intraoperative use. The advantage of this new method is planning on preoperative X-ray imaging instead of MRI or CT scans. Therefore, there is a reduction in time and efficiency in the logistic process, costs, and a decrease in radiation dosage to patients in CT usage. First experiences with X-ray-based PSI (3X-technology) showed a similar prediction of implant size by this new technique compared to planning on CT-based images in 70-78% of cases for femoral- and tibial implant size, respectively. When allowing for a difference of ±1 size, the value went up to 95.7% and 100% for femoral- and tibial component size, respectively [20]. Massé et al. conducted a study on X-PSI [8]. They showed a prediction of implant size by X-PSI within one size-difference in 95.6% of cases for the femoral component, and 100% of cases for the tibial component, compared to intraoperative used implant size. The same researchers also found that the accuracy of the

X-ray-based guides to reproduce the preoperative planned hip-knee-ankle angle (HKA) was within 3° in 86% of cases [8]. However, no direct comparison between X-ray-based and MRI-based planning for PSI has been assessed to date.

This study was designed to share the preliminary experiences with X-PSI in direct comparison with MRI-based PSI planning in the same patient, planned by the same surgeon. Additional to predicted implant size, differences between resection thickness and angles were also compared between both planning modalities. The authors hypothesised that predicting implant size and resection thickness will be similar in X-PSI planning compared to MRI-based PSI planning for TKA.

## METHODS

### *Imaging technique X-PSI*

Prior to surgery, all patients underwent a weight-bearing full-length radiograph (FLR) acquisition in anteroposterior (AP), and lateral (LAT) views according to the protocol of the manufacturer (Zimmer Biomet 1836.1-GLBL). Two calibration straps with X-ray markers were placed at least 10 cm proximal and distal from the knee joint line on the patient's leg. The patient was positioned in a standing position with the leg in extension, weight-bearing on both legs. No repositioning of the markers was permitted during the procedure. Source to Image Distance (SID) value was fixed during the acquisition of all radiographs. The knee joint, femoral head contour, ankle, and the entire X-ray markers were visible on the final AP and lateral stitched images (Figure 1). For this study, a special trained technician directed each weight-bearing FLR with strict patient positioning.

The FLR images were transferred to Zimmer Biomet to reconstruct 3D models. The following specific bony landmarks were registered for the femur; femoral head centre, the middle of the intercondylar notch, anterior cortex, medial and lateral posterior condyles, medial and lateral epicondyles, and medial and lateral distal condyles. For the tibia, the following landmarks were registered; tibial canal entry point, medial and lateral plateau, most medial point, medial third of the tibial tuberosity, fibular head point, posterior sulcus point, and medial and lateral malleoli (Figure 2). Additionally, the femoral and tibial bone contours were defined on the images (Figure 3). A mean 3D bone model for the femur and tibia was positioned and scaled inside the patient-specific shapes. This mean bone model is a gender- and laterality-specific model created from CT images of a library of healthy knees. An automatic bone deformation was performed to match the 3D mean bone model to the patient-specific contours. Finally, an estimated cartilage thickness was applied to the contours of the femur and tibia, on the medial and lateral side separately. The cartilage thickness was calculated as half the distance between the bone surface, between the most distal point of the condyle and the adjacent tibial plateau. The constructed model was then used to plan the location and orientation of the knee replacement implant components as in other PSI modalities. This default plan was sent to the surgeon for adjustments and approval.

**Figure 1 Example of full-length radiograph in anteroposterior and lateral with X-PSI markers**

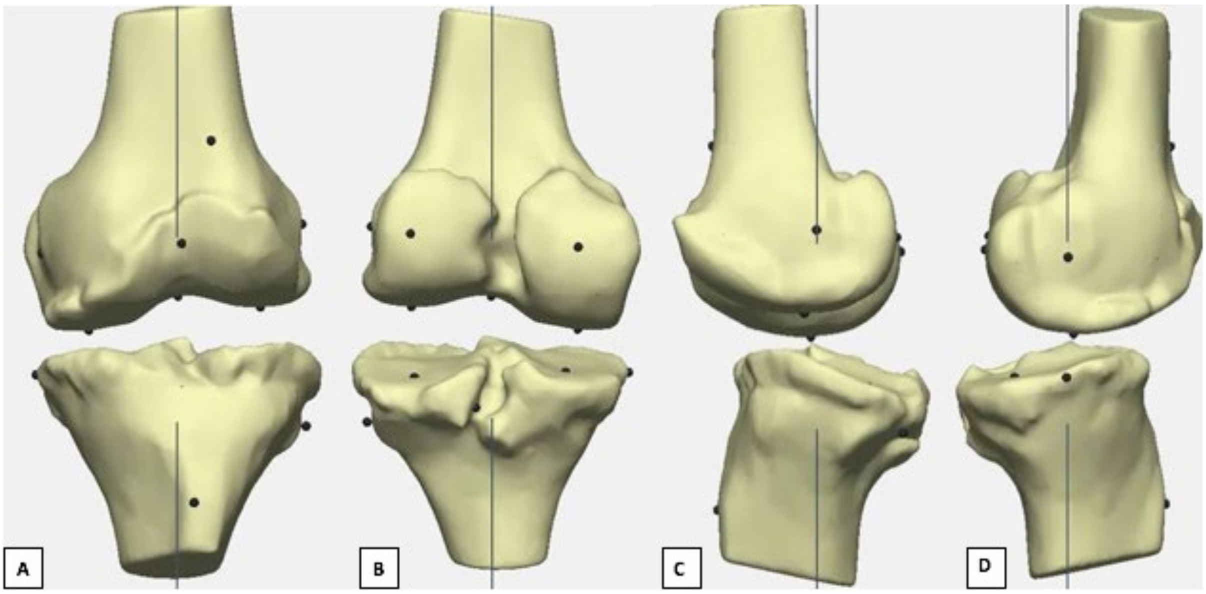


**Figure 2 Specific bony landmarks used in X-PSI**

*A: Anterior view; B: Posterior view; C: lateral view; D: medial view.*

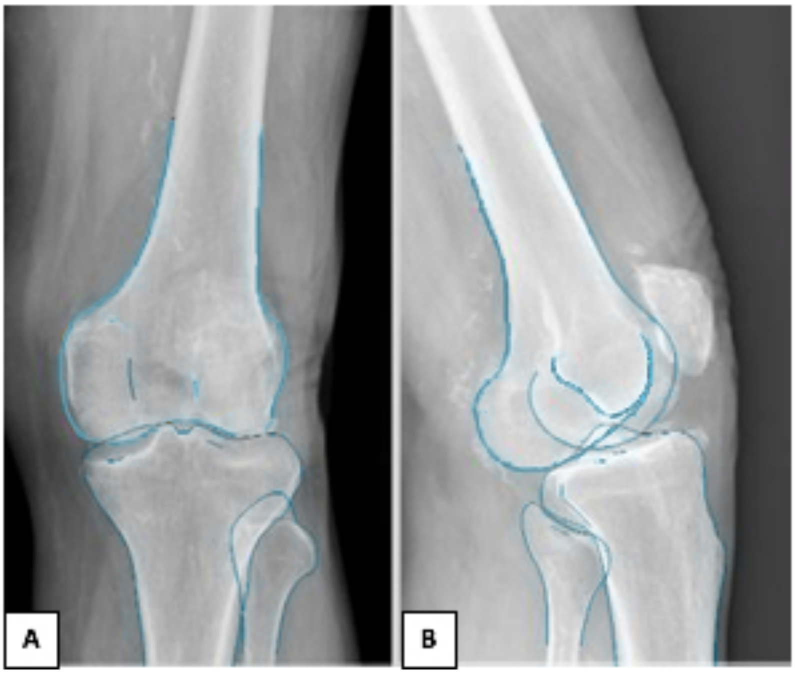


**Figure 3 Defined femoral and tibial bone contours in X-PSI on radiograph**

*A: Anteroposterior view; B: Lateral view.*

### *Study group*

The study group consisted of 20 consecutive patients assigned to undergo TKA for primary osteoarthritis of the knee using PSI (Signature™ Personalised Patient Care, Zimmer-Biomet, Warsaw, IN, USA), based on a preoperative MRI performed in the Zuyderland Medical Centre (Sittard-Geleen, The Netherlands). Furthermore, all patients underwent an FLR for additional planning using the X-PSI technology. Both MRI and FLR images were used to create two personalised templates to position and align the total knee prosthesis. One high-volume orthopaedic surgeon, specialised in knee surgery and experienced with PSI, performed all preoperative planning based on both X-ray- and MRI- images, using the matching software of the manufacturer. With the chosen mechanical alignment technique, the surgeon aimed for a horizontal joint line and a neutral mechanical axis.

Institutional review board (METC Z, Heerlen, the Netherlands) approval was obtained for this study (trial number 17-N-11).

### *Outcome measurements*

For all individual subjects, absolute differences in preoperative planning using both imaging modalities were evaluated for the following parameters: femoral- and tibial implant size, femoral resection (medial-distal, lateral-distal, medial-posterior, and lateral-posterior), tibial resection (medial and lateral), femoral flexion-extension angle, femoral- and tibial varus/valgus angle, posterior slope tibia, tibial rotation, and femoral- and tibial rotation. All absolute differences were calculated by subtracting the value obtained on MRI-based planning from the value planned with X-PSI.

## RESULTS

The study group consisted of 20 consecutive patients assigned to undergo TKA. Four of the knees evaluated had a valgus HKA, the other sixteen were varus knees. An overview of preoperative knee alignment is given in Figure 4.

Determination of femoral- and tibial implant size was identical in X-PSI and MRI-based PSI planning for 7 (35%) and 9 (45%) cases, respectively. Planned femoral implant size was within one size difference in 19 (95%) cases, and within one size difference in 18 (90%) cases for tibial implant size. Tibial implant sizes tended to be smaller when using X-PSI planning compared to the MRI-based planning of the same patient. An overview of planned implant size differences is shown in Table 1 and Figure 5.

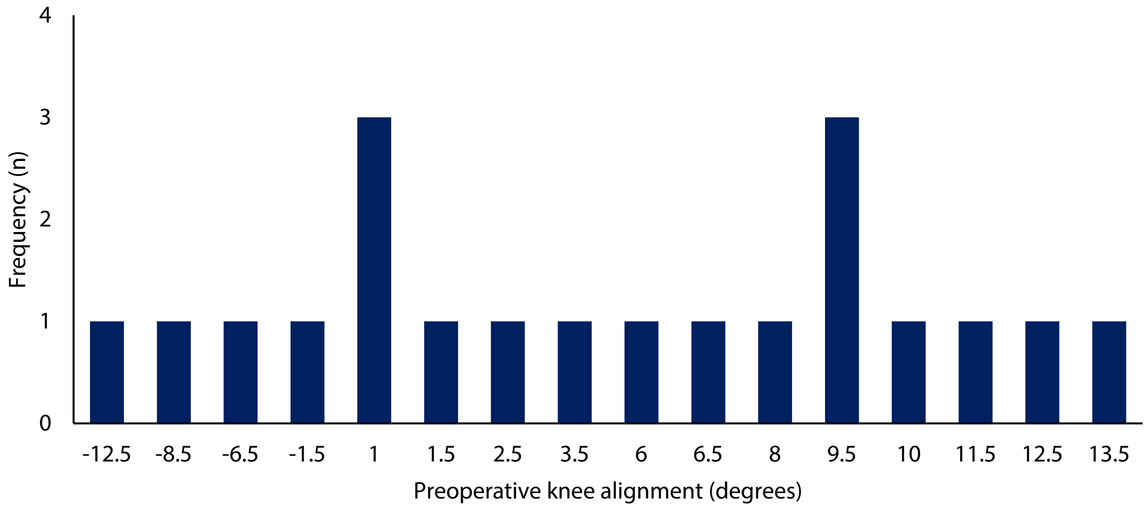


**Figure 4 Frequency of preoperative hip-knee-ankle angle in degrees**

*Negative values represent valgus hip-knee-ankle angle, positive values represent varus hip-knee-ankle angle.*

**Table 1 The frequency of differences in planned implant sizes between X-PSI planning and MRI-based planning**

| Size difference | Femoral component size n (%) | Tibial component size n (%) |
|---|---|---|
| -2 | 1 (5) | - |
| -1 | 7 (35) | - |
| 0 | 7 (35) | 9 (45) |
| 1 | 5 (25) | 9 (45) |
| 2 | - | 2 (10) |

*The difference represents the planned implant size on MRI-based planning minus X-PSI planning.*

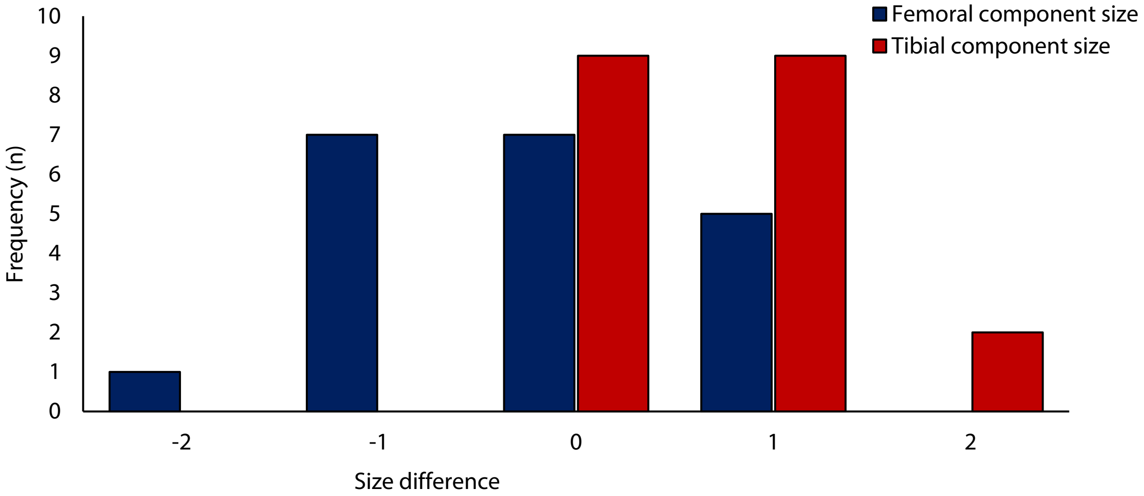


**Figure 5 The frequency of differences in planned implant sizes between X-PSI planning and MRI-based planning**

*The difference represents the planned implant size on MRI-based planning minus X-PSI planning.*

The frequency of differences between resection thickness between MRI-based planning and X-PSI planning is shown in Table 2, Figure 6, and Figure 7. Femoral resection levels were more equivalent when comparing the two planning modalities within one patient, whereas more variation was observed between tibial resection levels. Femoral resection levels were within a 1.5mm difference compared to X-PSI planning in 75-90% of patients. Tibial resection on the medial side was higher in all X-PSI planning than the same patients' MRI-based planning. Two millimetres or more resection difference was found in 15 cases (75%), with 12 cases (60%) in the range of 3 to 5mm resection difference. The differences were smaller in magnitude for lateral tibial resection than those observed for medial tibial resection. Nonetheless, 13 patients (65%) showed more resection in MRI-based planning, of which 9 (45%) cases showed a difference of more than 2mm.

**Table 2 The frequency of differences in resection planes between X-PSI planning and MRI-based planning**

| Resection difference (mm) | Femoral resection |  |  |  | Tibial resection |  |
|---|---|---|---|---|---|---|
|  | MD<br>n (%) | LD<br>n (%) | MP<br>n (%) | LP<br>n (%) | medial<br>n (%) | lateral<br>n (%) |
| >-5 | - | - | - | - | 1 (5) | - |
| -3 to -5 | - | - | - | - | 12 (60) | - |
| -2.5 | - | - | - | 1 (5) | 1 (5) | - |
| -2 | 1 (5) | 1 (5) | 2 (10) | 1 (5) | 1 (5) | 1 (5) |
| -1.5 | 2 (10) | 3 (15) | 5 (25) | 2 (10) | 1 (5) | 1 (5) |
| -1 | 1 (5) | 3 (15) | 6 (30) | 4 (20) | - | 1 (5) |
| -0.5 | 6 (30) | 2 (10) | 1 (5) | 4 (20) | 4 (20) | - |
| 0 | 2 (10) | 2 (10) | 3(15) | 2 (10) | - | 4 (20) |
| 0.5 | 1 (5) | 3 (15) | 2 (10) | 1 (5) | - | - |
| 1 | 1 (5) | 1 (5) | 1 (5) | 3(15) | - | 1 (5) |
| 1.5 | 3 (15) | 1 (5) | - | 1 (5) | - | 3 (15) |
| 2 | - | - | - | - | - | 5 (25) |
| 2.5 | - | 1 (5) | - | - | - | 2 (10) |
| 3-5 | 3 (15) | 3 (15) | - | 1 (5) | - | 2 (10) |
| >5 | - | - | - | - | - | - |

*The difference represents the resection in millimeters on MRI-based planning minus X-PSI planning.*
*MD, medial-distal; LD, lateral-distal; MP, medial-posterior; LP, lateral-posterior.*

The frequency of differences between the number of degrees between X-PSI planning and MRI-based planning of femoral flexion-extension angle are displayed in Table 3.
For 3 parameters (femoral varus/valgus angle (0 degrees), posterior slope tibia (3 degrees), tibial rotation from anteroposterior axis (0 degrees)), no changes to the proposed planning were made, resulting in identical planning of parameters in both modalities. Femoral rotation was, in all cases, unchanged from the default planning in both planning modalities. A single case in the X-ray-based planning group tibial varus/valgus was planned in 1-degree varus, in all other cases tibial varus/valgus was planned in neutral alignment.

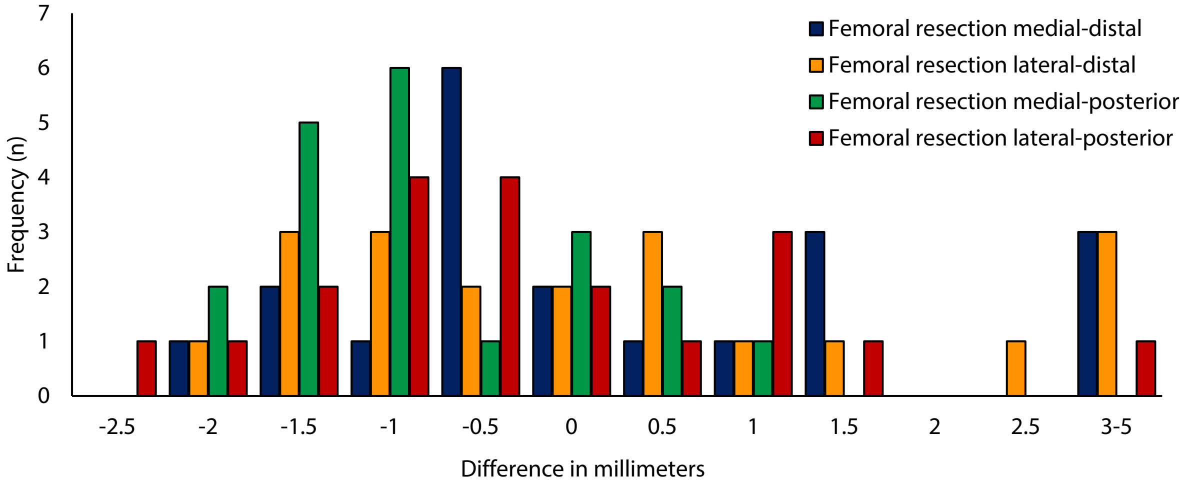


**Figure 6 The frequency of differences in millimeters of planned femoral resection between X-PSI™ planning and MRI-based planning**

*The difference represents the resection in millimeters on MRI-based planning minus X-PSI™ planning.*

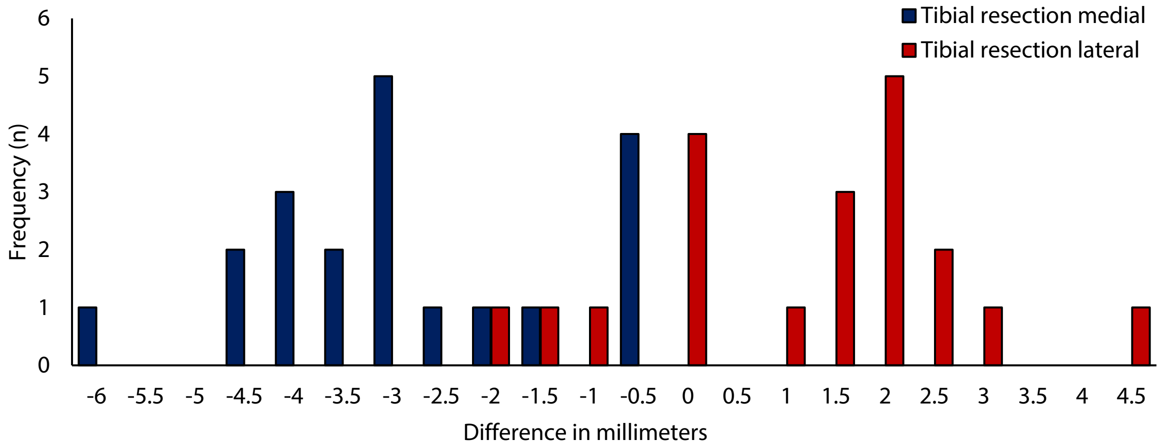


**Figure 7 The frequency of differences in millimeters of planned tibial resection between X-PSI™ planning and MRI-based planning**

*The difference represents the resection in millimeters on MRI-based planning minus X-PSI™ planning.*

**Table 3 The frequency of differences in the number of degrees between X-PSI™ planning and MRI-based planning of femoral flexion-extension angle**

| Resection difference (mm) | Femoral flexion-extension angle n (%) |
|---|---|
| -4 | 2 (10) |
| -3.7 | 1 (5) |
| -2.6 | 1 (5) |
| -2.5 | 2 (10) |
| -2 | 5 (25) |
| -1.8 | 1 (5) |
| -1.5 | 2 (10) |
| -1 | 4 (20) |
| 0 | 1 (5) |
| 0.5 | 1 (5) |

*The difference represents the angle in degrees on MRI-based planning minus X-PSI™ planning.*

## DISCUSSION

The authors hypothesised that predicting implant size and resection thickness will be similar in X-PSI planning compared to MRI-based PSI planning for TKA. This study shows that planned implant size was within one size difference between X-PSI versus MRI-based planning in 95% cases for femoral implant size and 90% cases for tibial implant size, respectively. Furthermore, femoral resection levels were more comparable when comparing both planning modalities within the same patient, whereas there was more variation between planned tibial resection levels.

Zheng et al. conducted a preoperative planning study where differences between X-ray- and CT-based PSI planning were evaluated in 23 cases. In this study, 78% of cases, X-ray-based PSI planned the same femoral component size as the CT-based method and 70% of the tibial implant size. When allowing for a difference of 1 size, this number changed to 96% for femoral implant size and 100% for tibial implant size [20]. These findings are in line with the present study's findings, but no information was given on the direction of size difference (smaller/larger). Massé et al. also compared implant size between X-PSI planning and intraoperative used component size. The surgery was executed according to the surgeon's preferred technique (MRI-based PSI, conventional instrumentation, or the readings from the navigation system). It was found that implant size within one size difference was the case for 95.6% and 100% for the femur and tibia components, respectively [8].

