Study and analysis of the evolution of knee arthroplasty surgery through its technological innovation

by

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ABSTRACT

Total Knee Arthroplasty (TKA) offers life-changing improvements for many patients; however, a considerable portion of 10-15% continue to experience dissatisfaction after the surgery. Given the rise in the aging population, increased insurance eligibility for TKA in patients with milder symptoms, and growing interest in robotic surgery, it is important to identify technology gaps that can improve overall patient outcomes. This analysis aims to map the network of processes and stakeholders involved in the TKA journey, from pre-operative planning to post-operative rehabilitation. It will examine existing technologies employed across stages of TKA, understanding their functionalities, evaluating their limitations, and assessing their impact on patient outcomes while identifying areas where investment in technology and innovation is most critical.

Through this investigation, the thesis seeks to shed light on the complexities of the TKA ecosystem, pinpointing some of its limitations and opportunities for technological advancement. This work serves as a decision-making guide, potentially empowering innovators to channel their resources toward impactful solutions that elevate both short and long-term patient outcomes following TKA surgery.

Thesis Supervisor: Joan Rubin
Title: Executive Director
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Acknowledgments

It has been an absolute privilege to study and work alongside so many talented individuals at MIT and learn from their expertise and experience. As my journey ends with the fulfillment of my degree, I am filled with a bittersweet mixture of emotions. I owe much acknowledgment to the many people who have supported, guided, and inspired me throughout my time here.

First, I would like to thank my family for their endless support and encouragement throughout these past three years. Niki, Soren, and Maziar, your belief in me and your support through this journey are the reasons that I could make this happen while working full-time. I owe you many weekends and afternoons, and I can't wait to spend more time with you.

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Contents

List of Figures

List of Tables

Abbreviations and Acronyms

TKA	Total Knee Arthroplasty
OA	Osteoarthritis
DVT	Deep vein thrombosis
NSAID	Non-Steroidal Anti-Inflammatory Drug
DSM	Design Structure Matrix or Dependency and Structure Modeling
AAOS	American Academy of Orthopedic Surgeons
AJRR	American Joint Replacement Registry
FOM	Figure of Merit
ROM	Range of Motion
TUG	Timed Up and Go
PROM	Patient-Reported Outcome Measures
KOS	Knee Outcome Survey
OKS	Oxford Knee Score
OKS-APQ	Oxford and Participation Questionnaire
PKIP	Patient Knee Implant Performance
EQ-5D-5L	5-Level EuroQol 5 Dimensions
SF-36	Short Form-36 outcome
SF-12	Short Form-12 outcome
NRS	Numeric Pain Rating Scale

CR	Cruciate retaining
PS	Posterior Stabilized
MB	Mobile Bearing
FB	Fixed Bearing
AM	Additive Manufacturing
Ti- 6Al-4V	Titanium-6Aluminum-4Vanadium
CPTi	Commercially Pure Titanium
Co-Cr-Mo	Cobalt-Chromium-Molybdenum
CPE	Conventional Polyethylene
MAO	Micro-Arc Oxidation
CAS	Computer-Assisted Surgery
ABN	Accelerometer-Based Navigation
MUA	Manipulation Under Anesthesia
RTKA	Robotic Total Knee Arthroplasty
VR	Virtual Reality
MA	Mechanical Alignment
AA	Anatomic Alignment
aMA	Adjusted Mechanical Alignment
KA	Kinematic Alignment
rKA	Restricted Kinematic Alignment
CMS	Medicare and Medicaid Services

NTAP	New Technology Add-on Payments
CT	Computed Tomography
MRI	Magnetic Resonance Imaging
PCL	Posterior cruciate ligament
MIS	Minimally Invasive Surgery
PRO	Patient-Reported Outcome
OR	Operating Room
ASC	Ambulatory Surgical Center

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Chapter 1

Introduction

Total Knee Arthroplasty (TKA), also known as Total Knee Replacement Surgery, is a widely performed surgical procedure that replaces the worn-out surfaces of the knee joint with artificial joint components [1]. TKA has the potential to significantly improve the lives of patients suffering from chronic knee pain and mobility limitations. The prevalence of TKA in the United States has increased dramatically in recent years. In 2017 alone, over 754,000 knee replacement surgeries were performed [1]. Shichman et al. reported that the annual volume of primary TKA in the United States rose from 188,118 in 2000 to 480,958 in 2019 [42]. Their model predicts a 139% increase by 2040 and a 469% increase by 2060 compared to the 2019 volume (Figure 1-1) [42].BCC research predicts that the global market for TKA will grow to $2.16B by 2026 (shown in Figure 1-2).

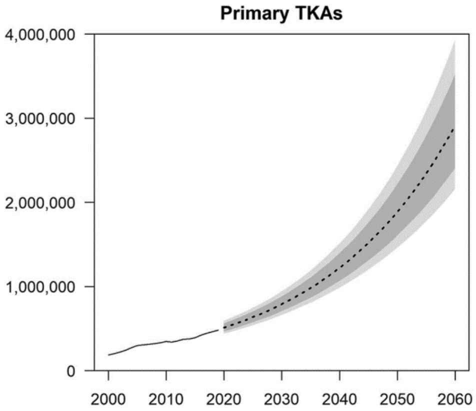
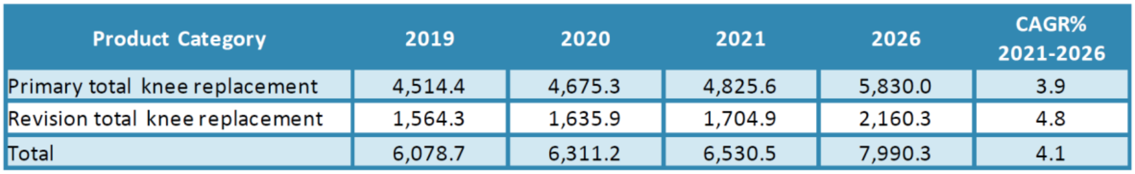


Figure 1-1 Primary TKAs are projected between 2020 and 2060. The black line depicts the observed CMS data (2000-2019), while the dotted line presents the point forecasts (2020-2060), with the dark gray and light gray areas representing 80% and 95% forecast intervals [42].



Product Category	2019	2020	2021	2026	CAGR% 2021-2026
Primary total knee replacement	4,514.4	4,675.3	4,825.6	5,830.0	3.9
Revision total knee replacement	1,564.3	1,635.9	1,704.9	2,160.3	4.8
Total	6,078.7	6,311.2	6,530.5	7,990.3	4.1

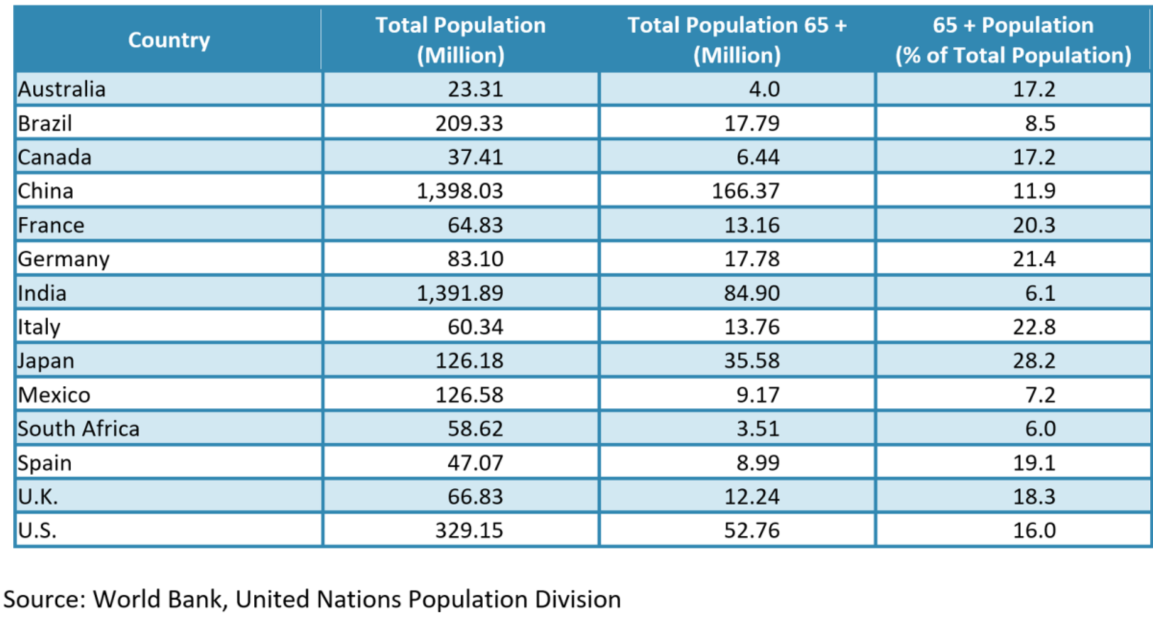
Figure 1-2 Global Market for Knee Replacement ($ Millions). Credit BCC Research Total Knee Replacement: Global Markets 2021

Osteoarthritis (OA) is the most common condition leading to TKA and is widely acknowledged as a primary source of disability and pain in the elderly population. Approximately 50% of individuals aged 65 years and older are affected by OA, with four out of five patients experiencing movement restrictions and one-quarter unable to perform daily activities [15]. In fact, with the rise in life expectancy, it is estimated that within the last three decades, OA has increased globally by 113.25%, from 247.5 million cases in 1990 to 527.81 million in 2019 [14].

Despite significant advancements in TKA, challenges and limitations still need to be addressed to enhance patient satisfaction and reduce healthcare costs. Treating OA presents a formidable challenge, as there are no effective therapeutic options to prevent or halt its progression, with TKA being the only end-stage therapy [19].

1.1 Thesis Motivation and Research Objectives

Despite the life-changing improvements offered by Total Knee Arthroplasty (TKA), 10-15% of patients continue to experience dissatisfaction after the surgery [43]-[45]. With an aging population (Figure 1-3) and the expansion of TKA insurance eligibility to patients with milder symptoms, it is crucial to identify technology gaps that can improve overall patient outcomes. By highlighting technology gaps in the TKA ecosystem, this thesis seeks to catalyze further technology innovation and foster more collaboration between stakeholders to develop novel solutions in this field.



Country	Total Population (Million)	Total Population 65 + (Million)	65 + Population (% of Total Population)
Australia	23.31	4.0	17.2
Brazil	209.33	17.79	8.5
Canada	37.41	6.44	17.2
China	1,398.03	166.37	11.9
France	64.83	13.16	20.3
Germany	83.10	17.78	21.4
India	1,391.89	84.90	6.1
Italy	60.34	13.76	22.8
Japan	126.18	35.58	28.2
Mexico	126.58	9.17	7.2
South Africa	58.62	3.51	6.0
Spain	47.07	8.99	19.1
U.K.	66.83	12.24	18.3
U.S.	329.15	52.76	16.0

Source: World Bank, United Nations Population Division

Figure 1-3 Global elderly population by country 2019 Million/%Total). Credit BCC Research Total Knee Replacement: Global Markets 2021

Understanding the TKA ecosystem and its technological landscape is one of the main goals of this thesis. This research aims to address the following key questions, organized around the essential aspects of the TKA ecosystem and its technological landscape:

1. **What are the critical junctions within the TKA workflow where technology plays a significant role?** This analysis will map the network of processes and stakeholders involved in a TKA journey -from pre-operative planning to post-operative rehabilitation - pinpointing the critical junctions where technology plays a major role.
2. **What are the existing technologies used in TKA procedures, and what are their limitations and impacts on patient outcomes?** This involves thoroughly evaluating the current state-of-the-art technology, understanding the existing technologies employed across all stages of TKA, delving into their functionalities, evaluating their limitations, and their impact on patient outcomes.
3. **Which combinations of technology in TKA provide the most value in terms of patient outcomes and cost-effectiveness?** This research will identify the most value-

generating combinations by analyzing and comparing different technology combinations, considering not just patient outcomes but also cost-effectiveness.

4. **Where is investment in technology, innovation, or collaboration most crucial within the TKA field?** The conclusion of this study will identify and expose these areas as understanding these limitations could potentially pave the way for others to join the pursuit of tackling these challenges.

1.2 Thesis Structure

The rest of this chapter provides a literature overview of the history of TKA, its associated risks, and limitations, setting the foundation for the subsequent chapters. Chapter 2 builds upon this foundation by deconstructing the TKA process as a system, illuminating the interconnections between each step and process. Chapters 3 and 4 delve into the different types of implants, fixtures, and assisting tools utilized in the pre-, intra-, and post-operative stages of TKA. These chapters provide a comprehensive evaluation of the current state-of-the-art technologies, their functionalities, limitations, and impacts on patient outcomes. Chapter 5 analyzes the effects of combining these technologies on patient outcomes and cost-effectiveness. By identifying the most value-generating technology combinations, this chapter contributes to the overall objective of highlighting areas where investment and innovation could potentially lead to significant improvements in TKA outcomes. Chapter 6 examines the findings from the previous chapters and explores the potential for technological advancements and innovations in the field of TKA. This chapter also discusses some of the current limitations and challenges faced by TKA technologies and identifies areas where further research and development are needed. Finally, in Chapter 7, the thesis summarizes the key findings and contributions of the research.

1.3 Background and History

Prosthetic limb products trace back long ago, as strong contenders for prosthetic leg use date back to 300 BC, found in a grave in Capua, Italy [46]. Figure 1-4 [47] shows a replica of the Capua leg. The limb was destroyed in a WWII air raid [48].

Figure 1-4 Replica of "the Capua leg." The original was dated to 300 BC [47].

Later, more practical prosthetic metal hands and hooks emerged in the 1600s [49], [50]. Throughout the 18th century, growing interest in musculoskeletal conditions led to the gradual development of what we now recognize as the field of orthopedics: The term itself, with potential roots in earlier French usage, gained wider recognition through publications such as Dr. Nicholas Andry's 1741 "Orthopédie," describing different methods to correct deformity in children [51], [52]. Early attempts in the 19th century focused on joint debridement and meniscectomy, such as the notable contributions of Scottish surgeon Sir William Fergusson [53], which was followed by resection arthroplasty in the late 19th and early 20th centuries [54]. These paved the way for the refinement of TKA in the latter half of the 20th century [55], leading to significant improvements in pain relief and functionality. In 1962, British orthopedic surgeon Sir John Charnley pioneered the first successful joint (hip) replacement surgery, opening the path for future advancements in joint replacement arthroplasty [10], [56] and spurring further advancements in joint replacement in general. Six years later, Dr. John Insall made a pivotal contribution to the field of knee arthroplasty by performing one of the first successful TKAs at the Hospital for Special

Surgery in New York [54], [57].

Today, millions of patients globally benefit from TKA's ability to restore joint function and improve the quality of their lives. It has become a commonly performed and effective surgical procedure, which involves the replacement of an affected patient's knee joint surfaces with prosthetic components known as implants. The femoral component of the TKA implant consists of a metal component that covers the distal end of the femur (thigh bone). The tibial (shin bone) component consists of the metal compartment and a medially graded polyethylene insert/spacer. The metal segment is the foundation for the implant's base, and the plastic spacer serves as a cushion between the two metal components.

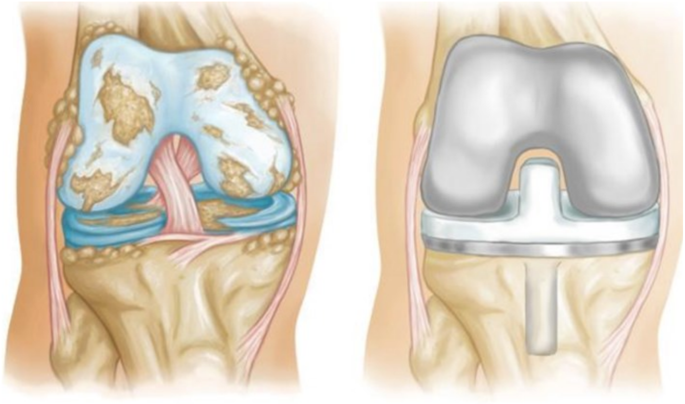


Figure 1-5 The knee with the patella component is not shown. (Left) Severe osteoarthritis. (Right) Tibial and Femoral metal implant and plastic spacer [1]

The concept of using cemented fixation in the tibial and femoral compartments with a metal-on-polyethylene condylar design was developed in the 1970s. Subsequent advancements in the field led to the refinement of this design and the introduction of non-cemented modalities [9], [19]. Over time, orthopedic procedures have become less invasive, leading to quicker patient recovery and better kinetic functionality on average.

1.4 Risks and Complications

Despite its remarkable efficacy, there are early and long-term potential risks and complications associated with the TKA procedure:

1.4.1 Early Complications

Infection: There is a small but significant risk of infection following TKA surgery, ranging from surgical site infection (up to 2%) [58] to deeper prosthetic joint infections (0.5-1.9%) [59], which could potentially lead to loss of a limb or even mortality.

Blood Clots: Deep vein thrombosis (DVT) is a complication that could potentially lead to life-threatening pulmonary embolisms and increase the risk of myocardial infarction (decreased blood flow to the heart) [63].

Stiffness and Pain: While significant pain relief is typically expected, some patients experience persistent stiffness (difficulty extending or flexing their knee) or even increased pain. Factors like component malalignment, patellar complications, or nerve injury are a few causes. Figure 1-4 [63], compares knee flexion or extension recovery range of motion for proper recovery and insufficient knee flexion.

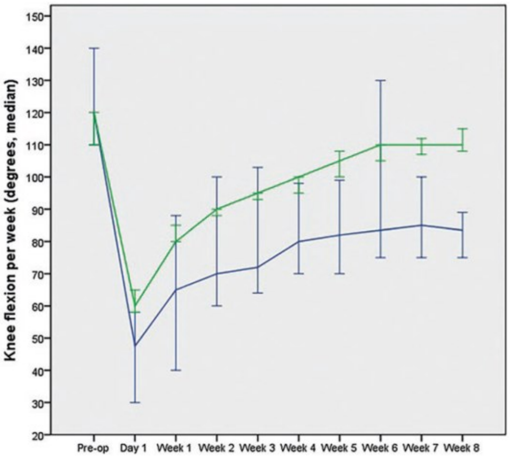


Figure 1-6 Flexion recovery: Green line: proper recovery range. The blue line is insufficient knee flexion [63].

Although rare, the peroneal nerve (Shown in Figure 1-5) is the most common nerve to become injured during the procedure, resulting in sensory loss, less motor control, dysesthesia (painful burning, tingling), or paresthesia (tickling sensation) [61]-[63].

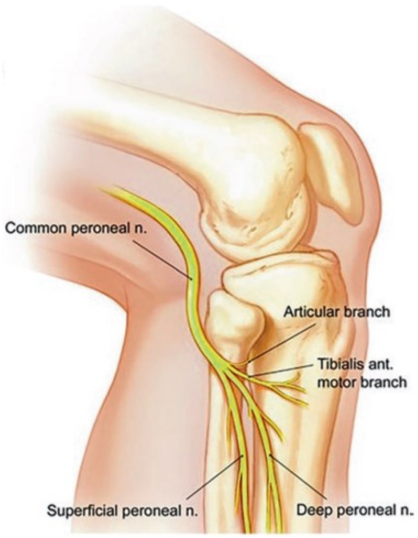


Figure 1-7 Peroneal nerve [64]

1.4.2 Long-term Complications

While TKA is generally a successful procedure, it is essential to be aware of the potential long-term complications that may arise. Understanding these complications is crucial for both patients and surgeons to make informed decisions and to drive advancements in the field. This section will discuss two major long-term complications: implant loosening and patellar complications.

Implant loosening: Over time, loosening of the prosthetic components can occur due to wear and tear or bone loss due to factors such as osteoporosis, which can lead to micromotion (slight movement) between the implant and bone [69]. This loosening of the implant can compromise the stability and function of the joint, manifesting as pain, stiffness, decreased range of motion, and instability in the knee. Another aspect is wear and tear in polyethylene and/or metallic compartments, which can potentially lead to the release of these particles into the body, resulting in the body's immune response and reabsorption of bone calcium minerals into the blood system and potentially loosening of the implant [63], [68], [69].

Patellar complications: Maltracking or instability of the kneecap (patella) can cause pain and dysfunction following TKA. In some cases, additional surgery may be required to address these issues [67]. Several factors can contribute to patellar complications, including pre-TKA valgus greater than 10 degrees, patellar thinness, and asymmetric bone cuts [67].

Chapter 2

System View

Total knee arthroplasty (TKA) is a complex and resource-intensive procedure that involves multiple stakeholders beyond the patient, including surgeons, nurses, anesthesiologists, and rehabilitation specialists. Understanding the patient's journey and the TKA procedure itself is crucial for identifying potential areas of improvement and optimizing patient outcomes. Figure 2-1 [71] illustrates a typical patient's journey for a TKA procedure, which consists of four main stages:

1. Pre-referral primary care, where the primary care physician provides non-operative options, such as physical therapy, weight management, medications, activity modification, and using assistive devices (e.g., braces). This stage is usually long, using a fair amount of trials, to ensure that all potential conservative treatments have been adequately explored and optimized before considering more invasive options like surgery. The goal at this stage is to manage the patient’s pain and improve their mobility through the least invasive method possible by allowing time to assess the patient's response to various therapies. Usually, non-operative options, such as weight loss, physical therapy, non-steroidal anti-inflammatory drugs (NSAIDs), bracing, and intra-articular injections, are tried before opting for TKA [60].
2. Assessment by a specialist, where usually (and most likely) radiology assessment of the bones and alignment is done.
3. In-hospital care, starting with the TKA surgery itself, involves the collaboration of various healthcare professionals, including surgeons, nurses, and anesthesiologists.
4. Post-surgery care, following the surgery and starting in the rehabilitation phase at

home or in a specialized facility.

A good understanding of the TKA procedure can be gained by identifying its key subsystems, main processes and their boundaries, stakeholders, and figures of merits. Decomposing the system will help unlock potential gaps and areas of improvement. The next section will evaluate the architecture of the TKA system and analyze its decomposition.