In the current study, there was a tendency for smaller tibia component size planning by X-PSI than the planning of the same patients executed on MRI-based plans. The planned femoral implant size tended to be smaller in the MRI-based planning. However, this tendency was less evident. Previous literature showed that CT-based models appeared to be slightly larger than the actual bones. In contrast, MRI-based models showed more significant differences and were smaller than the actual bones [17]. Previous authors postulated some reasons for differences between MRI and CT-based PSI. CT-based guides cannot account for the residual cartilage, and therefore the cutting guide may sit more eccentrically on patients' bony anatomy than MRI guides [2]. This may result in a difference in component size. The same effect may be accountable for differences in component size and differences in resection in the current study using X-PSI planning, where an estimation of articular cartilage is added to the 3D models produced by the manufacturer. To date, no direct comparison of MRI and X-PSI has been described in previous literature.

Femoral resection levels were more comparable within the planning of patients, whereas there was more variation between tibial resection levels. Notably, the difference in medial tibial resection is apparent, where 75% of cases had >2mm more resection with X-PSI compared to MRI-based plannings. Most knees were varus knees (sixteen out of twenty, 80%), where less remaining cartilage on the medial tibia can be expected. After determining the bony landmarks and contours, an estimated cartilage thickness was added to the 3D bone model. This was calculated as half the distance between the bone surface, between the most distal point of the condyle and the adjacent tibial plateau. With MRI-based planning the cartilage is visible on the image, so it is considered in reconstruction as is. Both planning modalities produce plans where resection thickness includes the (calculated) cartilage layer. Since this amount might be different between the estimation and the thickness on MRI, this might explain the difference in resection thicknesses. However, in a intraoperative situation the X-PSI moulds are bone referenced. Therefore, incorrect estimated cartilage thicknesses are not affecting the fit of the moulds intraoperatively.

There are a couple of potential advantages of X-ray-based PSI compared to PSI based on MRI or CT.

Substituting CT or MRI for standard X-ray imaging will reduce the costs significantly. Also, radiation dosage is much lower in X-ray imaging than in CT imaging, whereas the dose on one knee could be 10-14 times higher in the latter [7]. In addition, leg alignment varies when in a supine or standing weight-bearing position [3, 13]. Therefore, as in X-ray-based PSI, evaluating preoperative leg alignment in a weight-bearing position would represent functional alignment.

Wu et al. created a 3-D reconstruction of knee anatomy from single-plane fluoroscopic X-ray sequences during kinematic activity, based on a nonlinear statistical shape model. They found good accuracy in reconstructing these 3-D bone models [18]. As they concluded, this may eliminate the need for prior 3-D imaging like CT or MRI and therefore reduce manual labour, cost and in the case of CT radiation dose. It may also provide more accurate patient information in motion compared to static imaging. The use of fluoroscopic X-ray sequence during actual movement of the knee to reconstruct knee anatomy may therefore be of added value in the future. Further research and development in this field are needed before this can be applied in clinical practice. The first step in this evolution is evaluating the use of static X-rays as an alternative for MRI- or CT-based PSI.

A strength of this study was that a special trained technician directed each FLR with high precision. However, in daily practice the quality of FLR are often technician depended and are not always done consistently. When the 3D model is based on an inaccurate FLR, this has negative consequences for the subsequent planning.

This study has some limitations. Firstly, patient numbers are small, and the results may only be seen as indications and as a first impression. Secondly, all plans were revised and approved by only one experienced surgeon. Even though this is also a strength, interobserver reliability evaluation by Intraclass Correlation Coefficients (ICC) between multiple surgeons might have been of additional value. Furthermore, however not the goal of this study, there was no comparison to per- or postoperative results nor clinical outcomes. The objective of this study was to achieve an insight of direct comparison of preoperative planning obtained by both X-PSI and MRI-based PSI. Even though the current study only presents preliminary experiences, X-ray-based PSI may become an appropriate alternative to standard PSI methods in the future. Additional studies are necessary for the evaluation of this new technology.

## CONCLUSION

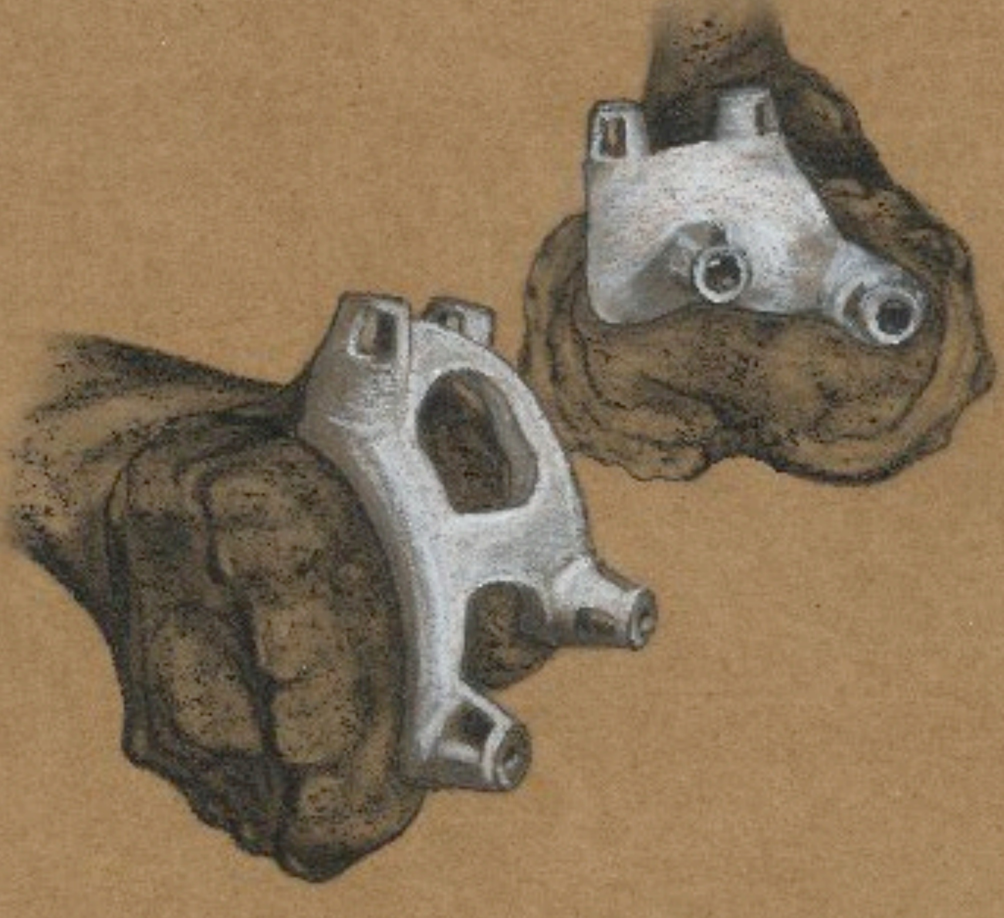
Preliminary experiences with X-PSI planning in direct comparison to MRI-based PSI planning shows that femoral resection levels were more comparable within the same patient, whereas there was more variation between planned tibial resection levels.

However, the planned implant size was within one size difference between MRI- versus X-ray-based planning in 90-95% of cases. Planning in TKA surgery is an evolving field with constant technical developments. Further research on X-ray-based PSI is needed to understand differences between planning modalities, and before application of this modality in all-day clinical use.

## REFERENCES

1. An VVG, Sivakumar BS, Phan K, Levy YD, Bruce WJM (2017). Accuracy of MRI-based vs. CT-based patient-specific instrumentation in total knee arthroplasty: A meta-analysis. J Orthop Sci, 22, 116-120.
2. Frye BM, Najim AA, Adams JB, Berend KR, Lombardi AV (2015). MRI is more accurate than CT for patient-specific total knee arthroplasty. Knee, 22, 609-612.
3. Fujii T, Sato T, Ariumi A, Omori G, Koga Y, Endo N (2020). A comparative study of weight-bearing and non-weight-bearing 3-dimensional lower extremity alignment in knee osteoarthritis. J Orthop Sci, 25, 874-879.
4. Hsu AR, Gross CE, Bhatia S, Levine BR (2012). Template-directed Instrumentation in Total Knee Arthroplasty: Cost Savings Analysis. Orthoped, 35(11), 1596-1600.
5. Issa K, Rifai A, McGrath MS, Callaghan JJ, Wright C, Malkani AL, Mont MA, McInerney VK (2013) Reliability of Templating with Patient-Specific Instrumentation in Total Knee Arthroplasty. J Knee Surg, 26, 429–434.
6. Kim YH, Park JW, Kim JS, Park SD (2014). The relationship between the survival of total knee arthroplasty and postoperative coronal, sagittal and rotational alignment of knee prosthesis. Int Orthop, 38, 379-385.
7. Koivisto J, Kiljunen T, Wolff J, Kortesniemi M (2013). Assessment of effective radiation dose of an extremity CBCT, MSCT and connventional X ray for knee area using MOSFET dosemeters. Radiat Prot Dosimetry, 157(4), 515-524.
8. Massé V, Ghate RS (2021). Using standard X-ray images to create 3D digital bone models and patient-matched guides for aiding implant positioning and sizing in total knee arthroplasty. Comput assist surg, 26(1), 31-40.
9. Nunley RM, Ellison BS, Ruh EL, Williams BM, Foreman K, Ford AD, Barrack RL (2012). Are patient-specific cutting blocks cost-effective for total knee arthroplasty? Clin Orthop Relat Res, 470, 889–894.
10. Parratte S, Pagnano MW, Trousdale RT, Berry DJ (2010). Effect of Postoperative Mechanical Axis Alignment on the Fifteen-Year Survival of Modern, Cemented Total Knee Replacements. J Bone Joint Surg Am, 92, 2143-2149.
11. Pfitzner T, Abdel MP, Roth P, Perka C, Hommel H (2014). Small Improvements in Mechanical Axis Alignment Achieved With MRI versus CT-based Patient-specific Instruments in TKA A Randomized Clinical Trial. Clin Orthop Relat Res, 472, 2913–2922.
12. Rivière C, Iranpour F, Auviet E, Howell S, Vendittoli PA, Cobb J, Parratte S (2017). Alignment options for total knee arthroplasty A systematic review. Orthop Traumatol Surg Res, 103, 1047-1056.

13. Schoenmakers DAL, Feczko PZ, Boonen B, Schotanus MGM, Kort NP, Emans PJ (2017). Measurement of lower limb alignment there are within-person differences between weight-bearing and non-weight-bearing measurement modalities. Knee Surg Sports Traumatol Arthrosc, 25, 3569–3575.
14. Schotanus MGM, Schoenmakers DAL, Sollie R, Kort NP (2017). Patient-specific instruments for total knee arthroplasty can accurately predict the component size as used peroperative. Knee Surg Sports Traumatol Arthrosc, 25(12), 3844-3848.
15. Schotanus MGM, Sollie R, Haaren van EH, Hendrickx RPM, Jansen EJP, Kort NP (2016). A radiological analysis of the difference between MRI- and CT-based patient-specific matched guides for total knee arthroplasty from the same manufacturer- a randomised controlled trial. Bone Joint J, 98-B, 786–92.
16. Schotanus MGM, Thijs E, Heijmans M, Vos R, Kort NP (2018). Favourable alignment outcomes with MRI-based patient-specific instruments in total knee arthroplasty. Knee Surg Sports Traumatol Arthrosc, 26, 2659–2668.
17. White D, Ghelule KL, Seedhom BB (2008). Accuracy of MRI vs CT imaging with particular reference to patient specific templates for total knee replacement surgery. Int J Med Robotics Comput Assist Surg, 4, 224–231.
18. Wu J, Mahfouz MR (2021). Reconstruction of knee anatomy from single-plane fluoroscopic x-ray based on a nonlinear statistical shape model. J Med Imaging, doi: 10.1117/1.JMI.8.1.016001.
19. Wu XD, Xiang BY, Schotanus MGM, Liu ZH, Chen Y, Huang W (2017). CT- versus MRI-based patient-specific instrumentation for total knee arthroplasty A systematic review and meta-analysis. Surg, 15, 336-348.
20. Zheng G, Hommel H, Akcoltekin A, Thelen B, Stifter J, Peersman G (2018). A novel technology for 3D knee prosthesis planning and treatment evaluation using 2D X-ray radiographs a clinical evaluation. Int J Comput Assist Radiol Surg, 13, 1151-1158.



# 7

# Computer-based pre- and intraoperative planning modalities for Total Knee Arthroplasty: A comprehensive review

Schoenmakers DAL, Dorling IM, Heymans MJFL, Kort NP, Boonen B, van Rhijn LW, Schotanus MGM

*J Orthop Exp Innov, 2024, https://doi.org/10.60118/001c.89963.*

## ABSTRACT

**Purpose:** Since the introduction of total knee arthroplasty (TKA) into modern medicine, many types of digital pre- and intraoperative planning methods have been introduced. Due to the abundance of planning modalities for TKA, physicians are posed with the challenge of which type to implement into their daily practice. In the current fast-paced and research-driven medical environment it is important to understand the differences between the computer-based pre- and intraoperative planning modalities for TKA.

**Methods:** The following databases were searched: MedLine, EMBASE, Web of Science, and the Cochrane Library. All articles were independently reviewed by the two reviewers (DS, ID). The following data were extracted, if available: study ID, country of conduction, type of planning modality or modalities, and the use and explanation of historical and currently employed pre- and intraoperative planning modalities for TKA.

**Results:** 39 studies were included into the systematic review. Computer-assisted surgery (CAS) represents a surgical concept where computer technology is used for surgical planning. CAS for TKA was introduced in the late 1980s. Subsequently, three different types of CAS were developed to plan TKA. The first type of CAS, computer-integrated instruments, also known as CAS navigation, provides a real-time view of anatomy and marked surgical instruments intraoperatively. For the second type of CAS, rapid prototyping, or 3D printing, was derived from CAS technology in which the development of patient specific instrumentation (PSI) for TKA followed. Furthermore, CAS aided the evolution of the third type of CAS for TKA: robotics.

**Conclusion:** With a high demand for TKA surgery, the challenge to achieve more accurate alignment, improved prosthesis survival, and improved patient satisfaction rates is a very topical one. Planning modalities for TKA were developed to address this demand. This comprehensive systematic review showed that the monumental development of digital planning modalities for TKA has led to a vast amount of well-researched options that surgeons can choose from and use in daily practice.

## INTRODUCTION

Over the years there has been an increasing demand for total knee arthroplasty (TKA) because of longer life expectancies, and rising expectations for quality of life and mobility in later life-years. Since the introduction of TKA into modern medicine, many types of pre- and intraoperative planning modalities for this surgery have been developed. Freehand techniques were swiftly augmented by intramedullary and extramedullary alignment guides which remain in use. However, these conventional alignment tools rely on direct visual inspection and assume a standard bone geometry, which does not apply to all patients. Multiple planning systems and software were developed to eliminate the need for these conventional alignment guides. The developers of these planning systems aimed to offer better alignment, survivorship of the prosthesis, and better clinical outcomes for patients receiving TKA, in an effort to reduce postoperative pain and loss of function. A rigorous amount of attention to pre- and intraoperative planning and their accompanying modalities are of importance to avoid implant failure as well as visualising the operation and foreseeing any potential pitfalls during surgery [1].

The first surgical planning for arthroplasty was performed using tracing paper and/or plastic overlays on standard radiographs [2, 3, 4]. Soon numerous computer-based preoperative planning software programs were developed to ease this process, in combination with the use of calibrated radiographic images. During the past decades, multiple new modalities for planning of TKA have been introduced, including computer-assisted navigation (CAS navigation) for TKA, patient-specific instrumentation (PSI) [5], and robot-assisted TKA [6]. With the introduction of new techniques and modalities, an abundance of research has been done to compare accuracy in alignment, cost-effectiveness and patient satisfaction rates between them. In general, successful TKA outcome is dependent on multiple factors such as surgical experience, patient demographics, preoperative patient reported outcome measures (PROMs), preoperative knee mobility, and patient expectations [7, 8]. Differences in outcomes between specific types of planning modalities for TKA have been investigated [9]. Yet, no full overview of computer-based pre- and intraoperative planning modalities and their method of use for TKA is available. With the current proliferation of available techniques, physicians are posed with the challenge of which type to implement into their daily practice and how to use them.

The aim of this systematic review was to give a comprehensive overview of historical and currently available digital pre- and intraoperative planning modalities for TKA. Furthermore, it aims to describe key elements of each surgical planning modalities and their method of use. In this review, based on articles found in the systematic review, the following types of CAS-based TKA were described: CAS navigation, PSI and robotics.

## METHODS

### *Review and protocol*

This systematic review was performed in line with the PRISMA-P statement for constructing a systematic review. The protocol for this systematic review has been registered in the PROSPERO database (protocol number CRD42023402165).

### *Search strategy and eligibility criteria*

The following databases were searched: OVID Medline, EMBASE.com, Web of Science (Clarivate), and the Cochrane Library (Wiley). No search limitations were applied. The first and final search was conducted on September the 3rd, 2022. Only titles in the English language were eligible for selection. The full search can be found in Appendix 1. All relevant titles in other languages are provided in Appendix 2.

Studies were included in the review if they met the following criteria:

- Articles which described computer-based pre- and/or intraoperative planning modalities for TKA.
- Articles which described patients undergoing TKA using computer-based pre- and/or intraoperative planning modalities, with explanation of the planning modality itself.

Articles were excluded if the authors solely investigated clinical outcomes. Furthermore, articles were excluded if they focused on non-digital planning modalities, singular tools for ligament balancing, reports on unicondylar knee arthroplasty or revision arthroplasty, case series, and case reports.

### *Study design and data collection*

The studies found in the search were de-duplicated and the remaining studies were assessed based on the eligibility criteria. All articles found in the search were independently reviewed by two reviewers (DS, ID) using Rayyan, a tool for the screening and selection of studies for systematic reviews [10]. The first assessment was performed using the available titles and abstracts (TiAb). After this assessment, the reviewers examined the remaining full text articles and independently decided whether articles were eligible for inclusion. Any disagreement between reviewers was resolved by discussion between the reviewers and if requisite a third reviewer (MS) was involved. After final inclusion of the articles, the following data was extracted: Study ID (author, year), country of study conduction, and type of planning modality or modalities. Furthermore, textual data extraction was performed on development, use and explanation of use of computer-based pre- and intraoperative planning modalities for TKA.

### *Data analysis*

This review is descriptive in nature; therefore, no statistical analysis or meta-analysis has been performed.

## RESULTS

### *Search results*

A full overview of the literature search and the selection process is provided in Figure 1. The systematic search in the abovementioned databases resulted in 7,913 hits. After deduplication 6,389 titles remained to be examined. These titles and abstracts were individually examined by the two reviewers (DS, ID) which resulted in 97 articles eligible for full-text analysis. After this analysis, 39 articles were included into the study (Table 1).

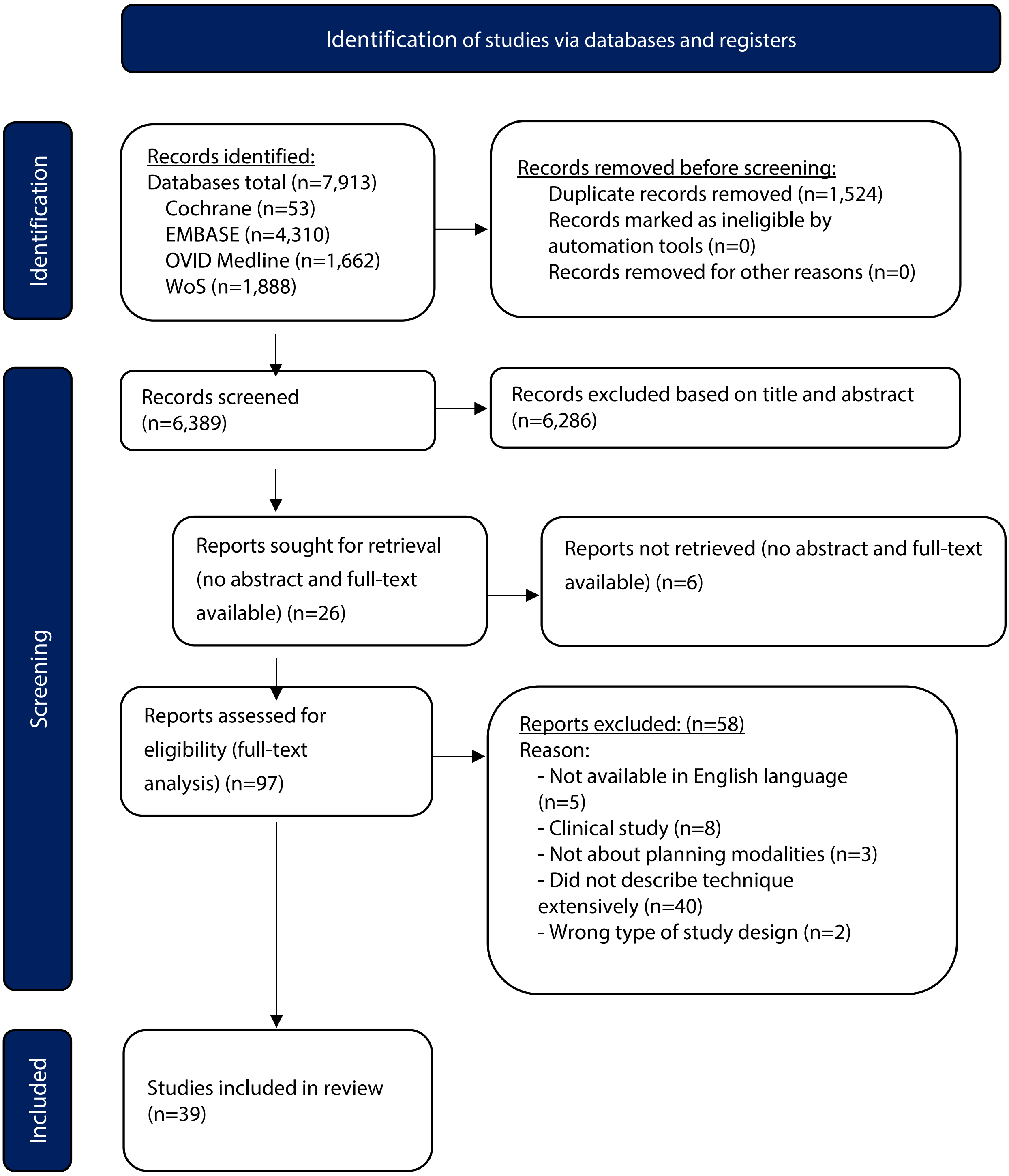


**Figure 1 PRISMA flowchart**

**Table 1 Included studies and study traits**

| Study number | Author | Year of publication | Country, or countries of study conduction | Study subject |
|---|---|---|---|---|
| 1 | Batailler et al. | 2020 | France | PSI, robotics |
| 2 | Batailler et al. | 2021 | France | Robotics |
| 3 | Bautista et al. | 2019 | Colombia, USA | Robotics |
| 4 | Calliess et al. | 2018 | Germany | Robotics |
| 5 | Chan et al. | 2020 | USA | Robotics |
| 6 | Chen et al. | 2018 | USA | Robotics |
| 7 | Ciever Bonfils et al. | 2020 | France, Australia | CAS navigation, robotics |
| 8 | Clathworthy et al. | 2022 | New Zealand | Robotics |
| 9 | Davies et al. | 2004 | United Kingdom | Robotics |
| 10 | Davies et al. | 2006 | United States | Robotics |
| 11 | Delp et al. | 1998 | United Kingdom, USA | CAS navigation |
| 12 | Desai et al. | 2011 | USA | CAS navigation |
| 13 | Ganpathi et al. | 2014 | United Kingdom | PSI |
| 14 | Gauci et al. | 2022 | France | PSI |
| 15 | Graichen et al. | 2020 | Germany, Thailand | CAS navigation, robotics |
| 16 | Jacofsky et al. | 2016 | USA | Robotics |
| 17, 18, 19, 20 | Jakopec | 2001, 2002, 2003, 2003 | United Kingdom | Robotics |
| 21 | Joskowicz et al. | 2017 | Israel | CAS navigation |
| 22 | Konan et al. | 2017 | United Kingdom | Robotics |
| 23 | Liow et al. | 2017 | Singapore | Robotics |
| 24 | Malvisi et al. | 2001 | Italy | Robotics |

**Table 1 Continued**

| Study number | Author | Year of publication | Country, or countries of study conduction | Study subject |
|---|---|---|---|---|
| 22 | Konan et al. | 2017 | United Kingdom | Robotics |
| 23 | Liow et al. | 2017 | Singapore | Robotics |
| 24 | Malvisi et al. | 2001 | Italy | Robotics |
| 25 | Merzger et al. | 2013 | Germany | CAS navigation |
| 26 | Mattei et al. | 2016 | Italy | PSI |
| 27 | McGovern et al. | 2011 | USA | PSI |
| 28 | Medical Advisory Secretariat | 2004 | Canada | CAS navigation, robotics |
| 29 | Muller et al. | 2000 | Germany | CAS navigation |
| 30 | Nathwani et al. | 2021 | United Kingdom | Robotics |
| 31 | Radermacher et al. | 1998 | Germany | CAS navigation |
| 32 | Roche et al. | 2018 | Germany | Robotics |
| 33 | Roche et al. | 2015 | Germany | Robotics |
| 34 | Siebert et al. | 2002 | Germany | Robotics |
| 35 | Sousa et al. | 2020 | USA | Robotics |
| 36 | St Mart et al. | 2021 | United Kingdom | Robotics |
| 37 | Wu et al. | 2021 | USA | Robotics |
| 38 | Xin Chen et al. | 2021 | China | Robotics |
| 39 | Yoge et al. | 2021 | USA | Robotics |

### ***Study results***

All of the 39 studies included into the systematic review are used for the following part of this article. First, a short history of CAS and its different subtypes will be introduced. Thereafter, an overview of these different CAS subtypes (CAS navigation, PSI and robotics for TKA) will be presented.

### *Computer-assisted surgery (CAS)*

CAS represents a surgical concept where computer technology is used for surgical planning. CAS was developed in the 1980s and early 1990s. In the following years, the use of CAS took off enormously, which also caused an increase in scientific interest. In 2000, the International Society for Computer Aided Surgery (ISCAS) was established. Ever since, CAS has brought a big change in tools and techniques on how surgeries are planned and executed in several medical disciplines.

CAS for TKA can be divided into three types; computer-integrated instruments for surgical navigation, image guided instruments for surgical planning, and robotic devices [11-13].

The first type of CAS, computer-integrated instruments, also known as CAS navigation, provides a real-time view of anatomy and marked surgical instruments intraoperatively. It uses 3D position sensors in order to visualise positional information of surgical instruments. The second type, image guided instruments, also patient-specific instrumentation (PSI), allows surgeons to create a three-dimensional (3D) preoperative plan. 3D-modelled guides manufactured from these plans guide the surgeon intraoperatively. The third type, robotic assisted surgery, provides intraoperative assistance to surgeons using a (semi-)active robotic arm [11-14].

All three types of CAS will be presented in more detail in the next sections.

### *CAS navigation*

The first type of CAS is CAS navigation.

#### *General concepts*

The first orthopaedic CAS navigation surgery was performed on a total hip replacement in 1992, by William Barger (Sacramento, California, USA). The first TKA using CAS navigation was executed in 1997 by Frederic Picard (Grenoble, France). [11, 12, 15].

CAS navigation is used to achieve a digital image that serves as a map for the surgeon intraoperatively. These CAS-systems provide positional information about surgical instruments relative to the bone in this digital map, but do not perform any part of the surgery [12, 14]. With this digital map, surgeons are able to use additional information to make decisions on where to make bony cuts and how much bone is to be resected in TKA.

Three different types of CAS navigation exist: preoperative imaging techniques, intraoperative imaging techniques, and image-free techniques.

The preoperative imaging techniques, also volumetric image-based navigation, uses information from either a CT- or MRI-scan. The image information is transferred into planning software which surgeons can utilise for preoperative decision-making. For the second technique, intraoperative imaging, such as fluoroscopy, is used for anatomical mapping of the knee. This informative map is utilised during the surgery and aids the surgeon in planning their bony cuts. In the image-free technique, kinematic joint information and/or morphologic bone information is determined intraoperatively. Using software, the collected data is then merged with an anatomical model to form a digital image. Infrared light-based trackers are most commonly used, whereas research on electromagnetic tracking has also been done [12].

For all above mentioned techniques the obtained anatomical information has to be registered in order for it to be used. In other words, within either computer programs or during digital tracking itself, certain anatomical landmarks have to be registered in the computer, so that it registers the anatomy of the patient's knee, or where the knee is within space [12].

After registration of landmarks has been completed, the programs can calculate bony resections and soft-tissue releases. Additionally, the surgeon is able to alter the computer-based planning to his or her wishes. When using CAS navigation, the computer-based programs assist the surgeon with planning, but ultimately planning is done by the surgeon [12].

After the initial planning has been performed, implementation during surgery follows. The image-free technique is the most used technique for computer-assisted navigated TKA [12, 14]. Therefore, the authors will focus primarily on the infrared-, image-free-based CAS navigation technique.

### *Surgical technique*

Image-free CAS navigation systems consist of an infrared light-based optoelectronic tracker. This tracker guides the placement of the cutting guides by measuring the 3D coordinates of sensors. The optical localiser must be installed about one metre from the surgical field, to visualise placed trackers [11, 12, 15, 16].

At the start of the surgery trackers with infrared light emitting or -reflecting diodes are placed in the femur and tibia to create reference frames. Different mechanical angles and the hip rotation centre are acquired by moving the hip, knee, and ankle in all directions. Next, bone morphing of anatomical landmarks such as the femoral condyles and tibial plateau is performed with a handpiece. The acquired points are combined to build up a 3D surface model of the patient's individual anatomy. Bone cutting guides with sensors are then placed. The localiser measures the 3D coordinates of all sensors and visualises this on the screen. The angles of the bone cuts will be calculated by the computer system depending on the position of the guides. Once the orientation of the jig is in the desired position, the jig is secured in place. The surgeon can then make the bone cuts following the planning on the screen. Once the bone cuts are completed, the surgery continues as a traditional TKA [11, 12, 15, 16].

### *Patient-specific instrumentation*

The second CAS system is patient-specific instrumentation.

Rapid prototyping (RP), also known as 3D printing, is a technology used to create templates of computer-generated designs. In the medical field, these 3D templates were first used by maxillo-facial surgeons and dentists [17]. The first described case of RP being used for TKA was in the United States in 2007 [18]. RP technology can be applied to create PSI moulds to perform TKA.

#### *General concept*

For PSI, a CT-, MRI-, or a combination of a MRI-scan with a long leg x-ray is used to create a preoperative plan constructed from patient specific imaging sets. When PSI was first developed, CT-imaging was applied to model the knee anatomy. Subsequently, software was used to create a personalised surgical plan for femoral and tibial resection planes. The personalised surgical plans were translated into 3D-modelled guides to fit the shape of each individual patient's femur and tibia [19]. However, as PSI developed, MRI-imaging became an available option, creating the potential to include the cartilage layer of the femur and tibia. Essentially, software programs transform 2D CT- or MRI-images into 3D rendered templates of the knee [20].

The computer program is then used to place digital 3D-modelled femoral and tibial implants on the computer model of the patient's knee [11, 21, 22]. This technology led to the development of the PSI concept, in which 3D-printed plastic moulds can be created to aid the placement of cutting jigs on the patient's knee during surgery. Instead of using the computer program itself to only plan component size and resection planes, the computer program is used to create corporeal objects to use intraoperatively [23]. With this technology either pin guides could be manufactured, which aid surgeons to place pin tracks for conventional cutting guides, or the models can have integrated cutting slots [17].

*Preoperative planning and surgical technique*

The preoperative scan is loaded into specific software systems. The surgeon can oversee the 3D modelled knee in the software system and evaluate the generated digital plan with bony resections. Several parameters, like the slope, rotation and bony resections can be assessed and altered within the system. The preoperative plan can be modified to the surgeon's wishes. Once an appropriate plan has been approved, the information within the software system is sent to a manufacturer and a mould is constructed [20, 23].

Intraoperatively, after the femoral and tibial bones are prepared for bony resection the PSI models are placed on the accommodating bone [24]. Osteophytes and/or cartilage defects should not be removed before placing the model when MRI-imaging has been used as the models are based on bone as well as cartilage. Contrary, when using CT-based PSI the surgeon is required to remove the cartilage and soft tissue under cutting block contact points to ensure accurate fit of the mould [20]. The models are used for the initial femoral and tibial cuts. If sufficient, the surgeon can continue the next steps of the surgery. If cutting planes are unacceptable, intraoperative modifications can be made in terms of cut thickness, however rotation, slope and angulation cannot be changed. Once the desired bony resections are made, the usual TKA procedure follows.

*Robotics for TKA*

The third CAS system used for TKA is robotics.

The use of robotics in medicine started in the 1980s when industrial robots were modified for use in the operating theatre. The robots were used to bear tools for surgeons at specific locations in neurosurgical cases. When the tools arrived at their designated location the surgeon took over to perform the surgical duty. The robots were purely used as passive positioning systems [25, 26].

Development of multiple robotic systems took place in the early to mid 1990s, mostly in neurosurgery, maxillofacial surgery, laparoscopic surgery, and orthopaedic surgery. This resulted in the first clinical trials for a robotic TKA in 1998 [26].

*General concepts*

In orthopaedic surgery, three types of robotic systems are in use: passive, active and semi-active or synergistic robots [27, 28]. The above-mentioned system is an example of a passive robot. The robot itself does not perform any surgical action but aids the surgeon in either: surgical simulation, preoperative planning or intraoperative navigation. An example of a passive robot in knee surgery is the BRIGIT™ robot, which eventually developed into the semi-active ROSA® robot [27-30].

The second type of robots is active robots. In TKA, active robots were the first generation of joint surgery robots used [30]. These robots carry out a specific task such as making bony cuts or reaming femoral cavities in hip surgery. The surgeon does not intervene in their surgical duties, but the systems contain a safety override allowing the surgeon to take over if needed. Some examples of these types of robots in knee surgery are ROBODOC® (now TsolutionOne®), and the CASPAR® robot [14, 27-35]. The third type of robots used in orthopaedic surgery are synergistic or semi-active systems. These robots work together with the surgeon and combine their skills to perform specific surgical steps. Examples used for TKA are the Acrobot®, MAKO®, VELYS™ Robotic Assisted Solution (VRAS), and Navio™. The synergistic system allows the surgeon to control the surgical strategy of the robot while the surgeon directly receives feedback when for instance making bony cuts in TKA [14, 25-30, 33, 36-39].

Among these three types, the semi-active systems are the most widely used robotic systems for TKA.

Additionally, to the above-mentioned different types of robotic systems, there are several possibilities for orientation and visualisation. Image-based systems rely on CT, MRI or X-rays to construct a virtual model of the knee based on CAS technology. A key advantage of these systems is the ability to perform preoperative planning. Imageless systems record bony landmarks intraoperatively to form a virtual reconstruction of the knee from a preloaded database of patient scans in the robotic software. Some robotic systems use a combination of both [27-29, 33, 35-43].

Two different software systems exist. Closed systems only use specific manufacturer approved implants, while open systems allow different implants designs from different manufacturers from an inventory. With open systems, general bony cuts can be planned, but techniques specific to a specific knee implant cannot be applied [27-29, 33, 42, 44].

### *Planning and surgical technique*

#### Active robotic systems

Active robot systems use a preoperative planning module where the surgeon determines position of implants on a preoperative CT scan (most used) or MRI [13, 33, 35]. Based on this preoperative plan, a specific machining plan is generated by the software. Fixed trackers are attached to the femur, tibia, and the surgical cutting tool. After additional pin-based contact registration, the plan is then used by the robotic system during surgery. The limb is immobilised and attached to the robot. In active systems, the robot mills or saws the bone, or places the jigs on the bone for manual cutting. Thus, active robotic systems are autonomous and operate under supervision of the surgeon. The surgeon does not provide any active input during these surgical steps, but the surgeon can alter or stop the robot at any time [13, 33, 35, 40].

Passive robotic systems

Passive robots utilise three types of methods for intraoperative navigation: volumetric image-based navigation in which CT, MRI or ultrasound images are used, fluoroscopic navigation which construct guiding maps intraoperatively, or imageless navigation [14]. The main concept is that the robotic system is used as a positioner for a guide or a jig [28, 29, 33, 45, 46]. Image-based surgery is performed by importing preoperative images into the system. Subsequently, validated algorithms create a virtual 3D model of the patient's knee. Imageless surgery is performed by stylus guided orientation of the leg and knee during surgery. When using the imageless method, the surgeon points out anatomic landmarks and performs mobilisation of the knee, which is of importance to gather information on the characteristics of the soft tissue balance of the knee. Using a camera and calibrated tracking pins inserted into the femur and tibia, the system creates a 3D rendered reference of the knee and where it is located within the OR [29, 33, 45, 46]. Whichever method is used, during surgery the robotic system uses the acquired information to place a cutting jig in the required position for the surgeon to make an accurate cut [29, 33, 45, 46].

Semi-active robotic systems

In the late 2000s, semi-active robots were developed for unicompartmental knee arthroplasty (UKA), and later for TKA as well [13, 15, 33, 40, 47]. Semi-active systems are under direct control of the surgeon. The surgeon performs the burring- or cutting procedure, but the robotic system will retract the cutting tool or provide alerts and feedback when the limits of a predefined operative region are reached [14, 33, 36-40]. Semi-active systems are able to do this by using image-based or imageless software and adapt based on the anatomy of the individual patient [48].

To create a virtual model of the knee intraoperatively, the surgeon places pin-tracking diodes in the femur and tibia, and registers anatomical landmarks with a navigation probe. The system uses an infra-red camera that tracks the attached diodes and the robotic arm. By moving the limb and knee, construction of the limb axis and calculation of gap balance are carried out. Within the computer system a template implant is placed in the desired position on the virtual model of the knee. Then, a high-speed burr or saw attached to the robotic arm performs bone resections. The system provides resistance and automatically stops when bony cuts go outside of the determined boundaries defined by the operative plan. The components are implanted by the surgeon [15, 27-29, 33, 34, 36-39, 43, 47-50].

## DISCUSSION

Due to the abundance of planning modalities for TKA, physicians are posed with the challenge of which type to implement into their daily practice. In this comprehensive review, the authors aimed to summarise the development and key elements of computer-based pre- and intraoperative planning modalities for TKA. In this review the authors described CAS, PSI and robotics for TKA.

CAS is an evolving field with continuously changing techniques and software. For TKA, technological developments such as computer software and execution tools are continuously invented to achieve more accurate alignment, better interaction with and understanding of soft-tissue balance, and subsequently improved prosthesis survival and patient satisfaction. The question of what kind of technological improvement will be most impactful remains. The future of CAS for TKA is promising however, especially since the rise of artificial intelligence (AI) which may be able to assist with planning and alignment. The possible role of AI is however not yet known.

In addition to these technological developments, different alignment strategies arose which in combination with CAS could improve clinical outcome, patient satisfaction, prosthetic alignment and implant survival. Theories regarding native knee alignment and knee phenotyping are currently being researched extensively.

Alignment has been designated as one of the factors that determine survivorship of the implant [51]. Since the introduction of TKA, the fixed alignment approach of mechanical alignment (MA) has been used as consistent targets for all knees [52-55]. MA has been, and still remains, the most common alignment technique for executing TKA which attempts a horizontal joint line, and a neutral mechanical axis [52-54, 56]. This results in an evenly distributed biomechanical loading on the femoral and tibial implants [56]. However, MA alters natural knee kinematics and balance, which may compromise functional outcomes.

To simulate the patient’s own pre-arthritic, or constitutional, alignment, multiple alignment philosophies arose as alternatives to MA and are gaining popularity [55]. Kinematic alignment (KA) has been suggested as a technique to recreate a patient's constitutional alignment, improving soft tissue balance and resulting in more natural knee movements with similar or better PROMs [53, 55, 57-60]. MA restores the 3D morphology of the native knee irrespective of anatomical extremes, therefore prioritising the patient's constitutional alignment over the generic target of a neutral axis. Nevertheless, KA may increase the risk of alignment-related early failures.

With the proliferation of CAS technology, resection thickness, alignment and joint gaps can be planned and/or assessed intraoperatively. As a result, functional alignment (FA) has been proposed as a technique to combine optimal mechanical alignment and balancing of the soft tissues. With the aid of CAS, the limb alignment and gaps can be planned or assessed in real-time by changing the implant position in all three planes, individualised to the patient's knee and gaps. Consequently, individualised alignment targets can be achieved reproducibly [54, 55]. This comprehensive systematic review aids in the understanding of the differences between computer-based planning modalities from which surgeons can choose to achieve the chosen alignment strategy.

In addition to the knowledge of alignment strategies themselves, understanding of constitutional knee alignment and different phenotypes is of utmost importance to choose an optimal alignment strategy in TKA. In patients with knee arthritis, asymmetric loss of the tibiofemoral joint space results in an altered mechanical hip-knee-ankle (HKA) angle compared to their pre-arthritic coronal knee alignment. Over the last years, research was conducted on estimation of the constitutional alignment before arthritic deformity occurred. Some authors proposed a formula to calculate the 'arithmetic HKA' (aHKA), from which the approximate constitutional alignment could be derived [61, 62]. Apart from aHKA, joint line obliquity (JLO) has been designated as an independent variable in knee alignment. This JLO in the coronal plane is parallel to the floor during walking or running as the centre of mass shifts laterally during single leg stance, with adduction of the hip joint [52, 54].

Recent literature highlighted the fact that the anatomy of the knee is variable, and consists of multiple phenotypes [63]. Based on the aHKA and JLO, the Coronal Plane Alignment of the Knee (CPAK) classification has been developed. This classification categorises knees in nine different phenotypes [64]. Knowledge of these functional knee phenotypes may enable the surgeon to identify which patients may benefit most from different alignment strategies where soft-tissue balance is prioritised [64].

With the acquired knowledge on alignment strategies, constitutional knee alignment, and different phenotypes, surgeons are guided to a better understanding of optimal positioning of a total knee prosthesis for specific groups of patients. This can be valuable toward personalised TKA. To achieve this in daily practice, future developments within CAS could be accommodating to accomplish personalised alignment goals as desired by the surgeon.

New technological developments occur constantly. Recently, Augmented Reality (AR) has been proposed as a technology that could improve accuracy in TKA, providing a more efficient and cost-effective solution. Fucentese et al. proposed that the use of AR glasses during surgery improves procedure efficiency, particularly when combined with single use instruments. Furthermore, it allows for better visualisation of the ligaments of the knee joint and tibial rotation during TKA implantation [65]. However, AR is currently in the early stages of research.

The strength of the present article is that it was performed in line with the PRISMA statement for performing a systematic review. The search was conducted by a clinical epidemiologist to ensure that relevant articles could be included.

Its flaw however, is the exclusion of non-English language and non-full text documents which could lead to reporting bias. Also, a fair amount of available literature is from the first or older computer-assisted technologies, while these change over time. Therefore, one cannot generalise the results of a certain CAS system to other systems as some techniques are outdated swiftly by continuous evolutions within and in between groups of techniques [14]. In addition to this, while the search was conducted systematically, one could not assume that certain valuable articles might have not been found within the margins of the search. Furthermore, this review described key elements of each surgical planning modality, and their method of use, objectively while experiences of use may differ in clinical practice.

As new techniques are researched and may become popularised it is of importance that clinical performance of planning modalities remain the top priority. At present, no clear answer can be given on which modality is superior. More research remains to be done to define better understanding of optimal positioning of a total knee prosthesis, and possibly develop the best possible planning modality for TKA.

## CONCLUSION

Over the past decades, technological advances using computer software such as CAS navigation, PSI, or robotics were developed to achieve improved clinical outcomes after TKA. With an abundance of available techniques, the author's goal was to create a clear overview for readers to understand the differences between available computer-based planning modalities. This review showed that the monumental development of digital planning modalities for TKA has led to a vast amount of well-researched options that surgeons can choose from and use in daily practice.

## REFERENCES

1. Tanzer M, Makhdom AM (2016). Preoperative planning in primary total knee arthroplasty. J Am Acad Orthop Surg, 24(4), 220-230.
2. Eggli S, Pisan M, Muller ME (1998). The value of preoperative planning for total hip arthroplasty. J Bone Joint Surg Br, 80, 382–390.
3. Knight JL, Atwater RD (1992). Preoperative planning for total hip arthroplasty: quantitating its utility and precision. J Arthroplasty, 7(suppl), 403–409.
4. Linclau L, Dokter G, Peene P (1993). Radiological aspects in preoperative planning and postoperative assessment of cementless total hip arthroplasty. Acta Orthop Belg, 59, 163–167.
5. Stulberg SD, Picard F, Saragaglia D (2000). Computer-assisted total knee replacement arthroplasty. Oper Tech Orthop, 10(1), 25-39.
6. Bellemans J, Vandenneucker H, Vanlauwe J (2007). Robot-assisted total knee arthroplasty. Clin Orthop Relat Res, 464, 111-116.
7. Lizaur A, Marco L, Cebrian R (1997). Preoperative factors influencing the range of movement after total knee arthroplasty for severe osteoarthritis. J Bone Joint Surg Br, 79(4), 626-629.
8. Lingard EA, Katz JN, Wright EA, Sledge CB (2004). Predicting the outcome of total knee arthroplasty. J Bone Joint Surg Am, 86(10), 2179-2186.
9. León-Muñoz VJ, Martínez-Martínez F, López-López M, Santonja-Medina F (2019). Patient-specific instrumentation in total knee arthroplasty. Expert Rev Med Devices, 16(7), 555-567.
10. Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A (2016). Rayyan - a web and mobile app for systematic reviews. Syst Rev, 5, 210, doi: 10.1186/s13643-016-0384-4.
11. Delp SL, Stulberg SD, Davies B, Picard F, Leitner F (1998). Computer Assisted Knee Replacement. Clinical Orthopaedics and Related Research, 354, 49-56.
12. Desai AS, Dramis A, Kendoff D, Board TN (2011). Critical review of the current practice for computer-assisted navigation in total knee replacement surgery: cost-effectiveness and clinical outcome. Curr Rev Musculoskelet Med, 4, 11–15.
13. Joskowicz L (2017). Computer-aided surgery meets predictive, preventive, and personalized medicine. EPMA Journal, 8, 1–4.
14. Medical Advisory Secretariat (2004). Computer-assisted hip and knee arthroplasty. Navigation and active robotic systems: an evidence-based analysis. Ontario Health Technology Assessment Series, 4(2).
15. Cievet-Bonfils,M, Batailler C, Lording, D, Servien, E, Lustig S (2020). Performing Patient-Specific Knee Replacement with Intra-Operative Planning and Assistive Device (CAS, Robotics). In Rivière, C, Vendittoli, PA (Eds.), Personalized Hip and Knee Joint Replacement, pp 311-319, https://doi.org/10.1007/978-3-030-24243-5_26.