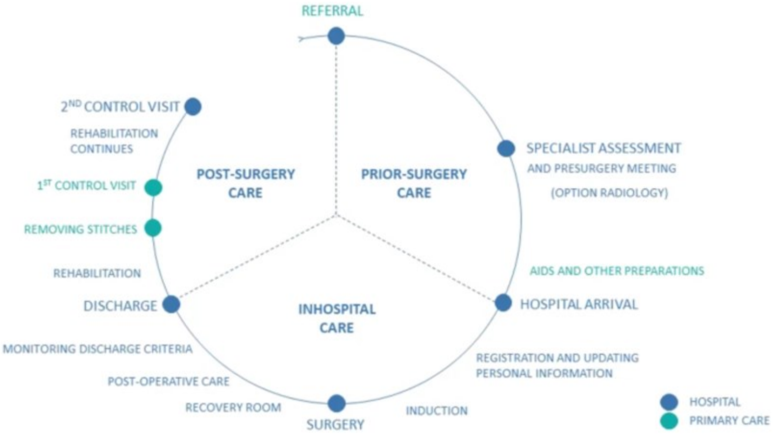
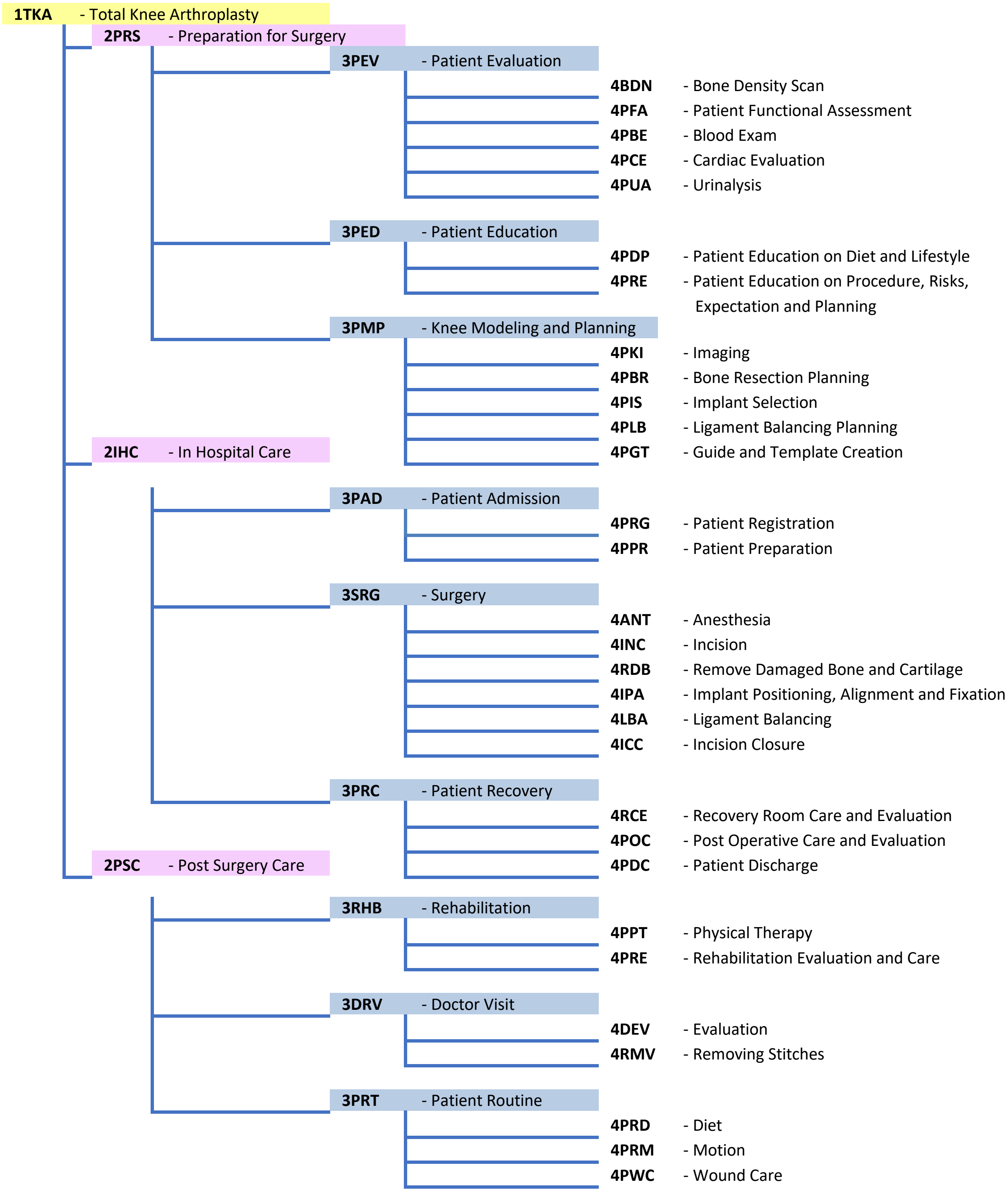


Figure 2-1 Overview of a patient's journey for TKA [71]

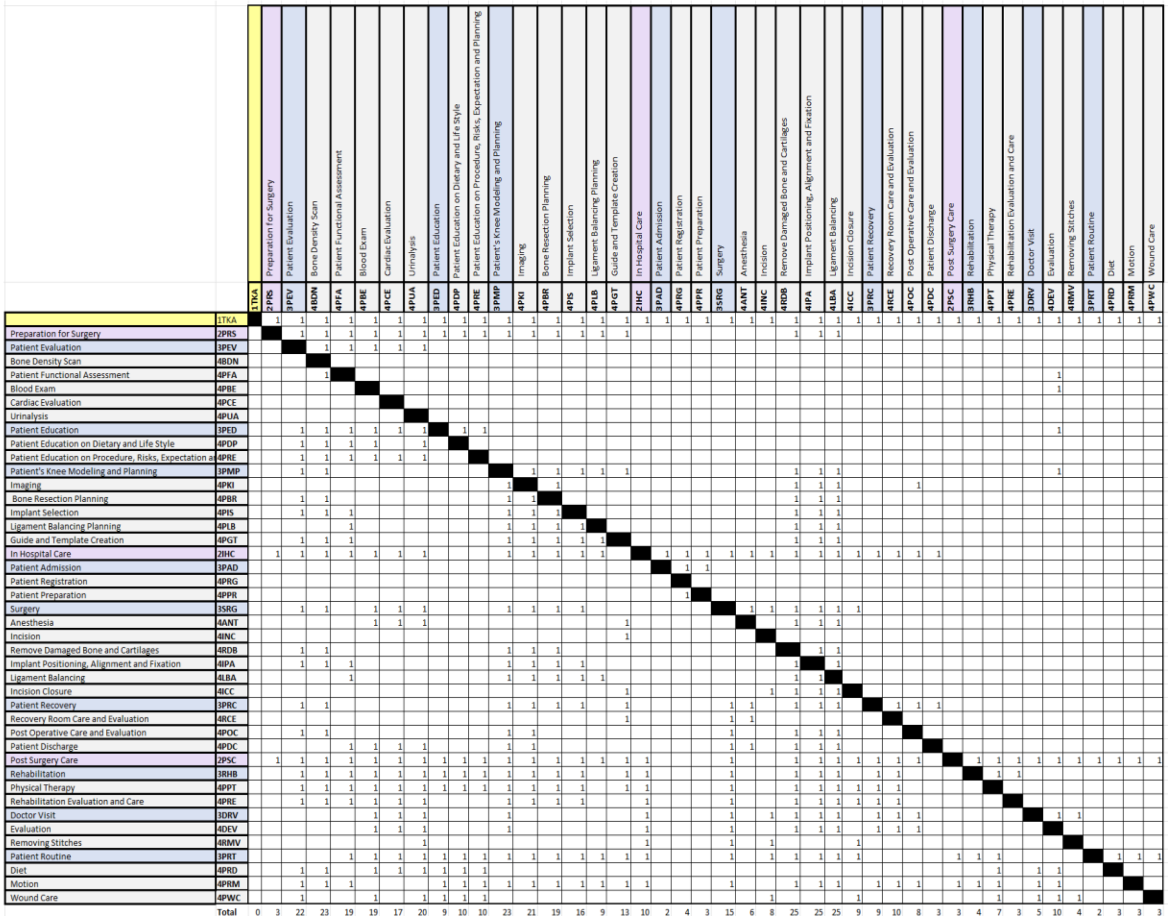
2.1 Design Structure Matrix Allocation

Design Structure Matrix, also known as Dependency and Structure Modeling (DSM), offers a systematic approach to managing complexity in systems. This methodology emphasizes the importance of identifying and analyzing the interactions (e.g., physical or organizational connections, mass, energy, or information flow) between different elements within a complex system. By mapping these interactions, DSM facilitates a detailed exploration of how system components interrelate, aiding in effectively managing dependencies and interfaces. DSM techniques dissect and optimize complex systems' architectures across different domains. For instance, in product development, DSM can be instrumental in streamlining the design process by identifying potential areas for integration or simplification. In organizational contexts, it helps delineate clear roles and communication pathways. Similarly, DSM helps optimize workflows in process engineering by pinpointing critical interdependencies that could impact performance. The DSM can be a useful tool in understanding the limitations of TKA surgery because it provides a structured approach to identify and analyze the complex interactions between various components and factors involved from pre- to post-procedure. To create a DSM, first, we analyze the TKA as a system level by level, as follows:



It is important to note that some of these elements (e.g., patient preparation, incision closure) are single steps, while others, such as rehabilitation, are recurring and may last for months, requiring multiple office visits and evaluations.

To understand how each step process or technology interacts and influences the other steps, each step/technology that enables the functionality of another element of the TKA system is identified and marked, as seen in the figure below.