16. Mezger U, Jendrewski C, Bartels M (2013). Navigation in surgery. Langenbecks Arch Surg, 398, 501–514.
17. Ganapathi M (2014). Patient specific guides for total knee replacements – A review. Orthop Trauma, 28(5), 315-321.
18. Chow JC, Torre PKD (2016). Patient-Specific Total Knee Arthroplasty. In Scuderi G, Tria A. (Eds.), Minimally Invasive Surgery in Orthopedics. Springer, Cham, pp 1319–1332, https://doi.org/10.1007/978-3-319-34109-5_124.
19. Batailler C, Swan J, Marinier ES, Servien E, Lustig S (2021). New Technologies in Knee Arthroplasty: Current Concepts. J Clin Med, 10, 47-65.
20. Mattei L, Pellegrino P, Calò M, Bistolfi A, Castoldi F (2016). Patient specific instrumentation in total knee arthroplasty: a state of the art. Ann Transl Med, 4(7), 126-132.
21. Müller W, Bockholt U, Voss G, Lahmer A, Börner M (2000). Planning System for Computer Assisted Total Knee Replacement. In Westwood JD et al (Eds.), Medicine Meets Virtual Reality. IOS Press, pp 214-219.
22. Radermacher K, Portheine F, Anton M, Zimolong A, Kaspers G, Rau G, Staudte HW (1998). Computer Assisted Orthopaedic Surgery With Image Based Individual Templates. Clin Orthop Relat Res, 354, 28-38.
23. Gauci MO (2022). Patient-specific guides in orthopedic surgery. Orthop Traumatol Surg Res, 108(1S), 103154, doi: 10.1016/j.otsr.2021.103154.
24. McGovern T (2011). Customized patient instrumentation for total knee arthroplasty: preoperative planning and intraoperative technique. Am J Orthop, 40(11), 9-12.
25. Davies BL, Harris SJ, Rodriguez y Baena F, Gomes P, Jakopec M (2004). Hands-On Robotic Surgery: Is This the Future? In Yang GZ, Jiang T (Eds.), MIAR 2004, LNCS 3150. Springer-Verlag Berlin Heidelberg, pp 27-37.
26. Davies BL, Rodriguez F, Jakopec M, Harris SJ, Barrett A, Gomes P, Henckel J, Cobb J (2006). The Acrobot system for robotic mis total knee and uni-condylar arthroplasty. Int J Humanoid Robot, 3(4), 415–428.
27. Jacofsky DJ, Allen M (2016). Robotics in Arthroplasty: A Comprehensive Review. J Arthroplasty, 31(10), 2353-2363.
28. Sousa PL, Sculco PK, Mayman DJ, Jerabek SA, Ast MP, Chalmers BP (2020). Robots in the Operating Room During Hip and Knee Arthroplasty. Curr Rev Musculoskelet Med, 13, 309–317.
29. St Mart JP, Goh EL (2021). The current state of robotics in total knee arthroplasty. EFORT Open Rev, 6, 270–279.
30. Chen X, Deng S, Sun M-L, He R (2022). Robotic arm-assisted arthroplasty: The latest developments. Chinese Journal of Traumatology, 25, 125–131.
31. Clatworthy M (2022). Patient-Specific TKA with the VELYS™ Robotic-Assisted Solution. Surgical Technology International, 40, 315-320.

32. Chan J, Auld TS, Stulberg B, Long WJ, Kreuzer S, Campanelli V, Liebelt R, Kissin YD (2020). Active Robotic Total Knee Arthroplasty (TKA): Initial Experience with the TSolution One® TKA System. Surg Technol Int, 37, 299-305.
33. Nathwani D, Shenoy R (2021). Latest Advances in Robot-Assisted Knee Arthroplasty. Surg Technol Int, 39, 331-337.
34. Chen AF, Kazarian GS, Jessop GW, Makhdom AM (2018). Robotic Technology in Orthopaedic Surgery. J Bone Joint Surg Am, 100, 1984-1992.
35. Siebert W, Mai S, Kober R, Heeckt PF (2002). Technique and first clinical results of robot-assisted total knee replacement. Knee, 9, 173–180.
36. Jakopec M, Harris SJ, Rodriguez y Baena F, Gomes P, Cobb J, Davies BL (2001). The First Clinical Application of a “Hands-on” Robotic Knee Surgery System. Comput Aided Surg, 6, 329-339.
37. Jakopec M, Harris SJ, Rodriguez y Baena F, Gomes P, Davies, BL (2002). Acrobot: a "hands-on" robot for total knee replacement surgery. 7th International Workshop on Advanced Motion Control. Proceedings (Cat. No.02TH8623), Maribor, Slovenia, pp 116-120, doi: 10.1109/AMC.2002.1026901.
38. Jakopec M, Rodriguez y Baena F, Harris SJ, Gomes P, Cobb J, Davies BL (2003). The Hands-On Orthopaedic Robot “Acrobot”: Early Clinical Trials of Total Knee Replacement Surgery. IEEE Trans Robot Autom, 19(5), 902-911.
39. Jakopec M, Harris SJ, Rodriguez y Baena F, Gomes P, Davies BL (2003). The Acrobot system for total knee replacement. Ind Robot Int J, 30(1), 61–66.
40. Konan S, Maden C, Robbins A (2017). Robotic surgery in hip and knee arthroplasty. British Journal of Hospital Medicine, 78(7), 378-384.
41. Graichen H, Lekkreusuwan K, Scior W (2019). How will digitalisation affect patient treatment in arthroplasty? Part I: Intraoperative aspects. J Orthop, 17, A1-A5.
42. Roche M (2015). Robotic and Sensor-Assisted Technologies in Knee Arthroplasty. Operative Techniques in Orthopaedics, 25(2), 127-149.
43. Wu M, Charalambous L, Penrose C, Belay E, Seyler TM (2021). Imageless Robotic Knee Arthroplasty. Oper Tech Orthop, 31(4), 1-12.
44. Liow MHL, Chin PL, Pang HN, Tay DK-J, Yeo S-J (2017). THINK surgical TSolution-One® (Robodoc) total knee arthroplasty. SICOT J, 3, 63-68.
45. Batailler C, Hannouche D, Benazzo F, Parratte S (2021). Concepts and techniques of a new robotically assisted technique for total knee arthroplasty: the ROSA knee system. Arch Orthop Trauma Surg, 141(12), 2049–2058.
46. Malvisi A, Marcacci M, Martelli S, Campion G, Fiorini P (2001). A Robotic System for Total Knee Replacement. In: Proceedings of the 2001 IEEE/ASME International Conference on Advanced Intelligent Mechatronics. Como, Italy, pp 1047–1052.
47. Bautista M, Manrique J, Hozack WJ (2019). Robotics in Total Knee Arthroplasty. J Knee Surg, 32(7), 600-606.

48. Calliess T, Ettinger M, Savov P, Karkosch R, Windhagen H (2018). Individualized alignment in total knee arthroplasty using image-based robotic assistance. Orthopäde, 47, 871-879.
49. Roche M (2021). The MAKO robotic-arm knee arthroplasty system. Archives of Orthopaedic and Trauma Surgery, 141, 2043-2047.
50. Yohe N, Mont MA, Chen Z, Sultan AA (2021). MAKO Robotic-Arm Assisted Total Knee Arthroplasty: Surgical Technique From the Office to the Operating Room. Surg Technol Int, 39, 375-385.
51. Werner FW, Ayers DC, Maletsky LP, Rullkoetter PJ (2005). The effect of valgus/varus malalignment on load distribution in total knee replacements. J Biomech, 38, 349–355.
52. MacDessi SJ, Oussedik S, Abdel MP, Victor J, Pagnano MW, Haddad FS (2023). The language of knee alignment: updated definitions and considerations for reporting outcomes in total knee arthroplasty. Bone Joint J, 105-B(2), 102–108.
53. Allen MM, Pagnano MW (2016). Neutral mechanical alignment: is it necessary? Bone Joint J, 98-B(1 Suppl A), 81–83.
54. Oussedik S, Abdel MP, Victor J, Pagnano MW, Haddad FS (2020). Alignment in total knee arthroplasty: what's in a name? Bone Joint J, 102-B(3), 276–279.
55. Karasavvidis T, Moldenhauer CAP, Haddad FS, Hirschmann MT, Pagnano MW, Vigdorchik JM (2023). Current Concepts in Alignment in Total Knee Arthroplasty. J Arthroplasty, 38(7S2), S29-S37.
56. Insall JN, Binazzi R, Soudry M, Mestriner LA (1985). Total knee arthroplasty. Clin Orthop Relat Res, 192, 13–22.
57. Lee YS, Howell SM, Won YY, Lee OS, Lee SH, Vahedi H, Teo SH (2017). Kinematic alignment is a possible alternative to mechanical alignment in total knee arthroplasty. Knee Surg Sports Traumatol Arthrosc, 25(11), 3467–3479.
58. Tian G, Wang L, Liu L, Zhang Y, Zuo L, Li J (2022). Kinematic alignment versus mechanical alignment in total knee arthroplasty: An up-to-date meta-analysis. J Orthop Surg (Hong Kong), 30(3), doi: 10.1177/10225536221125952.
59. Gao ZX, Long NJ, Zhang SY, Yu W, Dai YX, Xiao C (2020). Comparison of Kinematic Alignment and Mechanical Alignment in Total Knee Arthroplasty: A Meta-analysis of Randomized Controlled Clinical Trials. Orthop Surg, 12, 1567–1578.
60. Howell SM, Howell SJ, Kuznik KT, Cohen J, Hull ML (2013). Does a kinematically aligned total knee arthroplasty restore function without failure regardless of alignment category? Clin Orthop Relat Res, 471, 1000–1007.
61. Griffiths-Jones W, Chen DB, Harris IA, Bellemans J, MacDessi SJ (2021). Arithmetic hip-knee-ankle angle (aHKA): an algorithm for estimating constitutional lower limb alignment in the arthritic patient population. Bone Jt Open, 2(5), 351–358.

62. MacDessi SJ, Griffiths-Jones W, Harris IA, Bellemans J, Chen DB (2020). The arithmetic HKA (aHKA) predicts the constitutional alignment of the arthritic knee compared to the normal contralateral knee: a matched-pairs radiographic study. Bone Jt Open, 1(7), 339–345.
63. Hirschmann MT, Moser LB, Amsler F, Behrend H, Leclerq V, Hess S (2019). Functional knee phenotypes: a novel classification for phenotyping the coronal lower limb alignment based on the native alignment in young non-osteoarthritic patients. Knee Surg Sports Traumatol Arthrosc, 27, 1394–1402.
64. MacDessi SJ, Griffiths-Jones W, Harris IA, Bellemans J, Chen DB (2021). Coronal Plane Alignment of the Knee (CPAK) classification. Bone Joint J, 103-B(2), 329–337.
65. Fucentese SF, Koch PP (2021). A novel augmented reality-based surgical guidance system for total knee arthroplasty. Arch Orthop Trauma Surg, 141(12), 2227–2233.

## APPENDIX 1 Literature Search: databases and search strings

**EMBASE September 3rd, 2022**

| # | Query | Results |
|---|---|---|
| 9 | #4 AND #8 | 4,310 |
| 8 | #5 OR #6 OR #7 | 157,482 |
| 7 | preoperative period'/de | 63,626 |
| 6 | 'intraoperative period'/de | 46,923 |
| 5 | ((preoperati* OR intraoperati* OR peroperati* OR 'patient specific' OR 'pre operati*' OR 'intra operati*' OR 'per operati*' OR patientspecific) NEAR/3 (plan* OR templat* OR evaluat*)):ti,ab,kw | 55,149 |
| 4 | #1 OR #2 OR #3 | 67,118 |
| 3 | (((knee OR knees OR 'knee joint*') NEAR/3 (arthroplast* OR replac* OR reconstruct* OR prosthe* OR implant* OR alloplast* OR plasty OR plasties)):ti,ab,kw) OR tka:ti,ab,kw OR kneearthroplast*:ti,ab,kw | 55,164 |
| 2 | 'knee prosthesis'/exp | 13,265 |
| 1 | 'knee arthroplasty'/exp | 52,578 |

**OVID Medline September 3rd, 2022**

| # | Query | Results |
|---|---|---|
| 1 | exp Arthroplasty, Replacement, Knee/ | 29,825 |
| 2 | exp Knee Prosthesis/ | 13,199 |
| 3 | (((knee or knees or 'knee joint*') and (arthroplast* or replac* or reconstruct* or prosthe* or implant* or alloplast* or plasty or plasties)) or tka or kneearthroplast*).mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] | 76,823 |
| 4 | 1 or 2 or 3 | 76,823 |
| 5 | ((Preoperati* or intraoperati* or peroperati* or 'patient specific' or 'pre operati*' or 'intra operati*' or 'per operati*' or patientspecific) adj3 (plan* or templat* or evaluat*)).mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] | 39,308 |
| 6 | 4 and 5 | 1,662 |

**Cochrane Library September 3rd, 2022**

| # | Query | Results |
|---|---|---|
| 1 | ((knee or knees or 'knee joint*') and (arthroplast* or replac* or reconstruct* or prosthe* or implant* or alloplast* or plasty or plasties)) or tka or kneearthroplast*:ti,ab,kw | 13,619 |
| 2 | ((preoperati* OR intraoperati* OR peroperati* OR 'patient specific' OR 'pre operati*' OR 'intra operati*' OR 'per operati*' OR patientspecific) n3 (plan* OR templat* OR evaluat*)):ti,ab,kw | 830 |
| 3 | #1 and #2 | 53 |

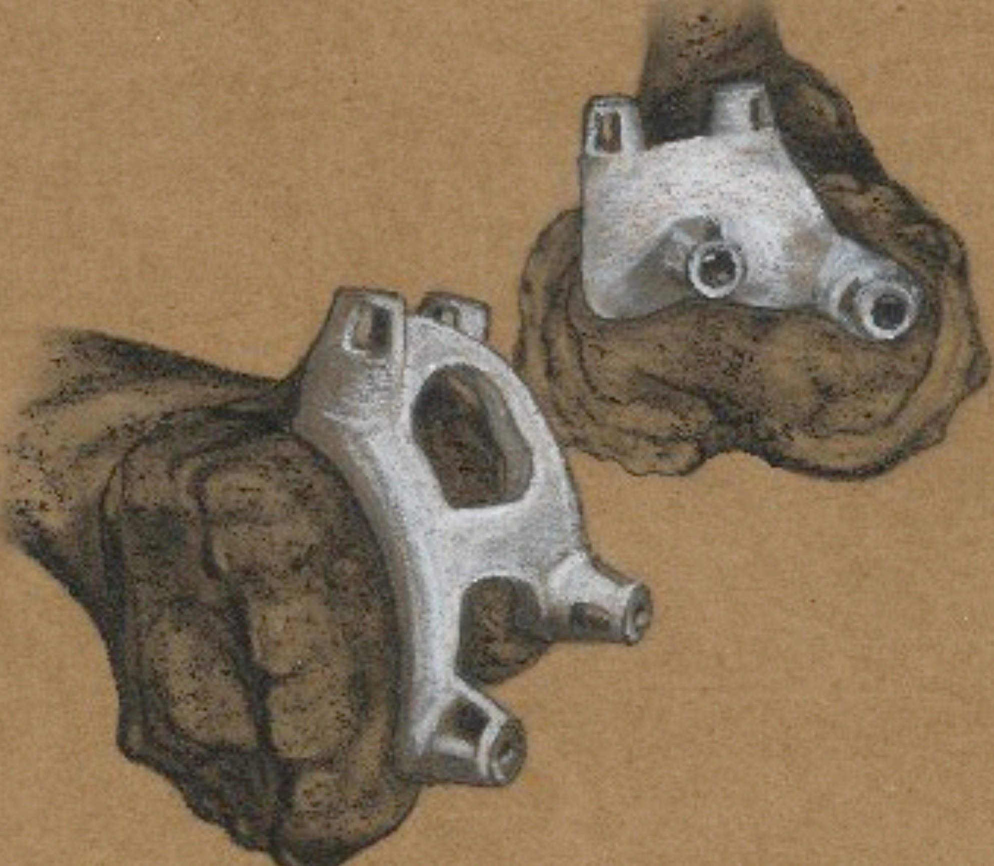
47 Cochrane Reviews
4 Cochrane Protocols
2 Trial

**Web of Science September 3rd, 2022**

| # | Query | Results |
|---|---|---|
| 3 | #1 AND #2 | 1,888 |
| 2 | (Preoperati* or intraoperati* or peroperati* or "patient specific" or "pre operati*" or "intra operati*" or "per operati*" or patientspecific) NEAR/3 (plan* or templat* or evaluat*) (Topic) | 40,432 |
| 1 | (((knee or knees or "knee joint*") and (arthroplast* or replac* or reconstruct* or prosthe* or implant* or alloplast* or plasty or plasties)) or tka or kneearthroplast*) (Topic) | 81,482 |

## APPENDIX 2 Relevant titles in non-English language

1. Huang YY, Yuan W (2018). Three-dimensional printing technology applied in knee diseases: Prosthesis matching and surgical planning. Chinese Journal of Tissue Engineering Research, 22(27), 4417-4422.
2. Hu HS, Wang JC, Xiong CZ, Yan LQ, Wang Q, Chen G (2014). Prosthesis size in total knee arthroplasty predicted using digital pre-operative plan. Chinese Journal of Tissue Engineering Research, 18(40), 6432-6437.
3. Tian H (2022). Robotic assisted artificial hip and knee arthroplasty is an inevitable trend in the future. Zhonghua yi xue za zhi, 102(1), 4-8.
4. Steinfeld Y, Yonai Y, Masarwa R, Berkovich Y (2021). Robotic Total Knee Arthroplasty. Harefuah, 160(11), 729-731.
5. Spaltenstein M, Allami B, Gardon R, Jolles BM (2014). Single use custom made instrumentation, the future of total knee arthroplasty? Revue Medicale Suisse, 10(455), 2424-2428.



# 8

# General discussion

## GENERAL DISCUSSION

This thesis aimed to enhance the knowledge to support clinical decision-making in computer-based total knee arthroplasty (TKA) planning. The thesis was divided into three sections: (1) Mechanical leg axis (MLA) measurements in weight-bearing and non-weight-bearing measurement modalities, (2) planning of patient-specific instrumentation (PSI) for TKA and its mid-term follow-up results, (3) X-ray-based PSI (X-PSI) and an overview of computer-based planning modalities for TKA.

In this chapter, the main findings and limitations of the previous chapters are discussed. Conclusions and recommendations for future studies are also presented in this chapter.

The foundation of this thesis started in the years that Zuyderland Medical Centre was using PSI for TKA regularly. Innovations in computer-assisted surgery (CAS) systems occurred during the time of this thesis. While the results for the first two sections of the thesis were being gathered, more recent innovations in the field led to the third section of this thesis. Techniques and tools continued to evolve, giving rise to new PSI systems like the X-PSI system presented in **Chapter 6.** Although this system did not achieve a global launch, its foundational principles were used for another innovation: robotics in TKA. Various robotic systems have been developed, with different possibilities for their use. **Chapter 7** was created to describe key elements of other computer-assisted surgical planning modalities and their method of use.

Concurrently, while some authors focused on innovations, literature on older CAS systems with longer follow-up results was being published. Despite being partially superseded by newer systems in clinical practice, the concepts of previous CAS systems remain crucial as they form the foundation of the newer ones. Thus, enhancing our understanding of these systems and their outcomes is still essential.

This thesis aimed to contribute valuable insights on measuring knee alignment, the planning of PSI in TKA, and the mid-term follow-up results of PSI. It also presented preliminary experiences with a novel planning modality in PSI and offered a comprehensive overview of computer-based planning modalities in TKA.

This thesis aimed to enhance the knowledge to empower clinical decision-making in computer-based TKA planning.

## Part 1 - Weight-bearing and non-weight-bearing leg alignment

This part assessed differences between MLA measurements in weight-bearing and non-weight-bearing measurement modalities.

**Chapter 2** revealed a mean difference of up to 2.5 degrees in within-person MLA measurements when comparing weight-bearing full-length radiographs (FLR) to non-weight-bearing measurement modalities (imageless CAS navigation or magnetic resonance imaging (MRI) based PSI).

Several authors identified differences in alignment and knee kinematics between weight-bearing and non-weight-bearing positions or imaging modalities [1,2]. Other factors may also contribute to differences. Hirschmann et al. found that knee flexion affected several knee joint movements in weight-bearing conditions. With higher degrees of flexion, progressive internal tibiofemoral rotation occurred, and a posterior shift of the femoral and tibial contact points occurred [3]. Factors like double or single-leg weight-bearing positions, higher body mass index, and end-stage osteoarthritis also contributed to discrepancies in coronal alignment between weight- and non-weight-bearing images [4,5].

**Chapter 2** only compared MLA measurements. No comparison of other angles was conducted. It also did not account for other factors like flexion deformity or ligamentous imbalance, which could affect MLA measurements on weight-bearing FLR.

Non-weight-bearing measurement modalities like computed tomography (CT) or MRI are used in PSI and other CAS systems that use these imaging modalities. Imageless modalities, like most CAS navigation systems and some robotics, create three-dimensional (3D) knee models in non-weight-bearing situations. Given the differences between weight- and non-weight-bearing conditions, this is an essential factor to consider when using these CAS systems for operative planning. In addition, follow-up after TKA is usually done with weight-bearing radiographs. Orthopaedic surgeons should be aware that differences exist.

Despite these differences in measurements, it remains to be seen if a difference of a couple of degrees impacts clinical outcomes in the short- and long-term.

In the future, it might be helpful to combine weight-bearing and non-weight-bearing information to provide surgeons with optimal details on the knee. However, optimal implant placement and alignment strategies for each patient still require further research. Their influence on long-term follow-up results, like implant survival and clinical outcomes, is still being determined. With technological developments, it might be possible to convert this knowledge into desired implant placement and intraoperative verification, encompassing placement angles and ligament balancing.

### Part II - Planning in Patient-Specific Instrumentation

The second part of this thesis focused on the PSI planning phase for TKA. It also presented mid-term follow-up of patients who underwent surgery using PSI.

In PSI, the manufacturer provides the orthopaedic surgeon with a preoperative plan that the surgeon can modify and approve. If a preoperative planning tool like PSI is used for TKA, it is essential to ascertain if repetitive planning by the surgeon leads to consistent results. Inaccuracies in these planning steps may lead to critical errors.

If a surgeon can predict the component implant size needed intraoperatively, it might improve operating room efficiency and decrease in-hospital stock. Exploring the differences between the default and approved plans and how they compare to intraoperative implant size is interesting to enhance the knowledge of this planning stage. If the approved plan matches the intraoperative results better, it underlines the importance of the surgeon approving each preoperative plan.

Additionally, **part II** also presented mid-term follow-up of patients who underwent surgery using PSI. Clinical follow-up studies are essential to evaluate treatments to enable comparison of outcomes with other treatments and estimate the associated benefits and costs.

The reliability of planning in PSI was assessed in **Chapter 3** by comparing repetitive preoperative planning within and between orthopaedic surgeons. Four experienced orthopaedic surgeons modified and approved 40 preoperative default plans three times. The intra- and interobserver reliability among preoperative planning by the surgeons was assessed.

The study revealed that planning of TKA using PSI by different surgeons resulted in an excellent agreement for implant sizes between surgeons and repeated planning by the same surgeon. Next to implant size, intra- and interobserver reliability demonstrated good to excellent agreement for 7 out of 12 remaining settings and 6 out of 12 parameters, respectively.

Notably, the agreement on implant size remained the same between the surgeons who made multiple changes to the proposed plans compared to those who made minimal adjustments. This suggests that more adjustments are required to change the implant's size. However, since cases were planned differently, it is still being determined what effect variations in the position of the knee prosthesis, despite resulting in the same implant size, would have on clinical outcomes. Like this research, other studies also focused on implant size as an outcome measure [6,7]. Although implant size is an easily measurable and comparable outcome, its relationship to clinical outcomes is unclear, and other factors may influence these outcomes more distinctly.

**Chapter 4** investigated the impact of preoperative default plan approval on the intraoperative implant size. The frequency and reason for intraoperative changes of the planned implant size were analysed. The clinical records of 293 patients who underwent surgery with PSI were reviewed for the actual implant size used. These implant sizes were compared to the manufacturer's preoperative default plans and the operating surgeon's approved plans.

The findings of **Chapter 4** indicated that the approved plans by the surgeon matched the intraoperatively used implant sizes more closely than the default plans provided by the manufacturer. Therefore, based on this chapter, we concluded that the operating surgeon should always validate and approve plans.

Similar findings were reported by Cucchi et al., who found significant differences between manufacturers and surgeons in accurately predicting implant sizes with CT-based PSI for TKA [8].

In both **Chapter 3** and **Chapter 4,** components of planning in PSI were analysed. Every surgeon approaches the planning of their surgical cases differently, with different priorities influenced by experience and/or preferences. Next to potential differences in the planning step, another variable aspect is how they would utilise the mould intraoperatively and how these intraoperative actions affect outcomes. Literature shows inconsistent results in the accuracy of bone resection based on PSI [9,10,11]. So, even with identical planning, the result may differ due to variations in resection cuts.

Furthermore, surgeons have personal preferences not only in the planning process, but also in the amount of knee laxity in the knees they operate on. These preferences might change based on patient gender, age, or other factors. This makes PSI not only patient-specific, but also in a certain way surgeon-specific. This complicates the comparison of results within groups. Hence, research often focuses on more definable outcomes like alignment and implant sizes.

By reviewing the default plan, surgeons evaluate the patient’s images in a structured way. By doing this, the operating surgeon can detect potential issues that may arise intraoperatively. The 3D virtual computer model changes based on the surgeon's modifications to the default plan. The visualisation of changes to the 3d model will aid the surgeon in planning. In this way, the surgeon will be optimally prepared for the surgery.
Beyond serving as an optimal preparation and visualisation tool for the surgeon, PSI could also have a valuable function in education. Training on patients and cadavers is considered the gold standard for learning and acquiring surgical skills. However, restrictions concerning patient safety, ethical dilemmas, and lack of availability must be considered. Consequently, representations in 3D emerge as beneficial educational tools, enhancing patients' comprehension and facilitating the understanding and skill development of medical students, residents, and surgeons [12,13].

Reviewing and modifying provided default plans by the surgeon is time-consuming.
Lambrechts et al. evaluated whether machine learning could improve manufacturers' default preoperative plans for TKA. Their machine learning-based preoperative plans, adjusted according to the surgeon's preferences, demonstrated a reduction of time needed to modify the preoperative plan before approval. These machine learning-based plans reduced the average number of corrections required by the surgeon by 39.71% [14].
It may be beneficial if machine learning could help an orthopaedic surgeon time-wise, without negatively influencing its potential for optimal preparation, visualisation and educational purposes. Although machine learning is still not widely applied in orthopaedics, its future application is anticipated to grow. The extent to which types of CAS will benefit from machine learning will become apparent as the field evolves.

In **Chapter 3 and 4** the planning process of PSI in TKA was evaluated. However, in recent years, an evolution of alignment strategies has occurred. Since planning is used to align the implants, understanding these alignment strategies and their consequences is essential.
The longevity of the total knee prosthesis is influenced by several factors, with alignment recognised as a crucial determinant [15,16]. Since the introduction of TKA, the consistent target for all knee prostheses has been the fixed alignment approach known as mechanical alignment (MA) [17,18]. With MA, the surgeon attempts to restore the MLA, which runs from

the hip joint's centre to the knee and ankle joints' centre. The femoral and tibial implants are placed perpendicular to this mechanical axis, achieving a horizontal joint line and a neutral mechanical axis. It has been, and remains, the predominant alignment method employed in TKA [17-19]. This alignment leads to an evenly distributed biomechanical loading on both implants [20]. PSI techniques have been developed mainly to achieve MA goals. However, concerns arose that MA could alter knee joint anatomy and balance, potentially adversely affecting functional outcomes [19].

Kinematic alignment (KA) is a different strategy aiming to restore the knee's pre-arthritic, or constitutional, alignment [17-19]. This strategy prioritises the individual's constitutional alignment over the generic target of a neutral axis. It, therefore aims to enhance soft tissue balance, facilitating more natural knee movements, potentially with comparable or superior clinical outcomes [17,19,21]. However, KA may increase the risk of alignment-related early failures. The restricted KA (rKA) concept has been proposed to decrease the risk of significant alignment outliers. This strategy sets boundaries on final limb alignment and implant positioning [17,19].

KA strategies focus on the restoration of constitutional lower limb alignment. However, determination of constitutional lower limb alignment can be challenging due to progressive joint deformity in knee OA. On top of that, varus- or valgus malalignment itself accelerates the OA progression, especially in more severe OA, possibly due to increased joint vulnerability [22].

An arithmetic hip–knee–ankle angle (aHKA) was invented to determine constitutional lower limb alignment, by measuring distances unaffected by joint space narrowing [23,24]. Constitutional alignment can also be approximated intraoperatively during computer-assisted TKA by stressing the collateral ligaments to reverse the direction of arthritic deformity, thereby producing a “stressed” HKA (sHKA) [25,26].

Recent literature has highlighted that the constitutional anatomy of the knee is variable and consists of multiple phenotypes [27]. Based on the aHKA and joint line obliquity, the Coronal Plane Alignment of the Knee (CPAK) classification has been developed. This classification categorises knees into nine different phenotypes [28]. A better understanding of the needs of individual patients may be facilitated by grouping patients according to these phenotypes. This knowledge may allow surgeons to identify which patients benefit most from alignment strategies where soft-tissue balance is prioritised [28].

With the acquired knowledge of alignment strategies, constitutional knee alignment, and the different phenotypes, surgeons are guided to a better understanding of the optimal positioning of a total knee prosthesis for specific groups of patients. Patients' follow-up results are needed to evaluate the effects on clinical outcomes. Further studies must determine the best individualised conservative and surgical treatment options, offer prognoses for osteoarthritis progression, and guide surgical intervention [29]. Future developments in CAS may provide the necessary support to accomplish personalised alignment goals as the surgeon desires.

**Chapter 5** presented the 5-year follow-up results of the first 200 TKAs performed using PSI. This chapter focused primarily on implant survival rate, (serious) adverse events, and patient-reported outcome measures (PROMs). Over five years, (partial) revision surgery was required in four patients (2%).
Previous research shows a total knee prosthesis survival of 90% after 20 years and approximately 82% of TKAs last 25 years [30]. The Dutch registry reports a 13-year revision rate of 6%, and a 5-year revision rate of 4% [31]. The revision percentage found in **Chapter 5** was low, but the small sample size (n=200) and short follow-up period warrant caution in interpreting these results. A cohort of 200 patients is small to investigate (serious) adverse events. More extensive databases would be valuable to evaluate this aspect.
Nonetheless, PROMs were consistent at five-year follow-up of TKAs using PSI. After 5 years, all median outcome scores for PROMs improved significantly from the preoperative values ($p \leq 0.05$). The median outcome scores were not significantly different between the 1- and 5-year follow-up moments, except for a significant decrease in EQ-VAS ($p \leq 0.05$) between these two follow-up moments.
This study did not compare PSI with conventional instrumentation or other surgical techniques. While improvements in PROMs from preoperative values are expected across all techniques, a comparative analysis of PROMs between surgical methods could be more insightful. However, it's important to note that PROMs are subjective and prone to bias.

Various authors found comparable or slightly superior alignment accuracy in PSI TKA compared to conventional instrumentation [32-37]. However, when functional outcomes and pain scores were compared, the current literature did not convincingly demonstrate the superiority of one technique over the other [32,36-40]. It is essential to acknowledge that PSI did not demonstrate convincing advantages compared to conventional instrumentation, especially on the clinical outcome level. Nonetheless, it also did not show worse outcomes. Although PSI has not achieved the desired results thus far, the potential of the technology in unusual cases and as an educational tool has been recognised [37].

The clinical impact of a few degrees of differences in alignment remains uncertain. These effects may also vary among the newly recognised phenotypes and the chosen alignment strategy. For all patients in this study, MA was the alignment strategy selected. Given recent insights, it is questionable whether surgical planning and execution are the predominant factors affecting clinical outcomes. Intraoperative decisions were not documented, like soft tissue release and choosing a certain amount of tightness. Yet, these factors could influence the outcomes too.

The same surgeon operated on all patients, which could affect the outcomes, while different surgeons might achieve varying results. Moreover, using other PSI systems and their imaging modalities (MRI- or CT-based) may yield different results. In **Chapters 2 through 5,** only one specific CAS navigation- and/or one particular PSI system was investigated. It was the system used in the hospital at the time the research was conducted. Stryker Precision Knee Navigation Software (Stryker Corp. Kalamazoo, Michigan USA) was used for the patients operated on by CAS navigation. The Signature™ system (Zimmer Biomet, Warsaw, IND, USA) was the PSI system used. Therefore, it must be emphasised that the results presented in this thesis do not automatically apply to other CAS navigation and PSI systems.

A recent systematic review comparing the cost-effectiveness of PSI with conventional instrumentation showed variable costs across several aspects of each surgical technique. Nonetheless, total costs per patient case were higher in PSI TKA [41]. Identifying methods to reduce imaging- and production costs could make PSI more economically competitive.

The reliability of a surgical planning tool is crucial. In **Chapter 3,** it was found that preoperative planning for TKA implant size using PSI demonstrated excellent intra- and interobserver reliability. **Chapter 4** emphasised that the approved plans by the operating surgeon matched the intraoperatively used implant sizes better than the default plans provided by the manufacturer. If needed implant sizes can be predicted, this could improve operating room efficiency and decrease in-hospital stock.

In addition to the patient-specific nature of PSI, PSI could be seen as doctor-specific since each surgeon has personal preferences in planning, but variations in intraoperative steps occur. What effect these variations have on the (clinical) outcome is hard to analyse in research. PSI may serve as an optimal preparation and visualisation tool for surgeons, especially in complex cases. It may also be beneficial as an educational tool.

In **Chapter 5,** consistent PROMs were found for a 5-year follow-up of TKA using PSI, with revision surgery being necessary in only a few cases. Literature needs to demonstrate superior results of PSI over other techniques convincingly. The effects of the new insights in alignment strategies, constitutional knee alignment, and the different phenotypes may contribute to a better understanding of optimal implant positioning in TKA. Improved understanding may affect (clinical) outcomes. Future developments in CAS and machine learning may provide the necessary support to accomplish these personalised alignment goals, hopefully leading to improved outcomes.

## Part III - Innovations in digital pre- and intraoperative planning modalities for TKA

New technological developments occur constantly in the current fast-paced and research-driven medical environment. In the field of TKA as well, innovations in digital pre- and intraoperative planning methods develop faster than ever. Multiple CAS options have become available over the last few years: a new era in TKA planning and execution.

**Chapter 6** presented the preliminary experiences of the new preoperative planning method X-PSI compared to MRI-based PSI planning. This novel planning method constructs 3D models of the knee using weight-bearing X-rays. It presents a potential low-cost alternative to CT and/or MRI-based PSI.

**Chapter 2** revealed a difference between weight-bearing and non-weight-bearing measurements of MLA. Previous PSI is CT or MRI-based. Since X-PSI uses weight-bearing X-rays, planning will be based on weight-bearing conditions.

The X-PSI models use an estimated cartilage thickness. This is done by equally dividing the space between the femur and tibia and presuming it represents the existing cartilage. A 'standard' amount of cartilage is added for areas without an opposing bone surface, like the posterior condyles. The resection planes are calculated, including added cartilage (Spokesman Zimmer Biomet, personal communication, June 28, 2023). This introduces potential biases due to the estimation of these cartilage thicknesses. While the X-PSI moulds are bone-referenced, the exact cartilage amount would be less critical for the fit of the moulds. However, it could still impact the precision of the preoperative planning, mainly if the goal would be to predict implant size and thereby reduce the number of surgical trays.

As it is a new technology, limited literature exists on X-ray-based PSI. Massé et al. found greater implant positioning accuracy using X-ray-based PSI guides compared to conventional instrumentation. The X-PSI imaging technology also showed potential in predicting implant sizes, potentially reducing the number of instrument trays required to enhance surgical efficiency [42]. Shetty et al. observed superior mechanical axis alignment based on the virtual cuts made with the X-ray-based PSI compared to the alignment based on the cuts made using conventional instrumentation [43]. These studies both have a very small sample size. Also, in the study by Shetty et al., the cuts by X-ray-based PSI were virtual and assessed via software intraoperatively.

Zimmer Biomet utilised the imaging techniques developed for X-PSI to validate the imaging method for the Rosa robot. However, with the introduction of the Rosa robot, no further investment in X-PSI was carried out due to a strategic shift within the company (Spokesman Zimmer Biomet, personal communication, June 9, 2023). The final measurements in a Rosa case originate from intraoperative landmarking, replacing the preoperative produced virtual 3D bone model. Besides X-ray-based planning, an MRI-based option for the Rosa robot exists. However, the MRI option for Rosa is not available (yet?) for the EMEA region (Europe, the Middle East, and Africa) due to the European Union Medical Device Regulation (Spokesman Zimmer Biomet, personal communication, June 25, 2023). These regulations dictate specific rules for submitting, assessing, and conducting clinical investigations with medical devices.

Similar to previous chapters, this chapter restricts its comparison to only one type of PSI: The Signature™ system (Zimmer Biomet, Warsaw, IND). Additionally, the chapter explores only one kind of X-ray-based PSI from the same manufacturer. Furthermore, it's important to note that these insights are based on the preliminary experiences of a single surgeon.

At the start of the research for this thesis, significant developments in CAS and TKA planning emerged every few years. In recent years, these developments have accelerated. Yet, many new technologies have evolved from the foundational principles of previous CAS methods. For example, PSI and CAS navigation principles are the foundation for most robotic systems. Understanding the basics is essential to understand the latest technology. This thesis aimed to enhance the understanding of CAS and computer-based planning methods for TKA, facilitating the ability to apply this knowledge to recent and future technological developments.

With all available computer-based pre- and intraoperative planning modalities for TKA, physicians are challenged to implement the most suitable modality into their daily practice. **Chapter 7** comprehensively overviews historical and current digital pre- and intraoperative planning modalities for TKA. Furthermore, it aimed to describe key elements of each surgical planning modality and their method of use.

These technologies are part of the evolving landscape of TKA to improve surgical precision and patient outcomes. We are currently witnessing an exciting phase in the technological evolution of TKA. However, despite the promising prospects of CAS, it did not prove the superiority of a specific system over other CAS systems or conventional instrumentation in clinical outcomes.
Like many technological developments, CAS systems seem to follow the Gartner Hype Cycle [44]. This Hype Cycle claims a technology's life cycle consists of five key phases (Figure 1).

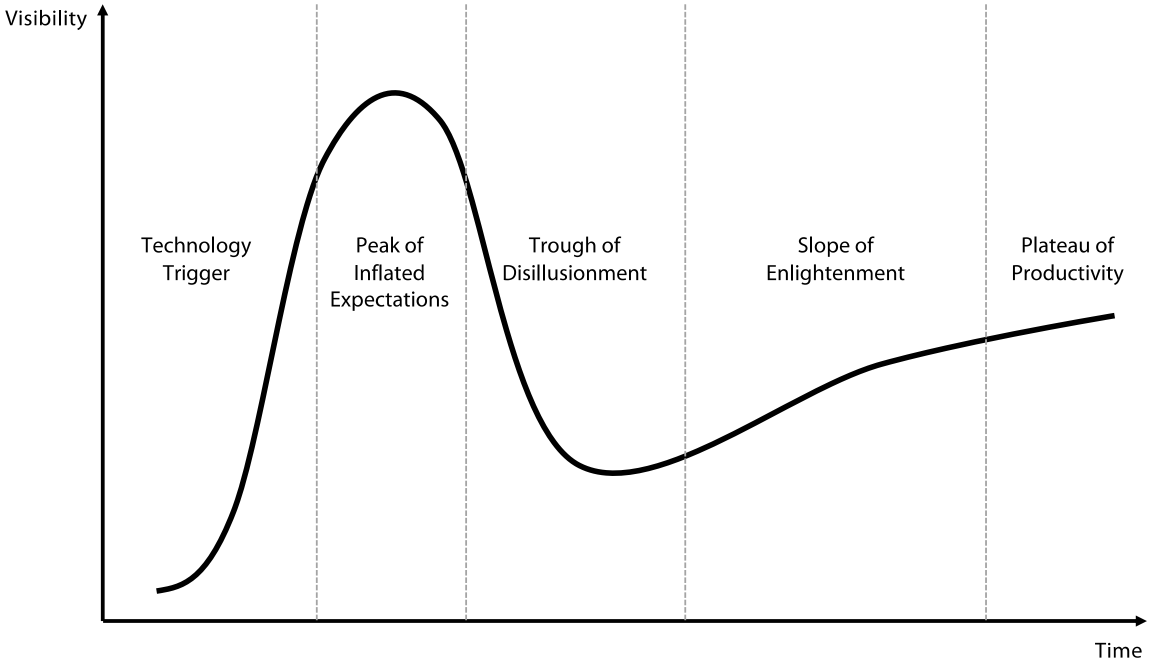


**Figure 1 Gartner Hype Cycle**

The first phase consists of a potential technology breakthrough. In the second phase, promising early results get published. Many authors reported improved implant positioning accuracy for all CAS systems and fewer outliers in achieving the planned limb alignment compared to conventional instrumentation [32-34,45-48]. They also found less blood loss, as these techniques do not require opening the intramedullary canal [49-51]. However, the technology must catch up to expectations in the third phase of the Gartner Hype Cycle as popularity surges. CAS, for instance, still needs to fulfil its promise of solving issues like patient dissatisfaction or improving functional outcomes. No apparent clinically significant effect on clinical outcomes or patient satisfaction has been associated with the available computer-based modalities for TKA thus far [32,36-40,47] Furthermore, compared to conventional instrumentation, the added costs and overall increased surgery time associated with all CAS technologies must be considered [52].

In the fourth phase, the benefits of the technology begin to crystallise, and a broader understanding is gained. Next-generation products appear from technology providers. In CAS, orthopaedic surgeons evaluated whether digital planning in CAS is an accurate navigation for better results. In the last face of Gartner's Hype Cycle, it reaches a plateau of productivity. Mainstream adoption starts with more clearly defined criteria. For CAS, some authors suggest a selective-use policy for technology-assisted TKA that prioritises technology assistance for those patients at a higher risk of revision. This could potentially meet the cost-effectiveness threshold in selected circumstances [53].

With new insights into osteoarthritis phenotypes and alignment strategies and the continued developments in CAS technology, the quest to improve planning in TKA, patient satisfaction, and prosthesis survival is ongoing. CAS systems for TKA may facilitate data-driven personalised care in decision-making, surgical planning, and execution.

## Future developments

New technological developments occur constantly. In recent years, artificial intelligence (AI) and machine learning have been applied in numerous aspects of our daily lives. AI is a field of computer science that designs systems performing tasks that typically necessitate human intelligence [54-57]. Machine learning, a subdivision of AI, enables computers to learn from data without explicitly programming [54-57].

In orthopaedics, these technologies have mainly been applied in medical imaging, from acquisition and reconstruction to analysis and interpretation. For knee-related healthcare specifically, it has been introduced for diagnosing osteoarthritis, predicting its progression, and predicting the clinical outcomes and potential complications following TKA [55,56].

Some authors explored the application of AI in PSI. Lambrechts et al. investigated whether machine learning could enhance manufacturers' default preoperative TKA planning provided by manufacturers to a surgeon [14].

Augmented Reality (AR) has also surfaced as a promising technology that could improve accuracy in TKA, providing a more efficient and cost-effective approach. AR-based surgical guidance systems could measure the impact of prosthesis alignment and soft tissue balance intraoperatively. Fucentese et al. proposed that employing AR glasses during surgery could improve the visualisation of knee joint ligaments and tibial rotation during TKA implantation [58]. Nonetheless, AR is currently in the early stages of research.

Despite the possible limitations of AI and AR, their transformative potential is undeniable, potentially providing orthopaedic surgeons with valuable tools in the future.

## Future studies

The past years have witnessed transformative shifts around TKA. So far, these developments did not translate to improved clinical outcomes. Also, factors like higher costs, surgical duration, and the learning curve play essential roles.

Achieving optimal outcomes in TKA starts much before the surgical intervention, with accurate preoperative planning playing an important role. This planning, on several levels, coupled with strict patient selection and realistic patient expectations, can hopefully improve surgical precision and patient outcomes. All developments will help to achieve the perception of a natural joint after TKA. More high-quality, long-term studies are needed to understand the clinical benefits of these existing technologies.

Next to technological development, introducing new alignment strategies, insights into constitutional knee alignment, and identifying various phenotypes could enhance our understanding of individual patient needs. These novel perspectives are reshaping the approach to TKA and the role CAS can play in planning and executing TKA. These innovations are part of the evolving TKA, which will continue to develop.

Innovations occur before long-term follow-up results and comparisons of previous techniques are fully understood. Orthopaedic surgeons and researchers will be challenged to find methods to asses these fast-paced innovations. CAS systems have the potential to acquire a lot of pre- and intraoperative data. This may aid in collecting data. Different aspects may be valuable to create a final treatment plan: patient characteristics, anatomical and biomechanical factors, patient expectations, cost analyses, outcomes from national and worldwide data registers in terms of revisions and implant survival, and clinical outcomes from previous literature. With rapid technological developments and the possible application of AI, researchers may have to evaluate optimal research methodologies critically.

CAS technologies so far have seen promises and pitfalls but helped in the evolution and understanding of these technologies. We are in a fascinating era with lots of development and changes. CAS offers a way to gather essential data for future growth and to combine new insights and knowledge on alignment strategies. Whether human surgeons or AI will eventually interpret this data effectively to improve patient satisfaction remains a future question. We might have to keep sharpening our 'cutting-edge' tools to place the perfect knee prosthesis.