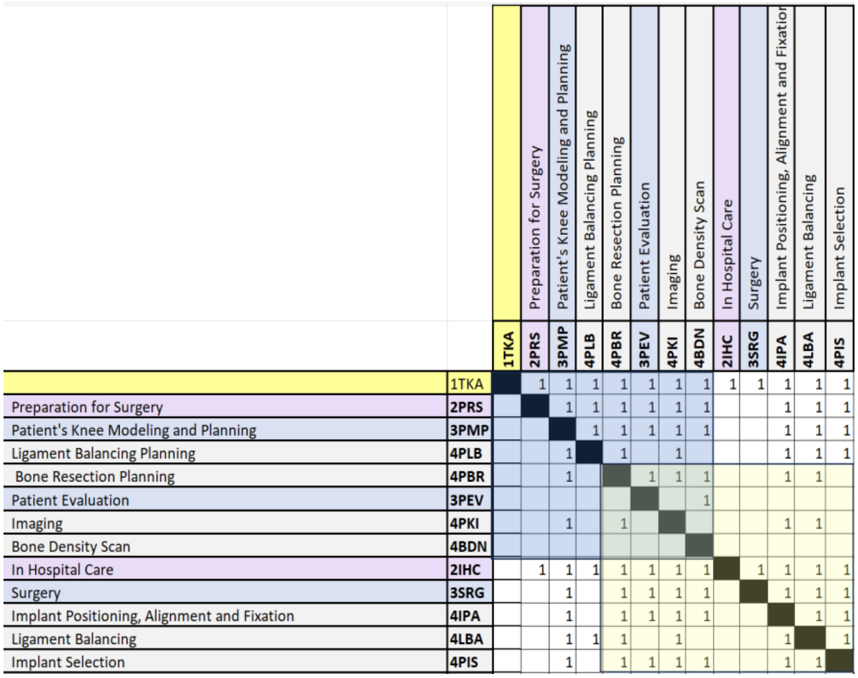


			Preparation for Surgery	Patient Evaluation	Bone Density Scan	Patient Functional Assessment	Blood Exam	Cardiac Evaluation	Urinalysis	Patient Education	Patient Education on Dietary and Life Style	Patient Education on Procedure, Risks, Expectation and Planning	Patient's Knee Modeling and Planning	Imaging	Bone Resection Planning	Implant Selection	Ligament Balancing Planning	Guide and Template Creation	In Hospital Care	Patient Admission	Patient Registration	Patient Preparation	Surgery	Anesthesia	Incision	Remove Damaged Bone and Cartilages	Implant Positioning, Alignment and Fixation	Ligament Balancing	Incision Closure	Patient Recovery	Recovery Room Care and Evaluation	Post Operative Care and Evaluation	Patient Discharge	Post Surgery Care	Rehabilitation	Physical Therapy	Rehabilitation Evaluation and Care	Doctor Visit	Evaluation	Removing Stitches	Patient Routine	Diet	Motion	Wound Care
		1TKA	2PRS	3PEV	4BDN	4PFA	4PBE	4PCE	4PUA	3PED	4PDP	4PRE	3PMP	4PKI	4PBR	4PIS	4PLB	4PGT	2IHC	3PAD	4PRG	4PPR	3SRG	4ANT	4INC	4RDB	4IPA	4LBA	4ICC	3PRC	4RCE	4POC	4PDC	2PSC	3RHB	4PPT	4PRE	3DRV	4DEV	4RMV	3PRT	4PRD	4PRM	4PWC
	1TKA	■	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Preparation for Surgery	2PRS		■	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1								1	1	1																
Patient Evaluation	3PEV			■	1	1	1	1	1																																			
Bone Density Scan	4BDN				■																																							
Patient Functional Assessment	4PFA				1	■																																	1					
Blood Exam	4PBE						■																																1					
Cardiac Evaluation	4PCE							■																																				
Urinalysis	4PUA								■																																			
Patient Education	3PED			1	1	1	1	1	1	■	1	1																											1					
Patient Education on Dietary and Life Style	4PDP			1	1	1	1		1		■																																	
Patient Education on Procedure, Risks, Expectation a	4PRE			1	1	1	1	1	1			■																																
Patient's Knee Modeling and Planning	3PMP			1	1								■	1	1	1	1	1								1	1	1											1					
Imaging	4PKI												1	■	1											1	1	1				1												
Bone Resection Planning	4PBR			1	1								1	1	■											1	1	1																
Implant Selection	4PIS			1	1	1							1	1	1	■										1	1	1																
Ligament Balancing Planning	4PLB					1							1	1	1	1	■									1	1	1																
Guide and Template Creation	4PGT			1	1	1							1	1	1	1	1	■								1	1	1																
In Hospital Care	2IHC		1	1	1	1	1	1	1				1	1	1	1	1		■	1	1	1	1	1	1	1	1	1	1	1	1	1	1											
Patient Admission	3PAD																			■	1	1																						
Patient Registration	4PRG																				■																							
Patient Preparation	4PPR																				1	■																						
Surgery	3SRG			1	1		1	1	1				1	1	1	1							■	1	1	1	1	1	1															
Anesthesia	4ANT						1	1	1									1						■		1	1	1																
Incision	4INC																	1							■																			
Remove Damaged Bone and Cartilages	4RDB			1	1								1	1	1											■	1	1																
Implant Positioning, Alignment and Fixation	4IPA			1	1	1							1	1	1	1										1	■	1																
Ligament Balancing	4LBA					1							1	1	1	1	1									1	1	■																
Incision Closure	4ICC																	1							1	1	1	1	■															
Patient Recovery	3PRC			1	1								1	1	1	1		1					1	1		1	1	1		■	1	1	1											
Recovery Room Care and Evaluation	4RCE																	1					1	1							■													
Post Operative Care and Evaluation	4POC			1	1								1	1									1			1	1	1				■												
Patient Discharge	4PDC					1	1	1	1				1	1									1	1		1	1	1					■											
Post Surgery Care	2PSC		1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1				1			1	1	1	1	1	1	1		■	1	1	1	1	1	1	1	1	1	1
Rehabilitation	3RHB			1	1	1	1	1	1	1	1	1	1	1	1	1		1	1				1			1	1	1		1	1				■	1	1							
Physical Therapy	4PPT			1	1	1	1	1	1	1	1	1	1	1	1	1		1	1				1			1	1	1	1	1	1					■								
Rehabilitation Evaluation and Care	4PRE			1	1	1	1	1	1				1	1	1	1			1				1			1	1	1	1	1	1						■							
Doctor Visit	3DRV						1	1	1				1						1				1		1	1	1	1		1	1	1						■	1	1				
Evaluation	4DEV						1	1	1				1						1				1			1	1	1		1	1	1							■					
Removing Stitches	4RMV								1										1				1		1				1											■				
Patient Routine	3PRT					1	1	1	1	1	1	1	1	1	1	1	1	1	1				1		1	1	1	1	1					1	1	1					■	1	1	1
Diet	4PRD			1	1		1	1	1	1	1	1																								1		1	1			■		
Motion	4PRM			1	1	1				1	1	1	1	1	1	1	1	1	1				1			1	1	1		1	1	1		1	1	1		1	1				■	
Wound Care	4PWC			1			1		1	1	1	1													1				1							1		1	1	1				■
	Total	0	3	22	23	19	19	17	20	9	10	10	23	21	19	16	9	13	10	2	4	3	15	6	8	25	25	25	9	9	10	8	3	3	4	7	3	5	10	4	2	3	3	3

Figure 2-2. 4-level DSM of TKA system decomposition

Clustering the entities in this DSM will enable us to minimize the interactions across stages of TKA and maximize the internal coherence within each of these stages [81]. Utilizing a clustering technique based on processes, the TKA architecture is grouped more functionally rather than by timeline.

This thesis aims to focus on analyzing the gap in technology for the first two clusters shown below, which have the most impact and have room for technology improvement.



			Preparation for Surgery	Patient's Knee Modeling and Planning	Ligament Balancing Planning	Bone Resection Planning	Patient Evaluation	Imaging	Bone Density Scan	In Hospital Care	Surgery	Implant Positioning, Alignment and Fixatio	Ligament Balancing	Implant Selection
		1TKA	**2PRS**	**3PMP**	**4PLB**	**4PBR**	**3PEV**	**4PKI**	**4BDN**	**2IHC**	**3SRG**	**4IPA**	**4LBA**	**4PIS**
	1TKA		1	1	1	1	1	1	1	1	1	1	1	1
Preparation for Surgery	**2PRS**			1	1	1	1	1	1			1	1	1
Patient's Knee Modeling and Planning	**3PMP**				1	1	1	1	1			1	1	1
Ligament Balancing Planning	**4PLB**			1		1		1				1	1	1
Bone Resection Planning	**4PBR**			1			1	1	1			1	1	
Patient Evaluation	**3PEV**								1					
Imaging	**4PKI**			1		1						1	1	
Bone Density Scan	**4BDN**													
In Hospital Care	**2IHC**		1	1	1	1	1	1	1		1	1	1	1
Surgery	**3SRG**			1		1	1	1	1			1	1	1
Implant Positioning, Alignment and Fixation	**4IPA**			1		1	1	1	1				1	1
Ligament Balancing	**4LBA**			1	1	1		1				1		1
Implant Selection	**4PIS**			1		1	1	1	1			1	1	

Figure 2-3. Zoomed-in 1rst Cluster DSM

2.2 Stakeholder Analysis

Here, we elaborate on the groups and individuals who have a stake in a TKA system. The primary beneficiary is the patient, as they will directly benefit from the performance of a TKA procedure. The surgeon, staff, and hospital management (healthcare providers) have professional and monetary interests in the procedure's effectiveness (short and long-term). Researchers and the American Academy of Orthopedic Surgeons (AAOS) provide data and evidence-based knowledge to the healthcare team, device manufacturers, and innovators. In 2012, AAOS launched the American Joint Replacement Registry (AJRR) database, which includes data on TKA procedures to track and monitor short and long-term outcomes, where many aspects, including but not limited to implant survival rate, functionality, quality of life, complications and revisions are recorded. These contributions by AAOS and researchers give insights into how to identify best practices and improve patient care. It also leads to generating data on the cost-effectiveness of various orthopedic treatments and procedures that could potentially help insurance companies update their policies and reimbursement practices for a TKA and its care. Moreover, these institutions' efforts offer educational resources to the healthcare team, focusing on new clinical or best practices and increasing patient outcomes, aligning with insurance companies' goals of potentially reducing the overall care cost. Manufacturers and innovators are incentivized by producing a product that results in high satisfaction for patients, the healthcare team, insurers, or regulators.

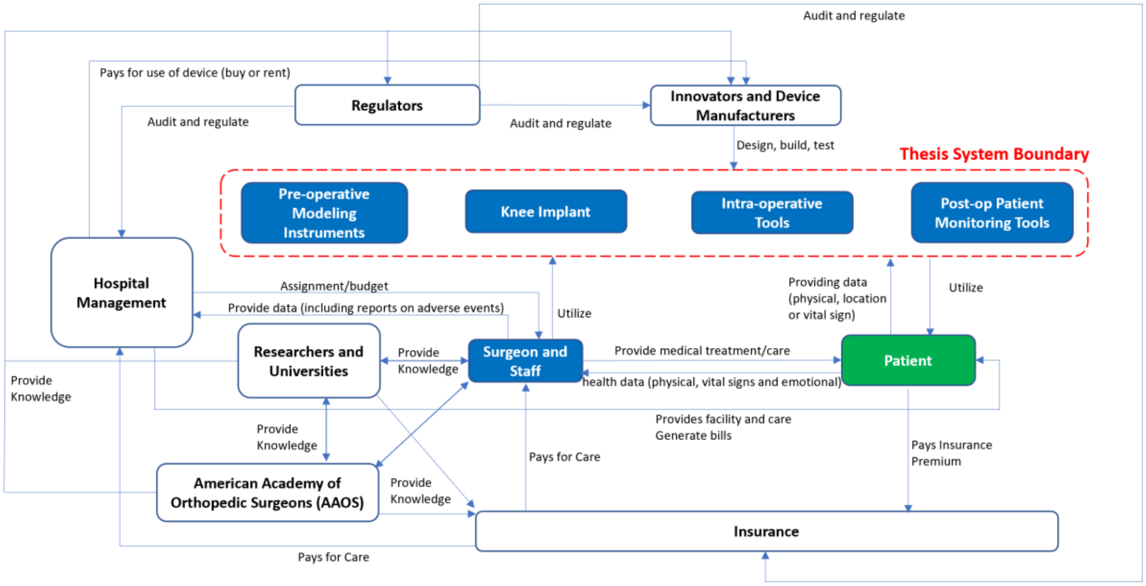


Figure 2-4 TKA Stakeholder view

The policies that regulators adopt impact insurance companies, healthcare provider teams, innovators, and device manufacturers. Their role revolves around establishing clear frameworks and protocols that ensure quality, safety, affordability, responsible practices, and accountability throughout the entire TKA journey. Through data monitoring and transparency mandates, regulators promote accountability and provide policies that prioritize patient safety first, as well as patient outcomes and cost-effectiveness. Their goal is to potentially act as a bridge between the healthcare providers/innovators/

manufacturers and insurers to facilitate their alignment and collaboration on patient wellbeing and cost by setting clear expectations and enforcing them.

2.3 Figures of Merit (FOM)

The table below shows a list of FOMs that can assess the TKA technology. Defining some of these factors can be nuanced as they encompass various aspects of recovery within a relative timeframe after the surgery. The first two FOMs, early functionality, and longevity are the primary merits more applicable to the TKA system considered in this research.

Early functionality or early functional recovery can be described as the initial stages of recovery after the surgery, where the patient begins to regain basic functional abilities in the knee joint. This could include activities such as walking, bending the knee, and performing simple movements. Assessing early functionality after surgery involves a mix of clinical evaluations, functional tests, and patient feedback reports. Defining early functionality can be challenging due to the lack of uniform standards; the specific tests and methods used vary across different studies and clinical settings, where the care team employs a diverse array of approaches to evaluate their patients' early progress and the knee's functionality. These tests and questionnaires aim to track postoperative recovery and identify deficits early on to guide rehabilitation in a timely manner.