## REFERENCES

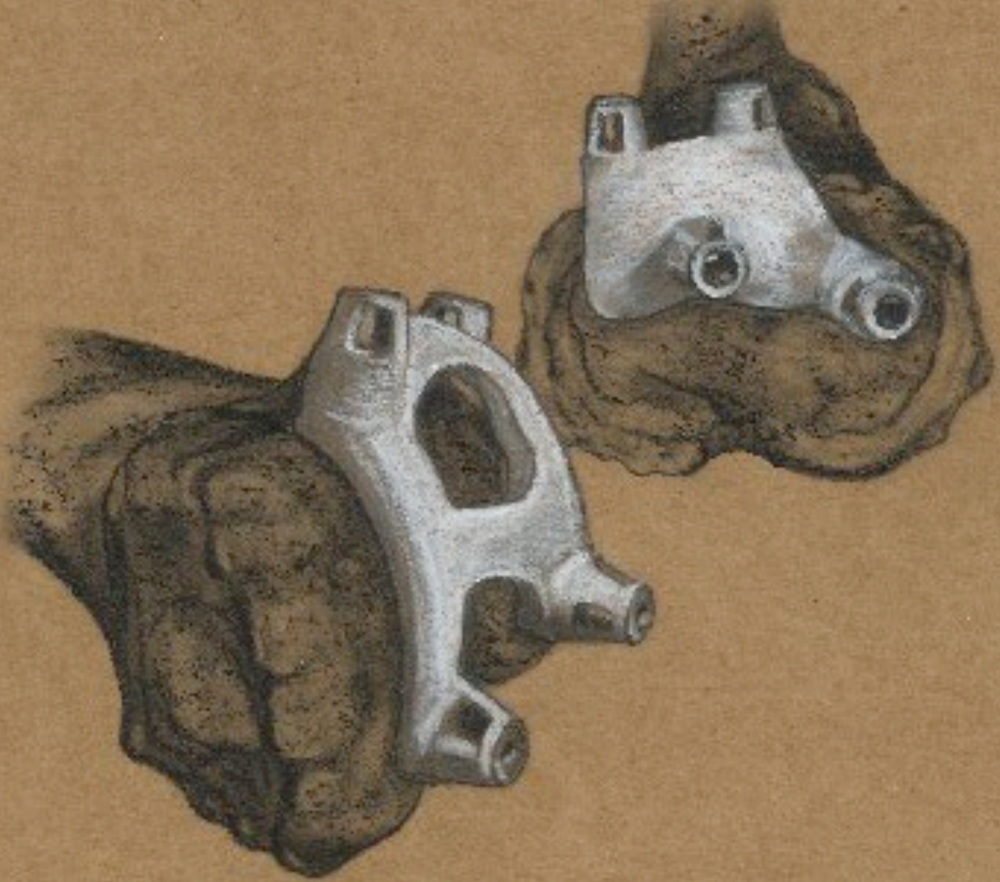
1. Hirschmann A, Buck FM, Fucentese SF, Pfirrmann CWA (2015). Upright CT of the knee: the effect of weight-bearing on joint alignment. Eur Radiol, 25, 3398-3404.
2. Paternostre F, Schwab PE, Thienpont E (2014). The difference between weight-bearing and non-weight-bearing alignment in patient-specific instrumentation planning. Knee Surg Sports Traumatol Arthrosc, 22, 674-679.
3. Hirschmann A, Buck FM, Herschel R, Pfirrmann CWA, Fucentese SF (2017). Upright weight-bearing CT of the knee during flexion: changes of the patellofemoral and tibiofemoral articulations between 0° and 120°. Knee Surg Sports Traumatol Arthrosc, 25, 853-862.
4. Yazdanpanah O, Karimi Mobarakeh M, Nakhaei M, Baneshi MR (2017). Comparison of Double and Single Leg Weight-Bearing Radiography in Determining Knee Alignment. Arch Bone Jt Surg, 5(3), 174-180.
5. Moon HS, Kim SH, Kwak DK, Lee SH, Lee YH, Yoo JH (2022). Factor affecting the discrepancy in the coronal alignment of the lower limb between the standing and supine radiographs. BMC Musculoskelet Disord, 23(1), 1136.
6. Issa K, Rifai A, McGrath MS, Callaghan JJ, Wright C, Malkani AL, Mont MA, McInerney VK (2013). Reliability of templating with patient-specific instrumentation in total knee arthroplasty. J Knee Surg, 26(6), 429-433.
7. Ettinger M, Claassen L, Paes P, Calliess T (2016). 2D versus 3D templating in total knee arthroplasty. Knee, 23(1), 149-151.
8. Cucchi D, Menon A, Compagnoni R, Ferrua P, Fossati C, Randelli P (2018). Significant differences between manufacturer and surgeon in the accuracy of final component size prediction with CT-based patient-specific instrumentation for total knee arthroplasty. Knee Surg Sports Traumatol Arthrosc, 26(11), 3317-3324.
9. Yuan L, Yang B, Wang X, Sun B, Zhang K, Yan Y, Liu J, Yao J (2021). The Bony Resection Accuracy with Patient-Specific Instruments during Total Knee Arthroplasty: A Retrospective Case Series Study. Biomed Res Int, 8674847.
10. Yamamura K, Inori F, Konishi S (2021). Evaluation of the accuracy of resected bone thickness based on patient-specific instrumentation during total knee arthroplasty. Arch Orthop Trauma Surg, 141(9), 1583-1590.
11. Levy YD, An VVG, Shean CJW, Groen FR, Walker PM, Bruce WJM (2017). The accuracy of bony resection from patient-specific guides during total knee arthroplasty. Knee Surg Sports Traumatol Arthrosc, 25(6), 1678-1685.
12. Maglara E, Angelis S, Solia E, Apostolopoulos AP, Tsakotos G, Vlasis K, Katsimantas A, Filippou DK (2020). Three-Dimensional (3D) Printing in Orthopedics Education. J Long Term Eff Med Implants, 30(4), 255-258.

13. Ejnisman L, Gobbato B, de França Camargo AF, Zancul E (2021). Three-Dimensional Printing in Orthopedics: from the Basics to Surgical Applications. Curr Rev Musculoskelet Med, 14(1), 1-8.
14. Lambrechts A, Wirix-Speetjens R, Maes F, Van Huffel S (2022). Artificial Intelligence Based Patient-Specific Preoperative Planning Algorithm for Total Knee Arthroplasty. Front Robot AI, 9, 840282.
15. Werner FW, Ayers DC, Maletsky LP, Rullkoetter PJ (2005). The effect of valgus/varus malalignment on load distribution in total knee replacements. J Biomech, 38, 349-355.
16. Kim YH, Park JW, Kim JS, Park SD (2014). The relationship between the survival of total knee arthroplasty and postoperative coronal, sagittal and rotational alignment of knee prosthesis. Int Orthop, 38(2), 379-385.
17. MacDessi SJ, Oussedik S, Abdel MP, Victor J, Pagnano MW, Haddad FS (2023). The language of knee alignment: updated definitions and considerations for reporting outcomes in total knee arthroplasty. Bone Joint J, 105-B(2), 102–108.
18. Oussedik S, Abdel MP, Victor J, Pagnano MW, Haddad FS (2020). Alignment in total knee arthroplasty: what's in a name? Bone Joint J, 102-B(3), 276-279.
19. Almaawi AM, Hutt JRB, Masse V, Lavigne M, Vendittoli PA (2017). The Impact of Mechanical and Restricted Kinematic Alignment on Knee Anatomy in Total Knee Arthroplasty. J Arthroplasty, 32(7), 2133-2140.
20. Insall JN, Binazzi R, Soudry M, Mestriner LA (1985). Total knee arthroplasty. Clin Orthop Relat Res, 5(192), 13–22.
21. Howell SM, Howell SJ, Kuznik KT, Cohen J, Hull ML (2013). Does a kinematically aligned total knee arthroplasty restore function without failure regardless of alignment category? Clin Orthop Relat Res, 471(3), 1000-1007.
22. Cerejo R, Dunlop DD, Cahue S, Channin D, Song J, Sharma L (2002). The influence of alignment on risk of knee osteoarthritis progression according to baseline stage of disease. Arthritis Rheum, 46(10), 2632-2636.
23. Griffiths-Jones W, Chen DB, Harris IA, Bellemans J, MacDessi SJ (2021). Arithmetic hip-knee-ankle angle (aHKA): An algorithm for estimating constitutional lower limb alignment in the arthritic patient population. Bone Jt Open, 2(5), 351-358.
24. MacDessi SJ, Griffiths-Jones W, Harris IA, Bellemans J, Chen DB (2020). The arithmetic HKA (aHKA) predicts the constitutional alignment of the arthritic knee compared to the normal contralateral knee: a matched-pairs radiographic study. Bone Jt Open. 2020 Nov 2;1(7):339-345.
25. McEwen P, Balendra G, Doma K (2019). Medial and lateral gap laxity differential in computer-assisted kinematic total knee arthroplasty. Bone Joint J, 101-B(3), 331-339.
26. Tarassoli P, Wood JA, Chen DB, Griffiths-Jones W, Bellemans J, MacDessi SJ (2022). Arithmetic hip-knee-ankle angle and stressed hip-knee-ankle angle: equivalent methods for estimating constitutional lower limb alignment in kinematically aligned total knee arthroplasty. Knee Surg Sports Traumatol Arthrosc, 30(9), 2980-2990.

27. Hirschmann MT, Moser LB, Amsler F, Behrend H, Leclerq V, Hess S. (2019). Functional knee phenotypes: a novel classification for phenotyping the coronal lower limb alignment based on the native alignment in young non-osteoarthritic patients. Knee Surg Sports Traumatol Arthrosc, 27: 1394–1402.
28. MacDessi SJ, Griffiths-Jones W, Harris IA, Bellemans J, Chen DB. (2021). Coronal Plane Alignment of the Knee (CPAK) classification. Bone Joint J, 103-B(2): 329–337.
29. Primorac D, Molnar V, Rod E, Jeleč Ž, Čukelj F, Matišić V, Vrdoljak T, Hudetz D, Hajsok H, Borić I (2020). Knee Osteoarthritis: A Review of Pathogenesis and State-Of-The-Art Non-Operative Therapeutic Considerations. Genes, 11(8), 854-888.
30. Evans JT, Walker RW, Evans JP, Blom AW, Sayers A, Whitehouse MR (2019). How long does a knee replacement last? A systematic review and meta-analysis of case series and national registry reports with more than 15 years of follow-up. Lancet, 393, 655–663.
31. Landelijke registratie orthopedische interventies (LROI) (2022). Mid- and long-term revision. Retrieved August 24, 2023, from https://www.lroi-report.nl/knee/survival-TKA/short-and-long-term-revision/
32. Anderl W, Pauzenberger L, Kölblinger R, Kiesselbach G, Brandl G, Laky B, Kriegleder B, Heuberer P, Schwameis E (2016). Patient-specific instrumentation improved mechanical alignment, while early clinical outcome was comparable to conventional instrumentation in TKA. Knee Surg Sports Traumatol Arthrosc, 24(1), 102-111.
33. Pauzenberger L, Munz M, Brandl G, Frank JK, Heuberer PR, Laky B, Schwameis E, Anderl W (2019). Patient-specific instrumentation improved three-dimensional accuracy in total knee arthroplasty: a comparative radiographic analysis of 1257 total knee arthroplasties. J Orthop Surg Res, 14(1), 437.
34. Ng VY, DeClaire JH, Berend KR, Gulick BC, Lombardi AV Jr (2012). Improved accuracy of alignment with patient-specific positioning guides compared with manual instrumentation in TKA. Clin Orthop Relat Res, 470(1), 99-107.
35. Victor J, Dujardin J, Vandenneucker H, Arnout N, Bellemans J (2014). Patient-specific guides do not improve accuracy in total knee arthroplasty: a prospective randomized controlled trial. Clin Orthop Relat Res, 472(1), 263-271.
36. Nam D, Park A, Stambough JB, Johnson SR, Nunley RM, Barrack RL (2016). The Mark Coventry Award: Custom Cutting Guides Do Not Improve Total Knee Arthroplasty Clinical Outcomes at 2 Years Followup. Clin Orthop Relat Res, 474(1), 40-46.
37. Keskinis A, Paraskevopoulos K, Diamantidis DE, Ververidis A, Fiska A, Tilkeridis K (2023). The Role of 3D-Printed Patient-Specific Instrumentation in Total Knee Arthroplasty: A Literature Review. Cureus, 15(8), e43321.
38. Boonen B, Schotanus MG, Kerens B, van der Weegen W, Hoekstra HJ, Kort NP (2016). No difference in clinical outcome between patient-matched positioning guides and conventional instrumented total knee arthroplasty two years post-operatively: a multicentre, double-blind, randomised controlled trial. Bone Joint J, 98-B(7), 939-44.

39. Rudran B, Magill H, Ponugoti N, Williams A, Ball S (2022). Functional outcomes in patient specific instrumentation vs. conventional instrumentation for total knee arthroplasty; a systematic review and meta-analysis of prospective studies. BMC Musculoskelet Disord, 23(1), 702.
40. Sassoon A, Nam D, Nunley R, Barrack R (2015). Systematic review of patient-specific instrumentation in total knee arthroplasty: new but not improved. Clin Orthop Relat Res, 473(1), 151-158.
41. Dorling IM, Geenen L, Heymans MJLF, Most J, Boonen B, Schotanus MGM (2023). Cost-effectiveness of patient specific *vs* conventional instrumentation for total knee arthroplasty: A systematic review and meta-analysis. World J Orthop, 14(6), 458-470.
42. Massé V, Ghate RS (2021). Using standard X-ray images to create 3D digital bone models and patient-matched guides for aiding implant positioning and sizing in total knee arthroplasty. Computer Assisted Surgery, 26:1, 31-40.
43. Shetty V, Shekhar S, Karade V, Maurya A, Sankar M, Wagh Y (2022). A Study of Surgical Accuracy with X-Ray-Based Patient-Specific Instrument (X3DPSI®) vs Conventional Instrument in Total Knee Arthroplasty Surgeries. Indian J Orthop, 56(7), 1240-1250.
44. Gartner (n.d.). Gartner Hype Cycle. Retrieved November 5, 2023, from https://www.gartner.com/en/research/methodologies/gartner-hype-cycle
45. Fu Y, Wang M, Liu Y, Fu Q. Alignment outcomes in navigated total knee arthroplasty: a meta-analysis (2012). Knee Surg Sports Traumatol Arthrosc, 20(6), 1075-1082.
46. Hetaimish BM, Khan MM, Simunovic N, Al-Harbi HH, Bhandari M, Zalzal PK. Meta-analysis of navigation vs conventional total knee arthroplasty (2012). J Arthroplasty, 27(6), 1177-1182.
47. Kayani B, Konan S, Ayuob A, Onochie E, Al-Jabri T, Haddad FS (2019). Robotic technology in total knee arthroplasty: a systematic review. EFORT Open Rev, 4(10), 611-617.
48. Hampp EL, Chughtai M, Scholl LY, Sodhi N, Bhowmik-Stoker M, Jacofsky DJ, Mont MA. Robotic-Arm Assisted Total Knee Arthroplasty Demonstrated Greater Accuracy and Precision to Plan Compared with Manual Techniques (2019). J Knee Surg, 32(3), 239-250.
49. Schnurr C, Csécsei G, Eysel P, König DP (2010). The effect of computer navigation on blood loss and transfusion rate in TKA. Orthopedics, 33(7), 474.
50. Cucchi D, Menon A, Zanini B, Compagnoni R, Ferrua P, Randelli P. Patient-Specific Instrumentation Affects Perioperative Blood Loss in Total Knee Arthroplasty. J Knee Surg. 2019 Jun;32(6):483-489.
51. Mancino F, Cacciola G, Malahias MA, De Filippis R, De Marco D, Di Matteo V, A G, Sculco PK, Maccauro G, De Martino I (2020). What are the benefits of robotic-assisted total knee arthroplasty over conventional manual total knee arthroplasty? A systematic review of comparative studies. Orthop Rev (Pavia), 12(1), 8657.
52. Christen B, Tanner L, Ettinger M, Bonnin MP, Koch PP, Calliess T (2022). Comparative Cost Analysis of Four Different Computer-Assisted Technologies to Implant a Total Knee Arthroplasty over Conventional Instrumentation. J Pers Med, 12(2), 184.

53. Hickey MD, Masri BA, Hodgson AJ (2023). Can Technology Assistance be Cost Effective in TKA? A Simulation-Based Analysis of a Risk-prioritized, Practice-specific Framework. Clin Orthop Relat Res, 481(1), 157-173.
54. Pesapane F, Codari M, Sardanelli F. Artificial intelligence in medical imaging: threat or opportunity? Radiologists again at the forefront of innovation in medicine (2018). Eur Radiol Exp, 2(1), 35.
55. Nich C, Behr J, Crenn V, Normand N, Mouchère H, d'Assignies G (2022). Applications of artificial intelligence and machine learning for the hip and knee surgeon: current state and implications for the future. Int Orthop, 46(5), 937-944.
56. Han XG, Tian W. Artificial intelligence in orthopedic surgery: current state and future perspective (2019). Chin Med J (Engl), 132(21), 2521-2523.
57. Bayliss L, Jones LD. The role of artificial intelligence and machine learning in predicting orthopaedic outcomes (2019). Bone Joint J, 101-B(12), 1476-1478.
58. Fucentese SF, Koch PP (2021). A novel augmented reality-based surgical guidance system for total knee arthroplasty. Arch Orthop Trauma Surg, 141(12), 2227-2233.



# 9

# Impact paragraph

# IMPACT PARAGRAPH

A robot that scans a patient's anatomy and walking pattern and decides on the best knee treatment based on the patient's complaints and expectations. Another robot performs a total knee arthroplasty (TKA) autonomously, customising the alignment and laxity of the knee to the patient’s unique needs. Can robots and artificial intelligence (AI) replace orthopaedic surgeons? Does it sound like a science fiction novel? Or is it a glimpse into the future of orthopaedic surgery?

At present, these scenarios are still far from real. However, fast-paced innovations in computer technology are increasingly impacting our daily lives and have also started to influence medical practices. Multiple computer-assisted surgery (CAS) systems have been developed for TKA in recent years: CAS navigation, patient-specific instrumentation (PSI), and robotics. All innovations aim to enhance outcomes for patients and simplify the tasks of the medical professional.

Despite advancements in CAS for TKA, patient dissatisfaction remains an issue in a significant percentage of patients, about 15% to 30%, with a third reporting residual symptoms at least one year after surgery. This raises questions about the effectiveness of CAS in TKA and its role in the future.

Knee osteoarthritis (OA) is a growing health concern due to the demographic shift towards an aging population and increasing obesity rates. After low-back pain, OA is the second leading musculoskeletal disorder in Disability Adjusted Life Years (DALYs) in the elderly population. This condition affects patients' quality of life and leads to a significant economic burden of over 89 billion USD annually. Knee and hip joint replacements are the most important contributors to these costs.

Knee OA emerges as the most prevalent subtype of OA in the Netherlands. It often leads to TKA when conservative treatment fails. Substantial progress has been made in prosthetic design, techniques, and materials since the introduction of the first TKA procedures in the late 1960s. An opportunity for further refinement has been sought in integrating computer technology. CAS arose as a possible solution to improve alignment and outcomes after TKA, potentially reducing knee OA's economic- and health burdens.

CAS for TKA includes CAS navigation, PSI, and robotic devices. Using infrared cameras and trackers, CAS navigation provides real-time visual guidance during TKA surgeries. PSI involves preoperative planning based on magnetic resonance imaging (MRI) or computed tomography (CT) scans and the intraoperative use of three-dimensional (3D)-printed moulds to guide bone cuts. Robotic surgery consists of several subtypes and represents the third type of CAS.

This thesis aimed to enhance the knowledge to empower clinical decision-making in computer-based TKA planning, focusing on PSI. PSI is still used in many clinical practices not only for primary TKA but also in revision cases, posttraumatic knees, and in specific instances like abnormal anatomy. It also forms the foundation of the newer robotic systems and future CAS systems. It is, therefore, of utmost importance that the planning of previous CAS systems like PSI is well understood to understand newer technologies.

Alignment of the prosthesis has been recognised as a crucial factor for implant survival. **Chapter 2** identified differences between weight- and non-weight-bearing measurements of the mechanical leg axis (MLA), highlighting the importance of considering these differences in surgical planning. The analysis of PSI planning in **Chapter 3** revealed excellent agreement in implant sizes between repeated plans by the same surgeon and between different surgeons. **Chapter 4** showed that validating and approving PSI plans by the surgeon matched the sizes of intraoperatively used implants better than the default plans provided by the manufacturer. These findings demonstrate that PSI can improve the predictability of implant sizes, potentially simplifying surgery planning and reducing in-hospital implant stock. **Chapter 5** showed consistent outcomes at 5-year follow-up of patients who underwent TKA with PSI compared to one-year post-surgery results. However, the long-term follow-up results of PSI remain to be published.

During this thesis's timespan, we learned that planning in TKA is a fast-evolving field where developments occur faster than ever. In **Chapter 6,** the preliminary planning experiences with a new weight-bearing X-ray-based PSI for TKA were evaluated, which could replace more expensive and time-consuming MRI- or CT-based PSI. Lastly, **Chapter 7** offered a comprehensive overview of the three CAS modalities, namely 1) CAS navigation, 2) PSI, and 3) robotics. It also described different subtypes within each modality and their method of use.

The rapid progression in CAS technologies presents a challenge: it becomes difficult to assess and compare long-term results due to new technologies continually being implemented into clinical practice before long-term follow-up results of previous CAS systems are available. Specific CAS systems, such as the X-ray-based PSI from **Chapter 6,** failed to achieve widespread usage as the manufacturer shifted the company focus to other technologies. Nonetheless, long-term evaluations are necessary to fully comprehend surgical innovations' impact and better understand the potential of newer CAS systems.

Next to innovations in CAS systems, the approach of knee OA and TKA changed with new alignment strategies and differentiation between knee phenotypes. The optimal alignment goals for each phenotype still need to be determined. Also, the long-term effects of these new approaches on surgical outcomes and whether they would benefit from being applied in older or newer CAS systems remain areas of investigation.

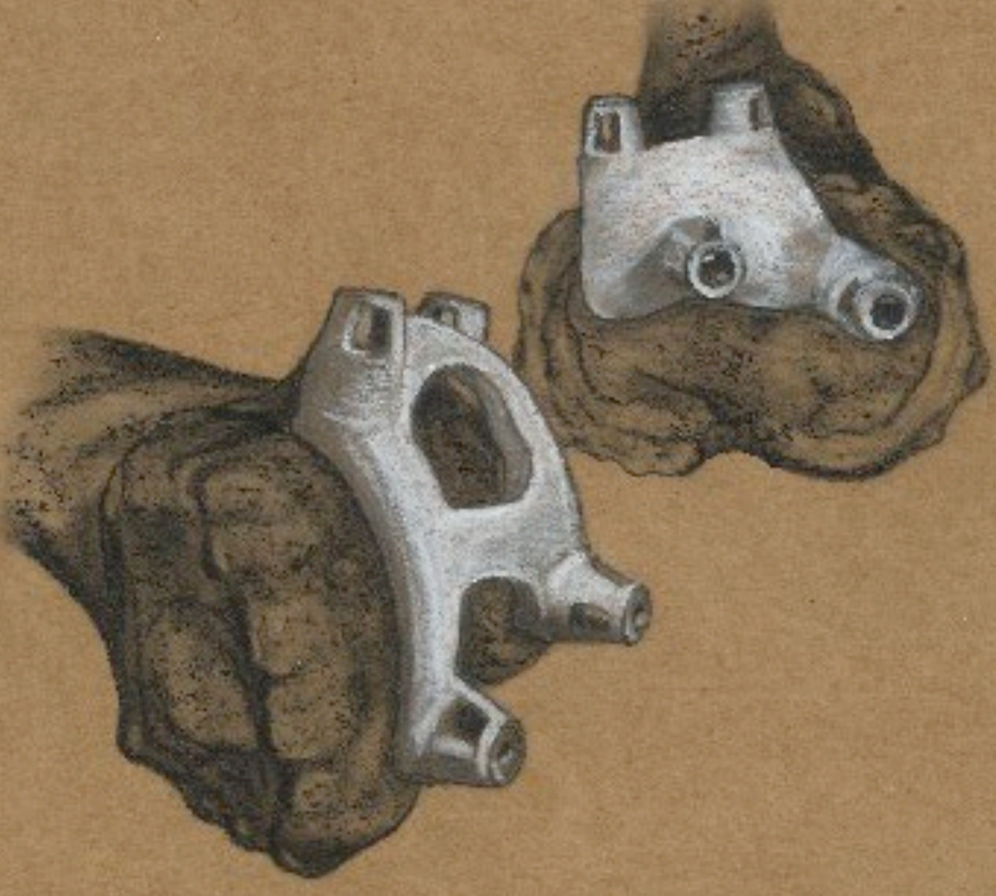
Most current research focuses on comparing the performance of CAS systems with conventional instrumentation or other CAS systems. Defining the goals in TKA and what role CAS can play in achieving them is essential. The potential of CAS to collect and save extensive pre- and intraoperative data, coupled with AI, could help formulate goals and patient subgroup identification in the future. CAS might be more beneficial for specific patient groups, and understanding these particular cases is crucial for its implementation to enhance outcomes and potentially its cost-effectiveness.

The findings of this thesis are particularly interesting for orthopaedic surgeons, healthcare policymakers, and patients with knee OA. Sharing of these findings is essential for the practical application of CAS.

Medical professionals can gain insights into planning in PSI and the differences between CAS systems. They can stay updated through medical journals and conferences where these subjects are presented. Improved surgical methods could reduce long-term healthcare costs, which is compelling for policymakers. Policymakers should understand the potential cost savings and benefits to the healthcare system. Patients would benefit from advancements that could lead to more prolonged knee implant survival and better clinical outcomes after TKA. Patients can learn about these advancements through healthcare providers, offering them a better understanding of how these technological advancements might impact their treatment options and outcomes.

Johann Wolfgang von Goethe's poem 'The Sorcerer's Apprentice' (German: 'Der Zauberlehrling', 1797) could be seen as a cautioning parallel. It was popularised in the 1940 Disney film 'Fantasia', with Mickey Mouse as the apprentice. The sorcerer's apprentice, left with chores, enchants a broom to fetch water - but doesn’t say how much water and doesn't know how to make the broom stop. Trying to stop the broom, the apprentice splits it in two with an axe, but each piece becomes a new broom that continues fetching water until the entire room becomes to flood. When all seems lost, the old sorcerer returns and breaks the spell. The poem concludes with the old sorcerer's statement that only a master should invoke powerful spirits. This story illustrates the potential consequences of misaligning human objectives with the capabilities of autonomous machines.

In conclusion, while the full realisation of AI and robotics in TKA surgery may still be in the future, this thesis provides research to empower clinical decision-making in computer-based TKA planning, focusing on PSI. Until today, patient dissatisfaction after TKA occurs in 15% to 30% of patients despite advancements in CAS for TKA. Knowledge of previous CAS technologies and defining clear goals is crucial to understanding future CAS innovations and their optimal application. Goethe's tale reminds us that in our eagerness to automate processes, we must recognise the need to consider the preconditions before automation. Progress should be seen as a process. Understanding the use of CAS and sharing knowledge is essential to ensure they benefit everyone involved: surgeons, policymakers, and, last but not least, patients.



# 10

## Summary

## Samenvatting

## Résumé

## SUMMARY

Osteoarthritis (OA) of the knee joint is a common degenerative disease, affecting more than 365 million individuals worldwide. It is the most prevalent subtype of OA in the Netherlands. In treating end-stage knee OA, the knee joint can be replaced with an artificial joint, known as total knee arthroplasty (TKA).
Over the last decades, computer technology has been developed for surgical planning to improve the accuracy and precision of component alignment, also called computer-assisted surgery (CAS). CAS for TKA can be classified into three types: CAS navigation, patient-specific instrumentation (PSI), and robotic devices.

CAS navigation uses computer technology to provide real-time visual guidance during TKA surgeries. It assists surgeons in aligning the knee implant by utilising infrared cameras and special trackers to capture and track the knee anatomy to construct a virtual 3D model of the knee on a monitor.
In PSI, the surgeon creates a preoperative plan based on MRI or CT images of the patient. From this 3D plan, moulds are manufactured that can be used intraoperatively to decide where to make the bone cuts. This determines the alignment of the knee prosthesis to be placed.
Lastly, robot-assisted surgery is the third type of CAS in orthopaedic surgery, with several types existing.

Planning in TKA is a fast-evolving field where developments occur more swiftly than ever. In this thesis, several aspects of TKA planning, especially by PSI, were evaluated.
This thesis was divided into three sections.
**Part I** investigated the differences between weight-bearing and non-weight-bearing leg alignment. **Part II** focused on the planning aspect of PSI for TKA and presented mid-term follow-up of patients operated with PSI. **Part III** presented the preliminary experiences of a novel method for preoperative planning in PSI. Furthermore, it gave an overview of computer-based planning modalities for TKA.

### Part I - Weight-bearing and non-weight-bearing leg alignment

The mechanical leg axis (MLA) is the line that runs from the centre of the hip joint to the centre of the knee and to the centre of the ankle joint. This axis is essential since the MLA is

recognised as a crucial determinant that influences the longevity of the total knee prosthesis.

MLA measurements can be conducted on weight-bearing full-length radiographs (FLR) of the complete leg or non-weight-bearing imaging modalities like MRI or CT. In CAS navigation and PSI, measurements and planning are based on non-weight-bearing images. **Chapter 2** aimed to evaluate if there is a difference in MLA between weight-bearing FLR and non-weight-bearing measurement modalities (CAS navigation and MRI-based PSI). It revealed a mean difference of up to 2.5 degrees in within-person MLA measurements when comparing weight-bearing FLR to non-weight-bearing measurement modalities (imageless CAS navigation or MRI-based PSI). This has implications for preoperative planning, performing TKA, and clinical follow-up after TKA surgery using weight-bearing and non-weight-bearing techniques.

### Part II - Planning in Patient-Specific Instrumentation

PSI in TKA uses individually designed disposable guides to determine intraoperative bone cuts. The manufacturer provides the surgeon with a digital proposed default plan, which the surgeon can modify before the moulds are produced. In **Chapter 3,** four orthopaedic surgeons revised and approved 40 preoperative default plans three times. The intra- and interobserver reliability among preoperative planning by the surgeons was assessed. The study revealed that planning of TKA using PSI by different surgeons resulted in an excellent agreement for implant sizes between surgeons and repeated planning by the same surgeon. Besides implant size, intra- and interobserver reliability demonstrated good to excellent agreement for 7 out of 12 remaining settings and 6 out of 12 parameters, respectively.

After modification of the proposed PSI plan, the surgeon approves the plan, and the information within the software system is sent to the manufacturer to construct the mould for intraoperative use. If the surgeon does not modify and approve the plan, the default plan is used for the construction of the mould. **Chapter 4** investigated the impact of approval of the preoperative PSI planning for TKA on the frequency and reason for intraoperative changes of the planned implant size. The validated and approved plans matched the sizes of intraoperatively used implants better than the default plans. This chapter concluded that the default planning provided by the technician must always be validated and approved by the operating surgeon.

**Chapter 5** presented the 5-year follow-up results of the first 200 TKAs performed with PSI, emphasising implant survival rate, (serious) adverse events, and patient-reported outcome measures (PROMs). Over five years, (partial) revision surgery was required in four patients (2%). PROMs were consistent at five-year follow-up of TKAs using PSI. After five years, all median outcome scores for PROMs improved significantly from the preoperative values ($p \leq 0.05$). The median outcome scores were not significantly different between the 1- and 5-year follow-up moments, except for a significant decrease in EQ-VAS ($p \leq 0.05$) between these two follow-up moments.

**Part III - Innovations in digital pre- and intraoperative planning modalities for TKA**
New technological developments occur constantly in the current fast-paced and research-driven medical environment. In the field of TKA, new innovations in digital pre- and intraoperative planning methods are developing faster than ever. Multiple CAS options have become available in recent years.

**Chapter 6** introduced the X-ray-based PSI (X-PSI™), a new method for preoperative planning of PSI-based TKA. This novel planning method constructs 3D models of the knees using X-rays. Alignment is, therefore, assessed under weight-bearing conditions. This chapter presented the preliminary experiences comparing preoperative planning of TKA with X-PSI™ to MRI-based planning for PSI. The planned implant size was within one size difference between X-PSI™ and MRI-based planning of the same patient in 95% of cases for femoral implant size and 90% of the cases for tibial implant size. Furthermore, femoral resection levels were comparable between both imaging modalities, whereas more variation was seen between planned tibial resection levels.

With all available computer-based pre- and intraoperative planning modalities for TKA, physicians are posed with the challenge of which type to implement into their daily practice. **Chapter 7** offered a comprehensive overview of historical and currently employed digital pre- and intraoperative planning modalities for TKA. It aimed to describe key elements of three CAS modalities, namely 1) CAS navigation, 2) PSI, and 3) Robotics. It also described different subtypes within each modality and their method of use.

# SAMENVATTING

Artrose van het kniegewricht is een wijdverspreide aandoening die wereldwijd meer dan 365 miljoen mensen raakt. Deze vorm van artrose is de meest voorkomende in Nederland. In het laatste stadium van de aandoening kan deze behandeld worden met een totale knieprothese (TKP), waarbij het beschadigde kniegewricht wordt vervangen door een kunstgewricht.
In de loop der jaren is de computertechnologie geavanceerder geworden en wordt deze toegepast bij operaties, beter bekend als Computer-Assisted Surgery (CAS). Binnen de orthopedie wordt computertechnologie onder andere toegepast om de precisie van de plaatsing van de protheseonderdelen te verfijnen. CAS voor TKP bestaat uit drie hoofdtypen: CAS-navigatie, patiëntspecifieke instrumentatie (PSI) en robot-geassisteerde chirurgie.

CAS-navigatie maakt gebruik van geavanceerde computertechnologie om chirurgen in realtime te begeleiden bij de plaatsing van de TKP. Dit gebeurt met behulp van infraroodcamera's en speciale sensoren die een 3D-beeld van de knie op een monitor weergeven. PSI hanteert een preoperatief plan gebaseerd op MRI- of CT-beelden van de patiënt, waaruit mallen worden gemaakt die tijdens de operatie helpen bij het bepalen van de juiste locatie voor de zaagvlakken. Robot-geassisteerde chirurgie is de derde ontwikkeling binnen CAS, waarbij diverse robotsystemen beschikbaar zijn om de chirurg te ondersteunen.

In deze scriptie worden verschillende aspecten van de planning van TKP's onder de loep genomen, waarbij in het bijzonder aandacht wordt besteed aan PSI. De inhoud is opgedeeld in drie delen. **Deel I** onderzocht de verschillen tussen belaste en onbelaste beenuitlijning. **Deel II** richtte zich op het planningsproces van PSI en presenteerde de middellange resultaten van patiënten geopereerd met PSI. **Deel III** introduceert een nieuwe methode voor preoperatieve planning in PSI. Bovendien gaf het een overzicht van verschillende CAS-methoden voor TKP.

### Deel I - Belaste en onbelaste beenuitlijning

De mechanische beenas (mechanical leg axis, MLA) is een lijn van het midden van het heupgewricht naar het midden van de knie en het midden van het enkelgewricht. Deze as is cruciaal omdat de MLA erkend wordt als factor die de levensduur van de TKP beïnvloedt.

MLA-metingen kunnen worden uitgevoerd op belaste röntgenfoto's van het gehele been, bekend als full-length radiographs (FLR), of met onbelaste beeldvorming zoals MRI of CT. Bij CAS-navigatie en PSI zijn metingen en planning gebaseerd op onbelaste beelden. **Hoofdstuk 2** evalueerde verschillen in MLA tussen belaste FLR en onbelaste beeldvorming (CAS-navigatie en MRI-gebaseerde PSI). Er werd een gemiddeld verschil van maximaal 2,5 graden gevonden tussen belaste FLR en onbelaste technieken wanneer beide metingen bij dezelfde patiënt uitgevoerd werden. Dit verschil is relevant voor de preoperatieve planning, de plaatsing van een TKP, en de klinische opvolging na de operatie en het gebruik van zowel belaste als onbelaste technieken op deze momenten.

### Deel II - Planning in Patiëntspecifieke Instrumentatie

PSI voor TKP gebruikt op maat gemaakte malletjes om de zaagvlakken tijdens de operatie te bepalen. De fabrikant levert een voorgesteld digitaal plan dat door de chirurg aangepast kan worden voor de productie van de mallen. Uit **Hoofdstuk 3** bleek dat vier orthopedische chirurgen 40 preoperatieve standaardplannen consistent wijzigden en goedkeurden. De maten van de knieprotheses toonden een uitstekende overeenstemming zowel tussen de chirurgen, alsook bij herhaalde planning door dezelfde chirurg. Een goede tot uitstekende overeenstemming werd verder gezien voor 7 van de 12 parameters als binnen één chirurg vergeleken werd, en voor 6 van de 12 parameters als de vergelijking werd gemaakt tussen de verschillende chirurgen.

Na aanpassing en goedkeuring van het PSI-plan door de chirurg, wordt de informatie naar de fabrikant gestuurd om de mal te maken die intra-operatief gebruikt zal gaan worden. Als de chirurg het plan niet wijzigt en goedkeurt, wordt het voorgestelde plan van de fabrikant gebruikt voor de vervaardiging van de mallen. In **Hoofdstuk 4** werd onderzocht wat de verschillen waren tussen de door de fabrikant voorgestelde plannen en de gewijzigde plannen door de chirurg, ten opzichte van de gebruikte implantaten tijdens de operatie. Dit onderzoek toonde aan dat de gevalideerde en goedgekeurde plannen beter overeenkwamen met de uiteindelijk gebruikte implantaatgroottes dan de standaardplannen. Dit hoofdstuk concludeerde derhalve dat de standaardplanning die door de fabrikant wordt geleverd, altijd moet worden gevalideerd en goedgekeurd door de opererende chirurg.

**Hoofdstuk 5** presenteerde de resultaten van een 5-jaar follow-up van de eerste 200 met PSI uitgevoerde TKP's, waarbij de focus lag op implantaatoverleving, complicaties en patiënt-gerapporteerde uitkomstmaten (in de vorm van Patient Reported Outcome Measures (PROMs)). Na vijf jaar was bij 2% van de patiënten (gedeeltelijke) revisiechirurgie uitgevoerd. Na 5 jaar, waren alle mediane PROMs significant verbetert ten opzichte van de preoperatieve waarden ($p \leq 0.05$). De mediane uitkomsten waren niet significant verschillend tussen de 1- en 5-jaars follow-up momenten, met uitzondering van een significante afname van de EQ-VAS ($p \leq 0.05$).

## Deel III - Innovaties in digitale pre- en intra-operatieve planningsmodaliteiten voor TKP

In het snel evoluerende veld van de medische technologie, vinden voortdurend nieuwe technologische ontwikkelingen plaats. Ook op het gebied van TKP, ontwikkelen nieuwe innovaties in digitale pre- en intra-operatieve planningsmethoden zich sneller dan ooit. De afgelopen jaren zijn diverse CAS-opties beschikbaar gekomen.

**Hoofdstuk 6** introduceerde X-PSI™, een nieuwe methode voor preoperatieve PSI-planning. Deze methode maakt op basis van röntgenfoto's 3D-modellen van de knieën, waardoor uitlijning in belaste toestand plaats kan vinden. In dit hoofdstuk werden de eerste ervaringen met de preoperatieve planning middels X-PSI vergeleken met planning op MRI-gebaseerde PSI. De geplande implantaatgrootte lag binnen maximaal één maatverschil in 95% van de gevallen van het femur en in 90% van de gevallen van de tibia. Verder werd gevonden dat de femorale resectieniveaus bij beiden planningstechnieken vergelijkbaar waren, terwijl er meer variatie werd gezien tussen de geplande tibiale resectieniveaus.

Met alle beschikbare computer-gebaseerde pre- en intra-operatieve planningsmodaliteiten voor TKP worden artsen geconfronteerd met de uitdaging welk type ze in hun dagelijkse praktijk moeten implementeren. **Hoofdstuk 7** bood een uitgebreid overzicht van historische en huidige digitale pre- en intra-operatieve planningsmodaliteiten voor TKP. Het doel was om de belangrijkste elementen van drie CAS-modaliteiten te beschrijven, namelijk 1) CAS-navigatie, 2) PSI, en 3) Robotica. Het beschreef ook verschillende subtypen binnen elke modaliteit en hun gebruiksmethode.

## RÉSUMÉ

L'arthrose de l'articulation du genou est une maladie dégénérative courante, touchant plus de 365 millions de personnes dans le monde. C'est le sous-type d'arthrose le plus répandu aux Pays-Bas. Dans le traitement de l'arthrose du genou en phase terminale, l'articulation peut être remplacée par une prothèse artificielle, connue sous le nom d'arthroplastie totale du genou (ATG).

Au cours des dernières décennies, la technologie informatique a été développée pour la planification chirurgicale afin d'améliorer la précision et l'exactitude de l'alignement des composants, également appelée Chirurgie Assistée par Ordinateur (Computer-Assisted Surgery (CAS)). Le CAS pour ATG peut être classé en trois types: navigation CAS, instrumentation spécifique au patient (Patient Specific Instrumentation (PSI)), et dispositifs robotiques.

La navigation CAS utilise la technologie informatique pour fournir une orientation visuelle en temps réel pendant les chirurgies ATG. Elle aide les chirurgiens à aligner l'implant du genou en utilisant des caméras infrarouges et des traceurs spéciaux pour capturer et suivre l'anatomie du genou afin de construire un modèle 3D virtuel du genou sur un moniteur. Dans le PSI, le chirurgien crée un plan préopératoire basé sur des images IRM ou CT du patient. À partir de ce plan 3D, des moules sont fabriqués qui peuvent être utilisés intraopératoirement pour décider où effectuer les coupes osseuses. Cela détermine l'alignement de la prothèse du genou à placer.

Enfin, la chirurgie assistée par robot est le troisième type de CAS en chirurgie orthopédique, avec plusieurs types existants.

La planification dans ATG est un domaine en rapide évolution où les développements se produisent plus rapidement que jamais. Dans cette thèse, plusieurs aspects de la planification ATG, en particulier par PSI, ont été évalués. Cette thèse a été divisée en trois sections. **La partie I** a étudié les différences entre l'alignement des jambes en charge et non en charge. **La partie II** s'est concentrée sur l'aspect de la planification du PSI pour ATG et a présenté le suivi à moyen terme des patients opérés avec PSI. **La partie III** a présenté les expériences préliminaires d'une nouvelle méthode de planification préopératoire en PSI. De plus, elle a donné un aperçu des modalités de planification informatisées pour ATG.

### *PARTIE 1 - Alignement des jambes en charge et non en charge*

L'axe mécanique des jambes (MLA) est la ligne qui va du centre de l'articulation de la hanche, au centre du genou et au centre de l'articulation de la cheville. Cet axe est important car le MLA est reconnu comme un déterminant crucial qui influence la longévité de la prothèse totale du genou.

Les mesures MLA peuvent être effectuées sur des radiographies de pleine longueur en charge (FLR) de la jambe complète, ou des modalités d'imagerie non en charge comme l'IRM ou le CT. Dans la navigation CAS et le PSI, les mesures et la planification sont basées sur des images non en charge. **Chapitre 2** visait à évaluer s'il existe une différence dans le MLA entre les FLR en charge et les modalités de mesure non en charge (navigation CAS sans image et PSI basé sur l'IRM). Il a révélé une différence moyenne allant jusqu'à 2,5 degrés dans les mesures MLA intra-individuelles en comparant les FLR en charge aux modalités de mesure non en charge (navigation CAS sans image ou PSI basé sur l'IRM). Cela a des implications pour la planification préopératoire, la réalisation de l'ATG et le suivi clinique après la chirurgie ATG en utilisant des techniques en charge et non en charge.

### *PARTIE 2 - Planification dans l'Instrumentation Spécifique au Patient*

Le PSI dans ATG utilise des guides jetables conçus individuellement pour déterminer les coupes osseuses intraopératoires. Le fabricant fournit au chirurgien un plan numérique proposé par défaut, qui peut être modifié par le chirurgien avant la production des moules. Dans **le Chapitre 3,** quatre chirurgiens orthopédiques ont modifié et approuvé 40 plans préopératoires par défaut trois fois. La fiabilité intra- et inter-observateurs parmi la planification préopératoire par les chirurgiens a été évaluée. L'étude a révélé que la planification de l'ATG utilisant PSI par différents chirurgiens a abouti à un excellent accord pour les tailles d'implant entre les chirurgiens ainsi que dans la planification répétée par le même chirurgien. Outre la taille de l'implant, la fiabilité intra- et interobservateur a montré un bon à excellent accord pour 7 des 12 paramètres restants et 6 sur 12 respectivement.

Après modification du plan PSI proposé, le chirurgien approuve le plan et les informations dans le système logiciel sont envoyées au fabricant pour construire le moule pour une utilisation intraopératoire. Si le chirurgien ne modifie pas et n'approuve pas le plan, le plan par défaut est utilisé pour la construction du moule. **Chapitre 4** a étudié l'impact de l'approbation de la planification préopératoire PSI pour ATG sur la fréquence et la raison des changements intraopératoires de la taille de l'implant prévu. Les plans validés et approuvés correspondaient mieux aux tailles des implants utilisés en intraopératoire que les plans par défaut. Ce chapitre a conclu que la planification par défaut fournie par le technicien doit toujours être validée et approuvée par le chirurgien opérant.

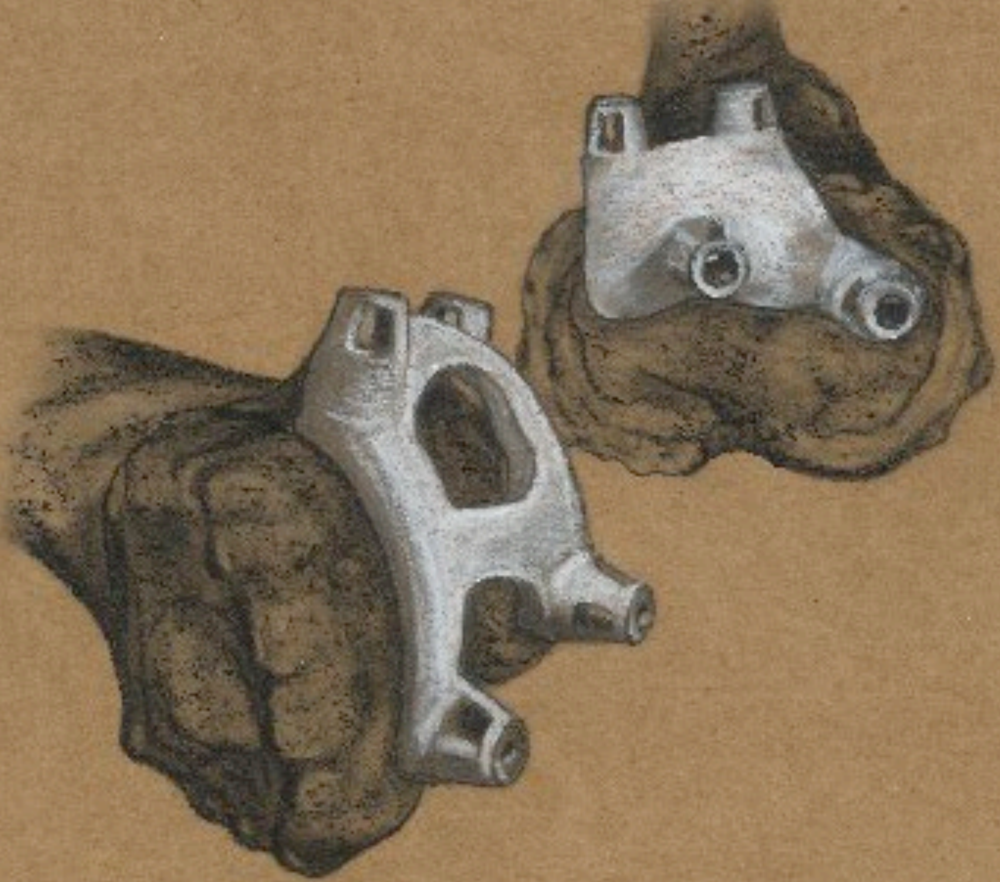
**Chapitre 5** a présenté les résultats du suivi à 5 ans des 200 premières ATG réalisées avec PSI, en mettant l'accent sur le taux de survie de l'implant, les événements (graves) indésirables et les mesures de résultats rapportées par les patients (PROMs). Après cinq ans, une (partielle) chirurgie de révision a été nécessaire chez quatre patients (2%). Les PROMs étaient constants lors du suivi à cinq ans des ATG utilisant PSI. Après 5 ans, tous les scores médians des résultats pour les PROMs se sont améliorés de manière significative par rapport aux valeurs préopératoires ($p \leq 0{,}05$). Les scores médians des résultats n'étaient pas significativement différents entre les moments de suivi à 1 et 5 ans, à l'exception d'une diminution significative de l'EQ-VAS ($p \leq 0{,}05$) entre ces deux moments de suivi.