Surgeons use a set of tests before and after surgery to assess the progress of patients undergoing TKA operation. These assessments include Range of Motion (ROM) tests, which are essential for activities like walking and stair climbing. Strength testing evaluates the muscles surrounding the knee, while functional tests like the Timed Up and Go (TUG) provide insights into the patient's mobility and recovery. Patient-reported outcome Measures (PROMs) and the Knee Outcome Survey (KOS) questionnaires help capture patients' views on their knee health and recovery. Oxford Knee Score (OKS) and its Activity and Participation Questionnaire (OKS-APQ) focus on pain and physical function of the treated knee. The Patient Knee Implant Performance (PKIP) score evaluates the performance of knee implants, whereas the 5-Level EuroQol 5 Dimensions (EQ-5D-5L) and the Short Form-36 outcome (SF-36) or SF-12 provide a broader assessment of the patient's general physical and mental health. These assessments are typically carried out at different stages within the recovery timeline, including one month, six weeks, three months, six months, one year, and two-year follow-up periods. [22], [23], [26], [72]-[74]. For the purpose of this thesis, we will define it as the % of a patient's recovery within a year at a follow-up visit.

To complement these evaluations, surgeons also conduct bilateral functional symmetry tests such as bilateral range of motion, symmetry in strength, and gait analysis. These tests identify discrepancies that could affect patient's balance and gait because of the imbalance between their knees.

Longevity in TKA is a critical goal for patients, surgeons, and insurers alike, as achieving a durable and functional knee joint replacement translates to improved quality of life and lower healthcare costs. Understanding the key factors influencing TKA longevity and evidence supporting their impact is crucial for optimizing both surgical and patient outcomes. The factors affecting the survivorship or longevity of a TKA implant and reasons for a revision TKA include the implant's physical durability (either metal or tibial polyethylene) [75], [78], infection [78], aseptic loosening [78], maintaining good knee function [77] patient- specific satisfaction questioner such as MACTAR [79] over a prolonged period.

Another figure of merit important to patients going through a TKA operation is residual pain, which is defined as a lingering or persistent pain that a patient may experience after the surgical procedure. It is not uncommon for some patients to experience mild to moderate residual pain. Several factors can contribute to pain after TKA, including but not limited to tissue repair, soft tissue manipulation during surgery, nerve sensitivity, muscle imbalance or weakness, mispositioning, and polyethylene wearing [63]. About 20% of patients experience postoperative persistent pain after TKA [150]. The amount of pain a patient encounters and their tolerance and acceptance towards it differ from person to person. Older patients generally have lower residual pain scores and a higher satisfaction rate with their outcomes after TKA compared to younger patients [28]. For example, Elmallah et al. found in [29] that older patients (≥75 years) had a mean pain score of 2.2 points on the Numeric Pain Rating Scale (NRS) compared to a mean pain score of 3.1 points for younger patients at 12 months checkup. The first three FOMs in Table 2-1 represent the key FOMs used in assessing this research. Although all FOMs, except cost, are subjective, the inclusion of early functionality and longevity in this analysis over residual pain is based on the objective measurability of the former (i.e., quantitatively assessment by using specific tests) compared to the inherently subjective nature of the latter. Residual pain FOM is purely subjective (i.e., varies widely among individuals influenced by physical, psychological, and social factors) and is indirectly reflected in the patient's early functionality and TKA longevity outcome.

Figure of Merit	Units	Description
Early Functionality	**[%]**	The % of patient ability to perform daily activities and mobility-related tasks at a 1-year follow-up visit.
Longevity	**[years]**	The duration for which a knee prosthesis is attached to the bone and effectively functional for a patient.
Cost	**[$]**	TKA Cost
Residual Pain	# between 1-10	Persisting pain that a patient may experience beyond 3-6 months after the surgical procedure.

Table 2-1 Figure of Merit Table

Chapter 3

Knee Implants

There are many different types of total knee implants available on the market today. The selection of an appropriate knee implant for a patient undergoing TKA is a multi-layer decision. This chapter reviews the broad landscape of knee implant options currently available. Numerous factors influence the specific brand and design ultimately chosen by an orthopedic surgeon, extending beyond a simple product listing. These key considerations include:

- Surgeon expertise and experience: Surgeons often favor implant types and brands with which they possess the most familiarity, practical experience and ones that they have seen better results among their patients.
- Patient characteristics: Individual factors such as knee anatomy, underlying pathology, age, body mass index, activity level, and overall health significantly impact implant suitability.
- Implant performance and cost: Surgeons evaluate the long-term performance record and associated costs of various implants before making a selection.
- Hospital vendor contracts: Certain hospitals may have established contracts with specific implant manufacturers, influencing surgical options.
- Insurance coverage: Insurance company policies and reimbursement agreements with the hospital can limit implant choices in certain cases.

Knee implants consist of several components that collaboratively constitute the replacement knee joint. The femoral component replicates the distal end of the femur (thigh bone), precisely curving around the bone to provide support and maintain natural joint shape. Its counterpart, the tibial component, replaces the proximal surface of the tibia (shin bone) and consists of two key parts: a flat metal platform for secure attachment and a tibial insert made of a durable material that facilitates smooth gliding and weight distribution during movement. Finally, the patellar component cushions the kneecap surface and can be electively used by the surgeon for patellar resurfacing for smoother interaction between the patella and other implant components during knee flexion and extension.

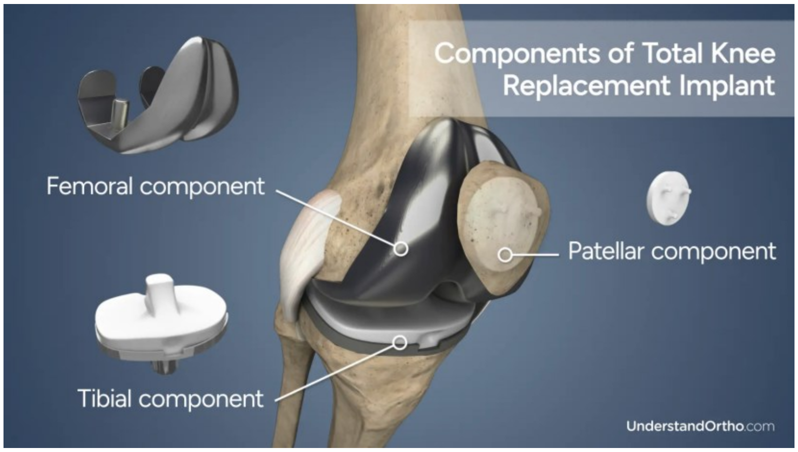


Figure 3-1 Total knee implant components [157]

Knee implants require highly specialized material with several crucial properties. They need to be biocompatible to minimize the risk of body rejection, toxicity and safety concerns [158]. This often involves using highly-regulated alloys and engineered plastics. They must withstand significant loads – bearing the patient's weight, absorbing impact, and enduring many flexion-extension cycles without breaking or deforming [158]. Beyond initial strength, the materials need to be long-lasting: resisting wear, fatigue, and corrosion for decades. Careful selection and design choices (e.g., mobile bearing or fixed bearing) are crucial for this long-term stability [158].

For enhanced stability and secure attachment to the bone, knee implants employ various fixation strategies. Some utilize bone cement, fixation screws (cortical or cancellous), or a combination of these methods. Cementless implants, on the other hand, rely on a porous surface and precise bone preparation to encourage bone ingrowth and achieve long-term stability.

There have been numerous development cycles (and failures and redesigns) in the history of TKA implants, resulting in over 150 types of knee implants available in the market today [1]. Figure 3-2 depicts the evolution of condylar TKA implants between 1970-1980 [164].

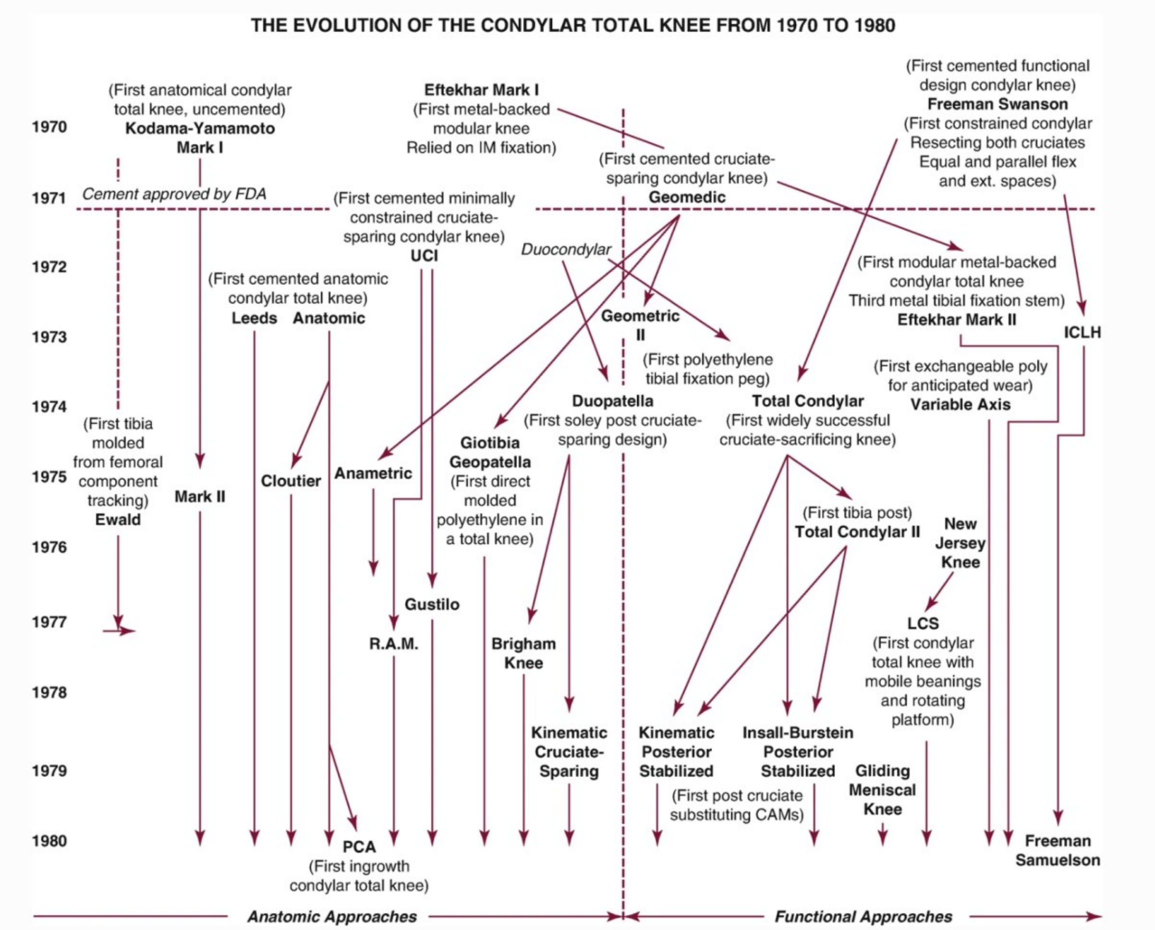


Figure 3-2. The condylar total knee evolution 1970-1980 [164]

Using various constraint types in knee implants allows surgeons to tailor treatment based on individual patients' specific ligament stability, bone quality, and alignment considerations.

Non-Constrained Implants: Non-constrained knee implants, such as cruciate-retaining (CR) implants, consist of separate upper and lower components without direct interconnection [165]. These implants rely on the relative stability of the medial and lateral ligaments, and in some cases, the posterior cruciate ligament, to facilitate coordinated knee movements, including flexion, extension, and rotation. The anterior cruciate ligament is typically removed before implantation, as it is often compromised by osteoarthritis. Non-constrained implants are suitable for patients with relatively stable ligaments and are designed to preserve natural knee kinematics [165].

Semi-Constrained Implants: Semi-constrained knee implants, such as posterior-stabilized implants, are utilized when the posterior cruciate ligament lacks sufficient stability and requires removal. These implants feature a hinge-like mechanism that connects the upper and lower components, providing stability in the absence of the cruciate ligaments. The hinge determines the range of motion for bending and straightening the knee. Semi-constrained implants are appropriate for patients with compromised posterior cruciate ligament function, enabling restoration of stability and joint movement [165].

Constrained Implants: Constrained, or "hinged," implants are designed for cases where both the medial and lateral ligaments exhibit inadequate stability [165]. These implants incorporate a hinged mechanism that firmly links the upper and lower components, supported by long stems that attach to the bone on each side. Constrained implants are employed in situations involving poor bone conditions, severe misalignments (such as knock knees or bow legs), and the need for enhanced stability beyond ligament support. By providing a fixed hinge, these implants offer substantial stability and support for patients with significant ligamentous deficiencies [165].

The advancements in knee implant technology continue to introduce new materials and designs. Here, we describe some recent advancements in knee implant technology, which have introduced novel materials and designs to enhance patient satisfaction and recovery.

3.1 Material

The metals commonly used in knee implants include titanium, cobalt-chromium alloys, and stainless steel. These metals are selected for their biocompatibility, mechanical strength, and corrosion resistance properties.

Titanium is a lightweight yet strong metal that is often used in knee implants. It has excellent biocompatibility and is known for its high strength-to-weight ratio and corrosion resistance. Titanium alloys, such as Titanium-6Aluminum-4Vanadium (Ti-6Al-4V) [169], are frequently employed in knee implant applications. For example, Stryker has developed Tritanium Advanced Fixation Technology [106] from Commercially Pure Titanium (CPTi) designed to mimic the trabecular bone, allowing the patient's bone to grow into the implant, creating a strong connection and enhancing long-term stability [3].

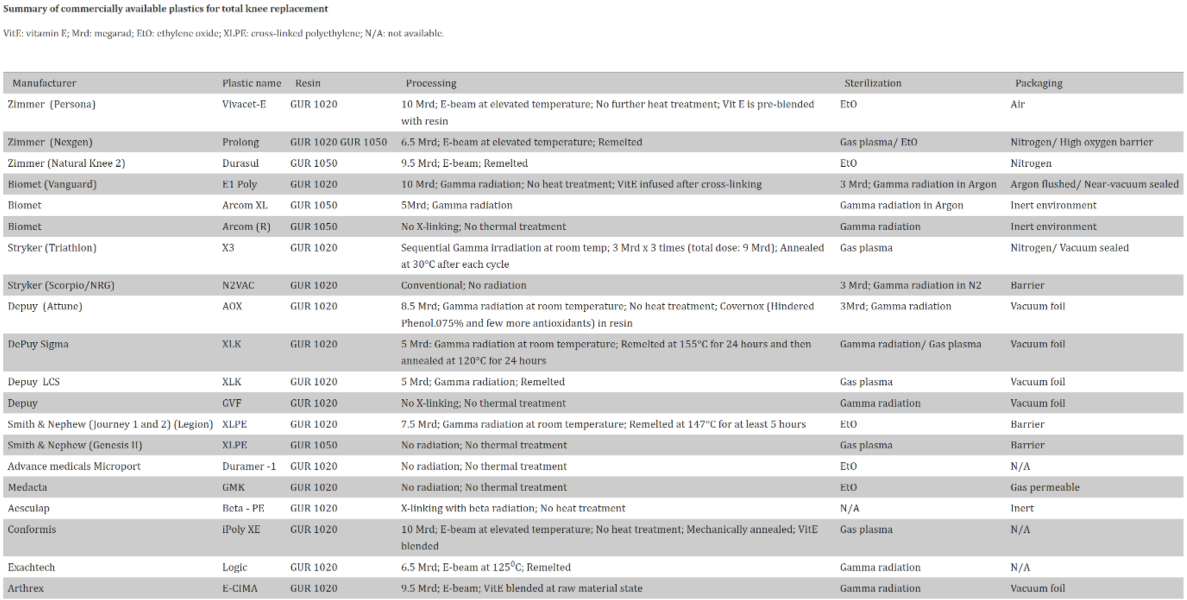
Cobalt-chromium alloys are another common option for knee implant materials. They offer excellent mechanical properties, including high strength and wear resistance. Cobalt-Chromium-Molybdenum (Co-Cr-Mo) alloys [161], [169], such as Co-Cr-Mo alloy ASTM F75, are widely used in orthopedic implants due to their biocompatibility and durability.

Stainless steel is another example that is occasionally used in knee implants. Stainless steel alloys, such as 316L [168], [169], provide good mechanical strength and corrosion resistance but are less favorable compared to other materials due to concerns about potential adverse reactions in some patients [169].

Ceramic materials, such as zirconia or alumina, are another type that is being explored for knee implants [161]-[163]. These materials have exceptional hardness, wear resistance, and biocompatibility. Ceramic-based implants offer the potential to reduce wear and improve longevity, providing a promising alternative to traditional metal implants.

Oxidized zirconium [167] is a modified form of zirconium metal that undergoes a surface oxidation process. This results in a ceramic-like surface layer that offers improved wear resistance and reduced friction compared to traditional metal implants. Oxidized zirconium implants may lead to decreased implant wear and potentially longer-lasting knee replacements.

Polyethylene, the plastic-like material used in the tibial bearing compartment of a knee implant, has shown improved longevity and performance using cross-linking techniques. For example, highly cross-linked polyethylene seems to exhibit improved wear resistance and decreased risk of debris generation compared to conventional polyethylene (CPE), making it desirable for younger patients [167]. However, its long-term performance for severe primary knee osteoarthritis (OA) patients has been debatable, as some research shows no advantage over conventional polyethylene in the 10-year follow-up [166]. Incorporating antioxidant addition (e.g., Vitamin E) into the bearing component is another method that is being introduced to overcome long-term oxidation [167]. Even though the technology has shown overall promising improvements in the fatigue strength of the insert, there is a lack of mid- and long-term research on its effect on TKA implants [167]. Figure 3-3 depicts the summary of commercially available bearing inserts for TKA implants [167].



Summary of commercially available plastics for total knee replacement

VitE: vitamin E; Mrd: megarad; EtO: ethylene oxide; XLPE: cross-linked polyethylene; N/A: not available.

Manufacturer	Plastic name	Resin	Processing	Sterilization	Packaging
Zimmer (Persona)	Vivacet-E	GUR 1020	10 Mrd; E-beam at elevated temperature; No further heat treatment; Vit E is pre-blended with resin	EtO	Air
Zimmer (Nexgen)	Prolong	GUR 1020 GUR 1050	6.5 Mrd; E-beam at elevated temperature; Remelted	Gas plasma/ EtO	Nitrogen/ High oxygen barrier
Zimmer (Natural Knee 2)	Durasul	GUR 1050	9.5 Mrd; E-beam; Remelted	EtO	Nitrogen
Biomet (Vanguard)	E1 Poly	GUR 1020	10 Mrd; Gamma radiation; No heat treatment; VitE infused after cross-linking	3 Mrd; Gamma radiation in Argon	Argon flushed/ Near-vacuum sealed
Biomet	Arcom XL	GUR 1050	5Mrd; Gamma radiation	Gamma radiation in Argon	Inert environment
Biomet	Arcom (R)	GUR 1050	No X-linking; No thermal treatment	Gamma radiation	Inert environment
Stryker (Triathlon)	X3	GUR 1020	Sequential Gamma irradiation at room temp; 3 Mrd x 3 times (total dose: 9 Mrd); Annealed at 30°C after each cycle	Gas plasma	Nitrogen/ Vacuum sealed
Stryker (Scorpio/NRG)	N2VAC	GUR 1020	Conventional; No radiation	3 Mrd; Gamma radiation in N2	Barrier
Depuy (Attune)	AOX	GUR 1020	8.5 Mrd; Gamma radiation at room temperature; No heat treatment; Covernox (Hindered Phenol.075% and few more antioxidants) in resin	3Mrd; Gamma radiation	Vacuum foil
DePuy Sigma	XLK	GUR 1020	5 Mrd: Gamma radiation at room temperature; Remelted at 155°C for 24 hours and then annealed at 120°C for 24 hours	Gamma radiation/ Gas plasma	Vacuum foil
Depuy LCS	XLK	GUR 1020	5 Mrd; Gamma radiation; Remelted	Gas plasma	Vacuum foil
Depuy	GVF	GUR 1020	No X-linking; No thermal treatment	Gamma radiation	Vacuum foil
Smith & Nephew (Journey 1 and 2) (Legion)	XLPE	GUR 1020	7.5 Mrd; Gamma radiation at room temperature; Remelted at 147°C for at least 5 hours	EtO	Barrier
Smith & Nephew (Genesis II)	XLPE	GUR 1050	No radiation; No thermal treatment	Gas plasma	Barrier
Advance medicals Microport	Duramer -1	GUR 1020	No radiation; No thermal treatment	EtO	N/A
Medacta	GMK	GUR 1020	No radiation; No thermal treatment	EtO	Gas permeable
Aesculap	Beta - PE	GUR 1020	X-linking with beta radiation; No heat treatment	N/A	Inert
Conformis	iPoly XE	GUR 1020	10 Mrd; E-beam at elevated temperature; No heat treatment; Mechanically annealed; VitE blended	Gas plasma	N/A
Exachtech	Logic	GUR 1020	6.5 Mrd; E-beam at 125^{0}C; Remelted	Gamma radiation	N/A
Arthrex	E-CIMA	GUR 1020	9.5 Mrd; E-beam; VitE blended at raw material state	Gamma radiation	Vacuum foil

Figure 3-3 Commercial available TKA bearing inserts in the market [167]

Another advancement is adding metal backing to tibial inserts, which feature a metal backing commonly made of cobalt-chromium or titanium alloy [114]. The metal backing provides structural support and stability to the polyethylene insert, particularly in cases where there may be compromised bone quality or surgical considerations.

3.2 Fixed or Mobile Bearing

Mobile bearing and fixed bearing (as shown in Figure 3-4) are two different designs that address the intricate dynamics between the tibial component (tibial tray) and the insert (bearing) component.

3.2.1 Fixed Bearing

In a fixed-bearing (FB) knee implant, the insert or bearing component is firmly attached or fixed to the tibial tray. The insert has no independent movement and remains fixed in its position within the tibial tray. During knee movement, the femoral component glides over the fixed insert. This design provides stability and is commonly used in traditional knee implant designs [161].