### *PARTIE 3 - Innovations dans les modalités de planification pré- et intraopératoires numériques pour ATG*

Dans l'environnement médical actuel rapide et axé sur la recherche, de nouveaux développements technologiques se produisent constamment. Dans le domaine de la ATG, de nouvelles innovations dans les méthodes de planification pré- et intraopératoires numériques se développent plus rapidement que jamais. Plusieurs options de CAS sont devenues disponibles ces dernières années.

**Chapitre 6** a introduit le PSI basé sur les rayons X (X-PSI™), une nouvelle méthode pour la planification préopératoire de l'ATG basée sur le PSI. Cette nouvelle méthode de planification construit des modèles 3D des genoux à l'aide de rayons X. L'alignement est donc évalué dans des conditions de charge. Ce chapitre a présenté les expériences préliminaires de comparaison de la planification préopératoire de l'ATG avec X-PSI™ à celle basée sur l'IRM pour le PSI. La taille d'implant prévue était dans une différence de taille maximale de 95 % des cas pour la taille de l'implant fémoral et de 90 % des cas pour la taille de l'implant tibial. De plus, les niveaux de résection fémorale étaient plus comparables entre les deux modalités d'imagerie, alors qu'une plus grande variation était observée entre les niveaux de résection tibiale planifiés.

Avec toutes les modalités de planification pré- et intra-opératoire basées sur l'ordinateur disponibles pour l'ATG, les médecins sont confrontés au défi de choisir le type à intégrer dans leur pratique quotidienne. **Chapitre 7** a offert un aperçu complet des modalités de planification digitale pré- et intra-opératoire historiques et actuellement utilisées pour l'ATG. Il visait à décrire les éléments clés de trois modalités de CAS, à savoir 1) la navigation CAS, 2) le PSI, et 3) la Robotique. Il a également décrit les différents sous-types au sein de chaque modalité et leur méthode d'utilisation.



# Appendices

Abbreviations
Publications
Dankwoord
Curriculum vitae

# ABBREVIATIONS

| | |
|---|---|
| 2D | Two-dimensional |
| 3D | Three-dimensional |
| Acrobot® | Active constraint robot |
| aHKA | Arithmetic hip-knee-ankle angle |
| AI | Artificial intelligence |
| AP | Anteroposterior |
| AR | Augmented reality |
| ASA | American Society of Anesthesiologists |
| BMI | Body mass index |
| BRIGIT™ | Bone Resection Instrument Guidance by Intelligent Telemanipulator |
| CAS | Computer-assisted surgery |
| CASPAR® | Computer-Assisted Surgical Planning And Robotics |
| CPAK | Coronal plane alignment of the knee |
| CT | Computed tomography |
| DALYs | Disability Adjusted Life Years |
| e.g. | exempli gratia (for example) |
| EMBASE | Excerpta Medica Database |
| EMEA | Europe, the Middle East, and Africa |
| EQ-5D | European Quality of Life 5 Dimensions Score |
| EQ-5D-3L | European Quality of Life 5 Dimensions 3 Level Version |
| EQ-VAS | European Quality of Life Visual Analog Scale |
| FA | Functional alignment |
| FLR | Full-length radiographs |
| HKA | Hip-knee-ankle angle |
| ICC | Intraclass correlation coefficients |
| ID | Identity document |
| IQR | Interquartile range |
| ISCAS | International Society for Computer Aided Surgery |
| JLO | Joint line obliquity |
| KA | Kinematic alignment |
| LAT | Lateral |
| MA | Mechanical alignment |
| MedLine | Medical Literature Analysis and Retrieval System Online |

| | |
|---|---|
| METC | Medical Ethics Committee |
| MLA | Mechanical leg axis |
| MRI | Magnetic resonance imaging |
| n | number |
| n.s. | not significant |
| NA | Not applicable |
| OA | Osteoarthritis |
| OKS | Oxford Knee Score |
| OR | Operation room |
| p | p-value |
| PRISMA-P | Preferred Reporting Items for Systematic Review and Meta-analysis Protocols |
| PROMs | Patient-reported outcome measures |
| PROSPERO | International Prospective Register of Systematic Reviews |
| PSI | Patient-specific instrumentation |
| rKA | Restricted kinematic alignment |
| ROSA® | Robotic Surgical Assistant |
| RP | Rapid prototyping |
| SD | Standard deviation |
| sHKA | Stressed hip-knee-ankle angle |
| SID | Source to image distance |
| SPECT | Single-photon emission computed tomography |
| SPSS | Statistical Package for the Social Sciences |
| TiAb | Titles and abstracts |
| TKA | Total knee arthroplasty |
| UKA | Unicompartmental knee arthroplasty |
| US | United States |
| USA | United States of America |
| VAS | Pain Visual Analogue Score |
| VRAS | VELYS™ Robotic Assisted Solution |
| vs | versus |
| WOMAC | Western Ontario and McMaster Universities Osteoarthritis Index |
| X-PSI | X-ray-based patient-specific instrumentation |

## PUBLICATIONS

**Schoenmakers DAL**, Feczko PZ, Boonen B, Schotanus MGM, Kort NP, Emans PJ. Measurement of lower limb alignment: there are within-person differences between weight-bearing and non-weight-bearing measurement modalities. Knee Surg Sports Traumatol Arthrosc, 2017, 25(11), 3569-3575.

Schotanus M, **Schoenmakers DAL**, Sollie R, Kort NP. Patient-specific instruments for total knee arthroplasty can accurately predict the component size as used peroperative. Knee Surg Sports Traumatol, 2017, 25(12), 3844-3848.

Van der Stok J, Hartholt KA, **Schoenmakers DAL**, Arts JJC. The available evidence on demineralised bone matrix in trauma and orthopaedic surgery – A systematic review. Bone Joint Res, 2017, 6(7), 423–432.

**Schoenmakers DAL**, Schotanus MGM, Boonen B, Kort NP. Consistency in patient-reported outcome measures after total knee arthroplasty using patient-specific instrumentation: a 5-year follow- up of 200 consecutive cases**.** Knee Surg Sports Traumatol Arthrosc, 2018, 26(6), 1800-1804.

**Schoenmakers DAL**, Theeuwen DMJ, Schotanus MGM, Jansen EJP, Haaren van EH, Hendrickx RPM, Kort NP. High intra- and interobserver reliability of planning implant size in MRI-based patient-specific instrumentation for total knee arthroplasty. Knee Surg Sports Traumatol Arthrosc, 2021, 29(2), 573-578.

**Schoenmakers DAL**, Schotanus MGM, Kort NP. Preoperative planning with X-PSI™ compared to MRI-based patient-specific instrumentation in total knee arthroplasty.
In review at J Clin Orthop Trauma, submitted August 2022.

**Schoenmakers DAL**, Dorling IM, Heymans MJFL, Kort NP, Boonen B, Rhijn van LW, Schotanus MGM. Computer-based pre- and intraoperative planning modalities for Total Knee Arthroplasty: A comprehensive review
J Orthop Exp Innov, 2024, https://doi.org/10.60118/001c.89963.

Theeuwen DMJ, **Schoenmakers DAL**, Scholtes MTM, Kalaai, S, Schotanus MGM, Boonen B. First long-term analysis of survival and clinical outcome in patient-specific instrumentation for total knee arthroplasty: follow-up of a prospective cohort study.
Acta Orthop Belg, 2024, 90, 51-56.

# DANKWOORD

Zoals zo velen vóór mij al hebben geschreven: een proefschrift schrijven doe je niet alleen. Ik kan dat alleen maar beamen, en dit proefschrift was nooit tot stand gekomen zonder de hulp en steun van de mensen om mij heen. Ik wil dan ook iedereen die heeft bijgedragen aan dit boekje, direct of indirect, hartelijk bedanken. Een aantal mensen wil ik in het bijzonder bedanken.

Te beginnen bij mijn promotieteam. Stuk voor stuk een aanvulling op elkaar. Ik wil beginnen met het bedanken van mijn promotor, **prof. dr. L.W. van Rhijn**. Beste **Lodewijk**, hartelijk dank voor je ideeën over de inhoud van dit proefschrift en de tijd die je hebt om genomen om mijn stukken kritisch door te lezen. Door jouw 'helikopter-view' zorgde je ervoor dat de rode draad duidelijk werd en bleef. Ik vind het knap hoe je altijd de juiste prikkelende vragen wist te stellen om mij aan het denken te zetten. Ondanks je drukke agenda wist je steeds weer tijd vrij te maken. Hartelijk dank!

Copromotoren **dr. M.G.M. Schotanus** en **dr. N.P. Kort**. Jullie hebben mij als ANIOS gevraagd of ik met jullie een promotietraject wilde starten. Dank voor deze kans en het vertrouwen. Zonder jullie was dit proefschrift er niet geweest.
Beste **Martijn**, beste Tinus, ik kon altijd bij je terecht met vragen en je was altijd bereid om mee te denken onder het genot van je 'standaard' sterke zwart uit de koffieautomaat. De verzameling mapjes met onderzoeken op je laptop is indrukwekkend. Ik ben dankbaar dat ik zoveel van je heb mogen leren.
Beste **Nanne**, enorm bedankt voor al de moeite en tijd die je in het lezen van de stukken hebt gestoken. Je kritische (klinische) blik en aanvullingen hebben de artikelen absoluut naar een hoger niveau gebracht. Ik ben dankbaar dat je deel uitmaakte van het team.

Leden van de beoordelingscommissie: hartelijk dank dat u bereid was om dit proefschrift te beoordelen.

Bijzondere dank aan de co-auteurs voor alle onmisbare hulp tijdens het schrijven van de verschillende artikelen voor dit proefschrift. **Dr. P.Z. Feczko** en **dr. P.J. Emans**, beste **Peter**, beste **Pieter**, mijn WESP begon bij jullie, waarbij ook data vanuit het Zuyderland gebruikt werd. Dank voor de begeleiding en het kritisch lezen van wat uiteindelijk mijn eerste wetenschappelijke publicatie werd! Hetzelfde geldt voor **dr. B. Boonen**, beste **Bert**, niet alleen bij dit eerste artikel was jij betrokken, maar bij een groot deel van dit proefschrift. Altijd had je wel aanvullingen of vragen waardoor het niveau van de artikelen absoluut verbeterde. Hartelijk dank hiervoor. **Rob** en **Dieuwertje,** bedankt voor de fijne samenwerking. Beste **dr. E.J.P. Jansen**, **dr. E.H. van Haaren** en **dr. R.P.M. Hendrickx**, beste **Edwin**, **Emil** en **Roel**, dank voor het wijzigen van de vele PSI-planningen en jullie hulp met het manuscript. Beste **Marion**, de 'Pubmed-tovenaar', enorm bedankt voor je hulp bij de search van het review en de gezellige meetings. **Isobel**, miss Majesty, het was heerlijk om samen te werken. Dank ook voor de theeleut-momentjes, je bent een topper!

Een apart woord van dank gaat uit naar de patiënten die hebben deelgenomen aan de onderzoeken. Zonder hun bereidwilligheid naar de follow-up momenten te komen en/of de vragenlijsten in te vullen was onderzoek niet mogelijk geweest.

Beste **stafleden orthopedie** en **traumachirurgie** van het **MUMC+**, dank voor alle leerzame momenten de afgelopen jaren. Al in het begin van mijn geneeskundeopleiding kon ik geregeld een dagje meekijken in de kliniek. **Drs. J.P.S. Hermus**, **Joris**, dank voor deze eerste kennismaking met de orthopedie. Vanaf dat moment is mijn enthousiasme voor de orthopedie onophoudelijk gegroeid wat resulteerde in mijn allereerste co-schap dat ik bij jullie doorbracht. Ik heb van jullie allen veel geleerd. **Dr. T.A.E.J. Boymans**, **Tim**, een bijzonder woord van dank voor jou, je fungeerde als een mentor gedurende mijn tijd in het MUMC+. Ik waardeer het enorm dat je zo onderwijs-minded bent. Ik heb veel van je geleerd. Ook alle andere **collega's** van de **gipskamer**, **poli**, **verpleegafdeling**, **operatiekamer** en **SEH** wil ik hartelijk bedanken voor de fijne samenwerking. Ditzelfde geldt voor de dames van het secretariaat orthopedie, met een extra woord van dank voor **Denise** voor het achter de schermen regelen van veel zaken voor dit boekje. Ook dank aan **Liesbeth**, **Margareth** en **Anita**. Fijn dat de deur altijd open stond om even bij te kletsen. **René**, **Chris** en **Liesbeth,** bedankt dat ik mijn eerste wetenschappelijke stappen samen met jullie kon zetten gedurende mijn geneeskundestudie.

Beste (oud) **stafleden orthopedie** en **traumachirurgie** van het **Zuyderland Medisch Centrum**, bij jullie begon ik als ANIOS wat mijn enthousiasme voor de orthopedie nog meer heeft aangesterkt. Wat een enorm fijne groep zijn jullie. Het was een voorrecht om in de afgelopen jaren met jullie te werken. Dank dat jullie allen op jullie eigen manier hebben geïnvesteerd in mijn opleiding. Ook wil ik jullie bedanken voor het begrip en de steun in de tijd dat ik het even extra nodig had. Ik ben door jullie allen enorm gegroeid als mens maar

zeker ook als dokter. Ik kijk uit naar het fellowship sport-orthopedie dat ik in 2024 bij jullie zal volgen. **Dr. E.J.P. Jansen** en **dr. I. Curfs**, **Edwin** en **Inez**, ontzettend bedankt voor het vertrouwen, we maken er een topjaar van!
Ook alle andere **collega's** van de **gipskamer**, **poli**, **secretariaat**, **zorgplanners verpleegafdeling**, **operatiekamer** en **SEH** wil ik uiteraard bedanken voor de fijne samenwerking tot dusver.

Beste **stafleden chirurgie** en **orthopedie** van het **Viecuri Medisch Centrum**, hartelijk dank voor de fantastische vooropleiding die ik bij jullie heb mogen volgen. Jullie prachtige groep en mooie vak hebben me zelfs wel eens (even) op de gedachte gebracht om chirurg te willen worden.

Beste **collega AIOS**, dank voor de geweldige opleidingstijd die we samen hebben gehad. Jullie hebben er zeker aan bijgedragen dat de afgelopen jaren voorbij zijn gevlogen! Natuurlijk ook dank aan alle **ANIOS** en **PA's** voor de fijne samenwerking.

**Sophía,** Fieke, wij kennen elkaar sinds 2009. Wat hebben we in die jaren veel mooie momenten samen meegemaakt! Ook in de minder mooie tijden vonden we veel steun bij elkaar. Ik waardeer onze gesprekken en dat je altijd in bent voor spontane plannen en avontuur. Ik ben dankbaar dat we vriendinnen zijn.

Wat heeft de studenten-klimvereniging MaasSAC me veel gebracht. Prachtige klimtripjes, een fantastisch bestuursjaar, maar bovenal dierbare vriendschappen. Jammer dat het grootste deel van jullie inmiddels uitgevlogen is naar andere hoeken van Nederland en we elkaar veel te weinig zien. **Marleen** en **Joris**, wat vind ik het fijn dat wij bevriend zijn. De bergen overwinnen we.. **Hanneke,** ik denk nog regelmatig terug aan onze prachtige reis in Patagonië. In die tijd had je net **Arne** leren kennen, wat een topstel zijn jullie! **Rutger** en **Meta**, ook jullie zie ik te weinig, maar het is altijd gezellig als we elkaar zien. **Sytze** en **Nienke**, wat waren onze wintersporttripjes toch tof. Fijn dat jullie 'half' nog in Maastricht wonen. **Gusta** en **Jan,** jullie winnen het wedstrijdje ver weg wonen. Jammer dat Nieuw-Zeeland zo enorm ver weg is, maar ik kom graag nog eens op bezoek! En dan alle andere MaasSAC'ers waarmee ik zoveel fijne momenten heb meegemaakt; **Anouk, Irene, Jesse, Maaike, Marijn, Matthijs, Michael, Nadia, Oliver, Pieter, Rianne, Rik, Ruth**, **Sabine, Sjoerd, Yon, Yuliya** en nog velen meer.. Wat een toptijd!
In het bijzonder wil ik **Chris** bedanken voor alle bijzondere en mooie jaren.

**Berry**, ik had nooit verwacht dat mijn leven zo zou veranderen na je uitspraak 'Je moet triathlon eens proberen..'. Maar ik ben je er enorm dankbaar voor! **Eva** en **Berry**, ik ga jullie missen als buren.
En dan, woorden schieten te kort voor de lieve 'Berry's Angels' (**Anke, Anne, Boukje, Elisa, Esther, Jacqueline, Heleen**, **Neiske** en **Nina**). Jullie zijn stuk voor stuk goud waard. Trainen met jullie is een feest, en de (wedstrijd)vakanties en tripjes samen zal ik nooit vergeten. Het was bijzonder om met een deel van jullie de Ironman in Kopenhagen te doen. Ik kijk uit naar meer mooie momenten samen. De triathlonmannen (**Bob, Filippo, Jeroen, Josef, Roel en Tony**) maken de TCM-familie compleet. Wat fijn dat we elkaar hebben leren kennen!
Verder bedankt aan alle andere TCM'ers voor de gezellige trainingsuurtjes (+koffie) in de Geusselt en andere gezellige momenten. **Guido**, dank voor de kletspauzes aan de zwembadrand tijdens de Tricenter-trainingen (sorry Berry..).

Een bijzonder woord van dank aan mijn paranimfen. Ik ben dankbaar dat jullie tijdens de verdediging achter me staan, zoals jullie dat ook de afgelopen jaren hebben gedaan.
**Elisa**, we leerden elkaar kennen op Oost33. Het was een eer je te mogen 'drillen' binnen het zaalwerk. Je bent een fantastische collega en een geweldige dokter; patiënten mogen zich gelukkig prijzen met jou als hun behandelaar. Daarnaast ben je een topvriendin. Ik ben dankbaar voor alle fantastische (sportieve) avonturen die we samen hebben meegemaakt; Hawaii, Cascais, wintersport.. Ik ben erg dankbaar met jou als mijn paranimf, maar zeker ook als vriendin.

**Michael**, we kennen elkaar inmiddels ruim 12 jaar, waarbij een mooie vriendschap is ontstaan. Altijd kon ik rekenen op je goede (levens)raad, zeker ook wat betreft m'n boekje. Daar ben ik je zeer erkentelijk voor. Zoals eerder gezegd ben je als een oudere broer voor me. Je enthousiasme voor wetenschap is inspirerend en aanstekelijk, naast je interesses op zóveel andere gebieden. Het is een eer om je naast me te hebben als paranimf.

**Famille Gautier et compagnie,** nous nous voyons trop rarement, mais c'est toujours un plaisir d'être en France. Je chéris les dîners de Noël qui prennent la moitié de la journée, la convivialité et les parties interminables de belote. Merci pour votre intérêt et votre soutien.
**Maman** et **Charlotte**, merci d'avoir vérifié mon résumé en français.

Lieve **Silvia**, **Thorwald** en **Quinty**, dank jullie wel voor de gezellige tijden en de support.

Lieve **Bart**, mijn kleine broertje, ondanks dat je groter bent dan ik. Ik ben enorm trots op je! Onze band is de afgelopen jaren steeds sterker geworden, dat vind ik erg fijn. Ik ben dankbaar dat ik je zus ben.

Lieve **pap** en **mam**, ik had me geen betere ouders kunnen wensen. Jullie onvoorwaardelijke liefde en steun hebben mij gevormd zoals ik nu ben. **Mam**, je bent de liefste en meest zorgzame persoon die ik ken. Waren er maar meer mensen zoals jij. **Pap**, je discipline en analytische blik zijn een voorbeeld voor me. Bij jou kan ik altijd terecht voor goede raad. Ik ben blij dat jullie genieten van jullie pensioen en prachtige reizen maken. Dank dat jullie er altijd voor ons zijn.

Tot slot, lieve **Jardy**, ondanks dat je alleen het laatste stuk van dit proefschrift hebt meegekregen, steunde je mij hierin zonder te aarzelen. De laatste loodjes zijn het zwaarst, maar je motiveerde en steunde me op de dagen waarin ik tot de late uurtjes nog achter de laptop te vinden was. Daar kan ik je niet genoeg voor bedanken. Fijn dat je zo onvoorwaardelijk achter me staat. Ik kijk uit naar onze volgende avonturen samen.

# CURRICULUM VITAE

Daphne Schoenmakers was born in Eindhoven, the Netherlands on May 9, 1990. In 2008, she graduated from high school (Athenaeum, Van Maerlant Lyceum, Eindhoven). She studied Health Sciences for one year after which she started her medical studies at Maastricht University in the Netherlands. Early in her studies she developed a special interest in the musculoskeletal system and orthopaedic surgery, which resulted in participation in science projects and clinical days at the orthopaedic surgery department in Maastricht University Medical Centre (MUMC+), Maastricht. In the last year of her medical studies, the foundation of this PhD thesis was laid at MUMC+, and the Orbis Medical Centre (currently Zuyderland Medical Centre), Sittard-Geleen, the Netherlands.

In August 2015 she finished her medical studies and started working as an orthopaedic resident (ANIOS) at the Orbis Medical Centre. In 2017 she started her career as an orthopaedic resident in training (AIOS) with 1.5 years of general surgical training at Viecuri Medical Centre, Venlo, the Netherlands. In 2018, she returned to the MUMC+ and Zuyderland Medical Centre, Sittard-Geleen and Heerlen, for her orthopaedic education.
During her residency she continued her research under supervision of prof. dr. Lodewijk W. van Rhijn, dr. Martijn G.M. Schotanus, and dr. Nanne P. Kort.

In October 2023, she completed her residency. In 2024, she is undertaking a fellowship in Sports Orthopaedics at Zuyderland Medical Centre.