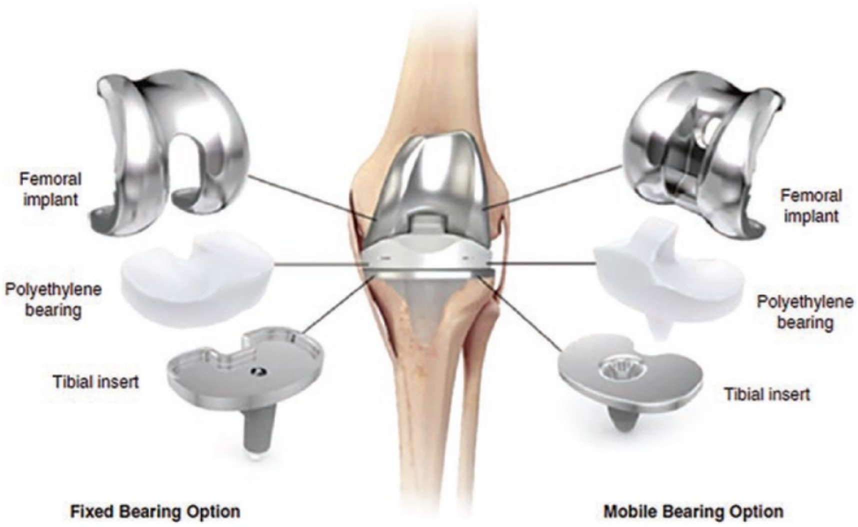


Figure 3-4- Fixed bearing and mobile bearing knee implant [161]

3.2.2 Mobile Bearing

In a mobile bearing (MB) knee implant, the insert or bearing component is designed to have some degree of independent movement within the tibial tray. It is not rigidly fixed but instead allows for slight rotation or translation. The mobile bearing insert can move or rotate slightly as the knee joint moves, mimicking the natural function of the knee. Mobile-bearing designs aim to distribute forces evenly across joint surfaces by enabling subtle insert mobility in response to knee movements, potentially mitigating wear and tear [161].

The choice between mobile bearing and fixed bearing designs depends on various factors, including the patient's condition, the surgeon's preference, and the specific implant system used [161], [170], [Surgeons #1-3]. Mobile-bearing knee implants are often considered in patients with good ligament stability, as they allow for more physiological movement and potentially lower stress on the implant components [161], [170]. However, fixed-bearing implants may be preferred in certain cases, such as patients with compromised ligament stability or specific anatomical considerations

[161], [170].

3.3 Bicruciate-Retaining

While the PCL safeguards against posterior tibial displacement, the ACL - for instance - controls anterior tibial translation and rotational stability. Traditional TKA often sacrifices the ACL to facilitate implant placement. Preserving these structures theoretically translates to a more natural knee feel and enhanced functional outcomes [158] specifically considering the substantial dissatisfaction rate in high-demanding patients [171]. Bicruciate-retaining knee implants are relatively new in TKA. While early bicruciate-retaining TKA implants have led to technical challenges and yielded variable results, recent design advancements show renewed promise for this knee replacement approach [171]. However, more systematic studies are needed to demonstrate the advantages of these implants in the short and long terms [158], [171].

3.4 Implant Fixation

Surgeons typically use cemented or cementless techniques to fix implant components to the patient's existing bone structure.

3.4.1 Cemented Knee Implant

In a cemented knee implant, a special bone cement, typically polymethylmethacrylate [158], is used to fix the implant components to the surrounding bone. The cement acts as an intermediary layer between the implant and the bone, providing a secure connection. The bone cement is applied to the prepared bone surface, and the implant components are then placed and pressed into the cement, which hardens, creating a stable bond between the implant and the bone. This method is commonly used in older patients, individuals with less bone quality, or in cases where immediate fixation is desired [8], [63], [75], [110], [121].

3.4.2 Cementless Knee Implant

Cementless knee implants are designed with porous surfaces on both the tibial and femoral components. These porous surfaces provide a rough texture that promotes bone in-growth, allowing the patient's bone to fuse with the implant over time [8], [98], [100], [121], [158]. The implant components are typically made of materials such as titanium or other biocompatible metals. This method is commonly used in younger, more active patients with good bone quality and the potential for long-term bone integration [98], [100], [121], [172].

The primary stability of a cementless implant comes from the close fit between the implant and the bone, along with the integration of bone into the porous surfaces [121]. This means that the success of the implant relies heavily on the accuracy of the surgical technique and the quality of the bone cuts. As Dr. Hannon, an orthopedic surgeon at the Mayo Clinic, states, "A cementless TKA requires increased accuracy with technique and relies on perfect cuts every time” [172].

3.4.3 Hybrid Fixation

As stated before, cemented epoxy offers immediate stability and the ability to be load-bearing, while cementless fixation promotes long-term bone preservation and mitigates potential future revisions. The hybrid fixation technique uses a cemented tibial tray for initial stability and minimizes cemented surface area by employing an uncemented femoral component. While initial reports suggest safety and reduced cement application time [173], a comprehensive understanding of its advantages and limitations requires further exploration. Hybrid fixation is a relatively new technique, and longer follow-up studies are needed to confirm its efficacy, durability, and selection criteria [174]. Therefore, this research will focus on the two traditional fixation methods for clarity.

The selection between cemented, cementless, and hybrid knee implants hinges on various factors, including patient age, bone quality, activity level, and surgeon preference. Each approach presents distinct advantages and considerations. Cemented implants offer immediate fixation and stability, but long-term durability may depend on the integrity of the cement. Cementless implants rely on bone in-growth for stability, which may take time to achieve fully, but they can provide long-term durability and potential for better bone preservation.

3.5 Gender-Specific Knee Implants

Manufacturers such as Zimmer Biomet, DePuy Synthes (a subsidiary of Johnson & Johnson), Stryker, and Smith & Nephew offer gender-specific knee implants. The anatomical differences between male and female knees primarily involve the bones' size, shape, and alignment and variations in soft tissue structures. Female knees generally have a narrower size and shape compared to male knees, with differences in the angles and slopes of the bones and ligament tensions [175]. These variations can theoretically impact joint stability, range of motion, and overall knee function. Gender-specific knee implants consider these differences by offering modifications in implant design, sizing, surfaces' shape, thickness, and contours. There is a lack of research into the comparison of various types of gender-specific implants with traditional implants [176].

3.6 Personalized Knee Implants

The field of knee implant technology has seen significant advancements in developing personalized knee implants, also referred to as patient-specific knee implants or custom knee implants. These innovative implants are designed to address the individual anatomical characteristics of patients, offering a tailored solution for optimal fit and alignment. Unlike standard off-the-shelf implants, personalized knee implants are created based on preoperative imaging data, such as Magnetic Resonance Imaging (MRI) or Computed Tomography (CT) scans, which enable a detailed analysis of the patient's knee anatomy.

Some of the benefits of personalized knee implants include enhanced fit and alignment, which theoretically contribute to improved functional outcomes and a more natural post-surgical experience. Personalized implants prioritize the preservation of healthy bone and minimize the removal of vital structures during surgery, leading to the potential for improved implant longevity.

The fabrication of personalized knee implants involves advanced manufacturing techniques such as additive manufacturing. This technology incorporates 3D hierarchical porous structures [177], [178] that mimic natural bone. This porosity plays a crucial role in promoting osseointegration, which offers a promising step towards improved bone growth, fixture, and longevity of the TKA surgery for patients. Traditionally, Micro-arc oxidation (MAO) has been used to enhance the building of porous titanium and titanium alloy structures used in TKA implants. In [177], Wang et al. offer a comprehensive overview of MAO's synergy with other technologies employed in the development of improved implants (see Table 3-1).

MAO combined with other treatments	Substrate	Surface morphology	Outcome	References
Combined application of MAO and hydrothermal method	3D-printed Ti6Al4V scaffolding	Micro-nano hybrid coating with moderate roughness	Enhance biocompatibility, osteogenesis, and osseointegration	Huang et al. (2021)
	3D Printed Macroporous Ti6Al4V Implants	Nanofibers on microporous walls	Improve three-dimensional porous Ti64 scaffold apatite *in vitro* and osseointegration *in vivo*	Xiu et al. (2017)
Combined application of MAO and ultrasound	Ti6Al4V alloy	Homogenized coating structure	Improve corrosion and wear resistance of coating	Xu et al. (2021)
Combined application of MAO and laser	Ti6Al4V titanium alloy plate	Microgrooves reduce liquid-solid contact angle and boost surface roughness	Significantly increase the proliferation and differentiation of MC3T3-E1 cells	Zheng et al. (2020)
	Ti6Al4V alloy	Pores are uniformly distributed, tiny, and thick	Higher hardness and better wear resistance	Wu et al. (2020)
MAO and bacteriostatic treatment	Grade 4 quality Cp-Ti discs	Adding calcium, phosphorus, and silver ions	Improve antibacterial efficiency while maintaining biological activity	Teker et al. (2015)
	Ti6Al4V titanium discs	Hydroxyapatite (HA) and Ag+	Good antibacterial activity	Muhaffel et al. (2016)
	Commercially pure titanium	Micro-porous with pore diameters of 1–4 µm	Reduce planktonic bacteria and *Staphylococcus aureus* in culture	Zhang et al. (2016)
	Ti6Al4V	Surface becomes smoother as pores get smaller and more average	Ti-MAO-Cu_2O group has the strongest antibacterial ability	Zhao et al. (2016)
	Ti6Al4V plate	Porous, uneven microstructure	Reduced planktonic and bacterial adherence	Zhou et al. (2019)
	Commercial Ti6Al4V plates	Double-layer structure, outer amorphous, inner polycrystalline	Good antibacterial activity is related to its strong electronic storage capacity	Wang et al. (2021c)
Combined application of MAO with sand blasting and acid etching	Titanium discs	Irregular valleys, micropores, and roughness	Enhanced biocompatibility, favourable for osteoblast differentiation	Deng et al. (2010)
MAO combined with other bioactive factors	3D-printed 600 µm pore Ti6Al4V plate	A numerous homogenously distributed pores	Promote osteogenesis and angiogenesis	Teng et al. (2019)

Table 3-1 Summary of Applications combined with MAO used in knee implant [177].

Chapter 4

Surgeon Assisting Tools and Methods

4.1 Imaging

Before a TKA procedure, an intricate model of the patient's knee is created through one of various imaging techniques, such as X-rays, CT scans, and MRIs. This detailed model serves as a roadmap for surgeons, enabling them to create a personalized surgical plan that guides critical aspects of the procedure, including bone resection, alignment corrections, and adjustments. These factors play a significant role in determining both the immediate and long-term outcomes of the TKA [18].

X-rays are the most frequently used imaging mode in TKA and serve as the first method of visualization. They provide basic bone anatomy, depicting joint spacing, patient leg deformity, and insights into the severity of advanced osteoarthritis [18]. However, X-rays have limitations in supplying comprehensive 3D anatomical information, such as soft tissue balancing and abnormalities, which are crucial for a complete understanding of the patient's knee.

To overcome these limitations, CT scans are often employed. A CT scan utilizes X-ray images captured from various angles around the body, which are then combined through computer processing to generate cross-sectional views or "slices" of the internal structures [179]. This technology includes bones, blood vessels, and soft tissue, offering a level of detail that surpasses standard X-ray examinations. CT scans excel at depicting bony structures, allowing for precise measurements and the creation of patient-specific 3D models. These models are essential for the development of personalized surgical plans and the selection of appropriate implant sizes and positioning.

Figure 4-1 showcases Stryker's Mako robot-enhanced planning screen based on preoperative CT. This technology allows surgeons to assess implant sizing, initial implant positioning, and finalize their preoperative plan [2].

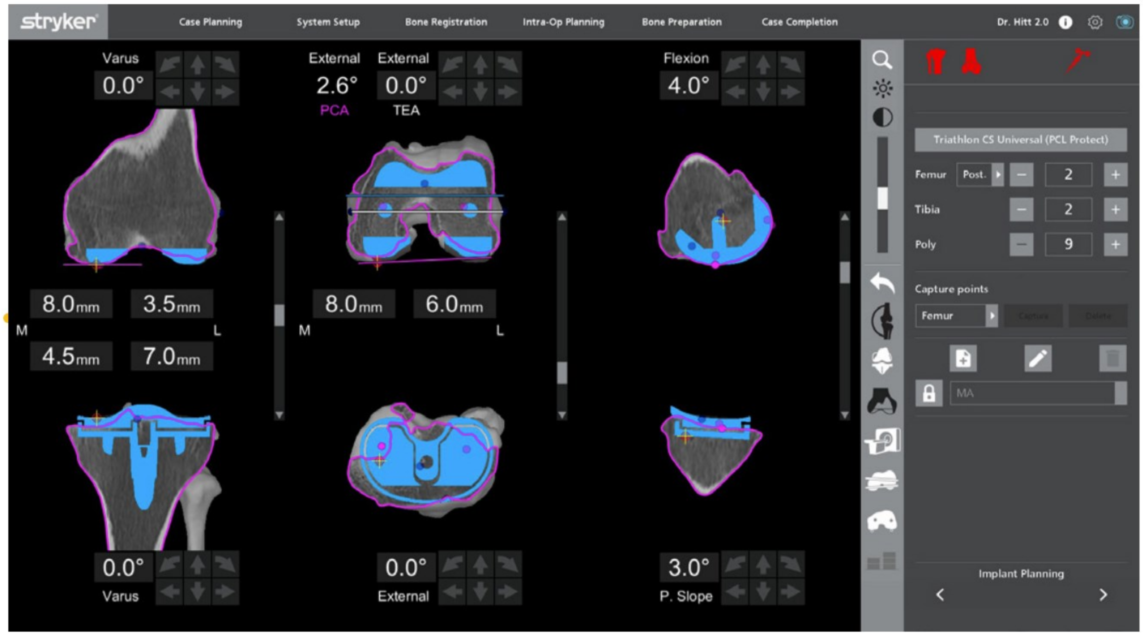


Figure 4-1 Mako Total Knee 2.0 3D CT-based pre-planning [2].

Fluoro imaging, or fluoroscopy, is an advanced medical imaging technology that provides real-time X-ray visualization of internal body structures. This technology allows for dynamic observation and guidance during surgeries and diagnostic tests. The system employs an instrumented image intensifier, capturing a series of images with specific markers that facilitate tracking of the instrument's position relative to the captured images [180].

In contrast, MRIs are utilized to visualize the joint’s bone structure and its soft tissues, which can be essential for assessing ligament integrity and cartilage damage. Due to its high cost, MRI technology is predominantly used for post-operation diagnostics. This includes identifying infections and evaluating loosening, wear, or malalignment following knee arthroplasty [18].

4.2 Computer-Assisted Surgery (CAS)

The use of computer navigation systems in TKA has seen a notable increase in recent years. First performed in Grenoble in 1997 by Drs Saragaglia, Picard, and Lebredonchel [181], these systems use preoperative or intraoperative imaging to create a virtual 3D model of the patient's knee, which then guides the surgeon throughout the procedure [18], [181], [182]. These navigation systems can be classified into two main categories: large-console and accelerometer-based hand-held navigation systems [182].

Large-console navigation systems for surgery are categorized into image-based and imageless systems. Image-based navigation systems utilize preoperative CT scans, fluoroscopy, or MRI to construct a 3D model of the patient's knee. This model is registered to the patient's anatomy during surgery using reference markers placed on the bone [18]. The surgeon can then employ the navigation system to guide bone resections, implants, and positioning. Imageless navigation systems do not require preoperative imaging. Instead, they rely on intraoperative patient anatomy registration using a combination of anatomical landmarks and kinematic data [18]. The surgeon can then use the navigation system to guide the procedure in a manner similar to image-based systems.

A large-console intra-operative navigation system consists of trackers, a localizer, and a computer workstation (shown in Figures 4-2 and 4-3). Trackers, which may be affixed to bones, surgical tools, or a probe during the procedure, are differentiated into 'passive,' typically reflective spheres, and 'active,' equipped with LEDs [183]. The localizer, often an optical camera, captures signals—either reflected from passive trackers or emitted by active ones—to ascertain their spatial positioning [183].

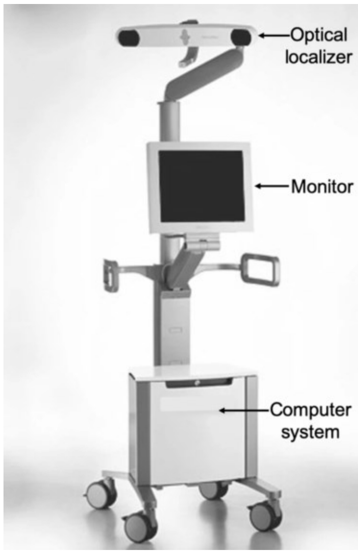


Figure 4-2 Large-console navigation system components [183]

Optical localizers are prevalent due to their efficiency, though they necessitate an unobstructed line of sight to the trackers for accurate detection. In contrast, electromagnetic systems possess a receiver capable of detecting tracker signals even without direct visibility, offering an alternative when line-of-sight maintenance is challenging. Figure 4-3 depicts how optical trackers are slotted into the cutting guide that is pinned to the femoral (A) or tibial (B) bone.

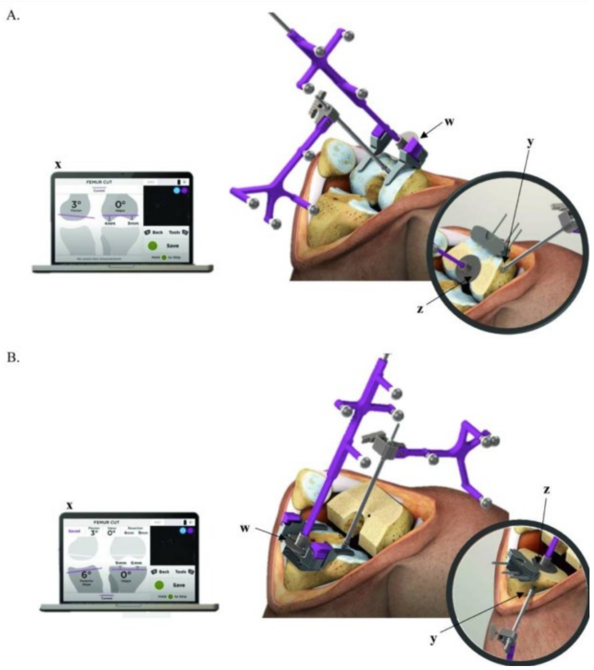


Figure 4-3 Imageless computer navigation device [184]

Handheld accelerometer-based navigation (ABN) tools have garnered attention in the TKA field as a noteworthy innovation, particularly for their cost-efficiency, as they eliminate the need for the significant capital expenses associated with surgical robots. Moreover, these tools do not require pre-operative imaging and are compatible with any standard implant, broadening their applicability and making them a versatile option for global use. However, these devices do not provide the sizing and visualization of the implant position with respect to the patient’s anatomy, osteophyte surface site visualization, and maintaining the position of the cutting tool that robotic surgery could potentially offer [195].

The Lantern® device, developed by OrthAlign, is a handheld navigation tool that calculates the angles required for femur and tibia resection, serving as a single-use device that works with all standard implant systems and provides intra-operative data on the patient's flexion and extension gaps.

Figure 4-4 Lantern® by OrthAlign. Credit OrthAlign website

Lantern® - compared to its predecessor KneeAlign® (shown in Figure 4-5)- has soft-tissue ligament balancing as an extra feature that facilitates the surgeon in achieving a balanced knee during their TKA surgery. Ligament balancing stands as a critical yet challenging objective, significantly affecting the surgery's outcome. Traditionally, experienced surgeons have depended on their intuitive sense to achieve this balance rather than a scientific perspective [5], [185]–[188]. The comfort caused by ligament balancing is influenced by various factors, including the patient's body composition, gender, joint laxity, degree of contracture, surgeon’s experience, and even the surgeon's daily condition [5], [189], [190]. This underscores the need for more research with an objective, scientifically grounded approach to ligament balancing in TKA procedures, as poor ligament balancing can lead to undesirable outcomes such as post-operative instability, stiffness, and discomfort, potentially necessitating revision surgery [5], [191].

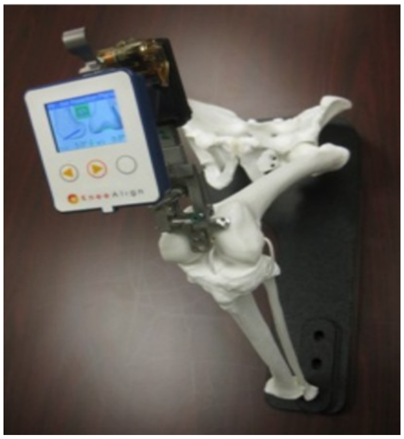


Figure 4-5 OrthAlign KneeAligh 2 system attached to a knee model. Credit: OrthAlign.

VeraSense by Stryker is another intra-operative tool that facilitates soft-tissue balancing. Its single-use sensor transmits quantitative real-time data wirelessly to an intraoperative monitor. Sava et al. have mentioned in [126] that employing VeraSense pressure sensors in TKA does not significantly enhance ROM, reoperation rates, or functional outcomes compared to conventional manual balancing techniques. Nevertheless, a notable decrease in manipulation under anesthesia (MUA) rates was observed in the group using VeraSense [126]. However, this factor might not justify the additional cost of using VeraSene as an individual tool in TKA surgery.

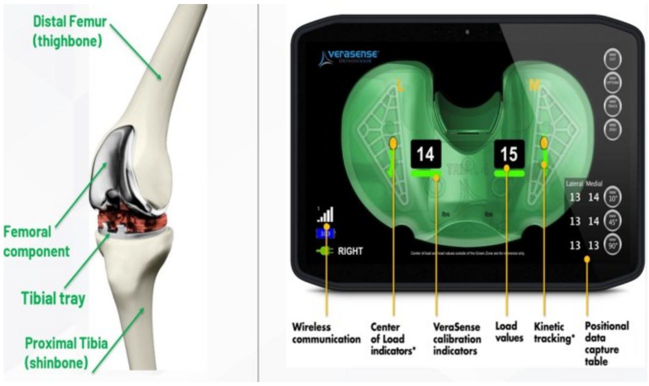


Figure 4-6 VeraSense by Stryker. Credit: Stryker

4.3 Robotic-Assisted Surgery

Robotic Total Knee Arthroplasty (RTKA) is a promising technology with vast potential. It integrates navigation technology with the robotic execution of bone resection, all under the surgeon's control. Using a preoperative or intraoperative mapping to plan the procedure in RTKA theoretically ensures that the outcome does not deviate from planned cutting planes and potentially enhances surgical precision. RTKA has come a long way from its early development in the 1980s, when the ACROBOT system was used for TKA surgery in 1988 in London [12]. Later, the ROBODOC system – initially designed for hip surgeries – was the first surgical robot approved by the FDA in 2008 and used in clinical settings [17]. One of the key advantages of robotics in knee arthroplasty is its ability to provide accurate and consistent bone resection through a robotic interface, regardless of the specific robotic system used [4], [16], [18], [20].

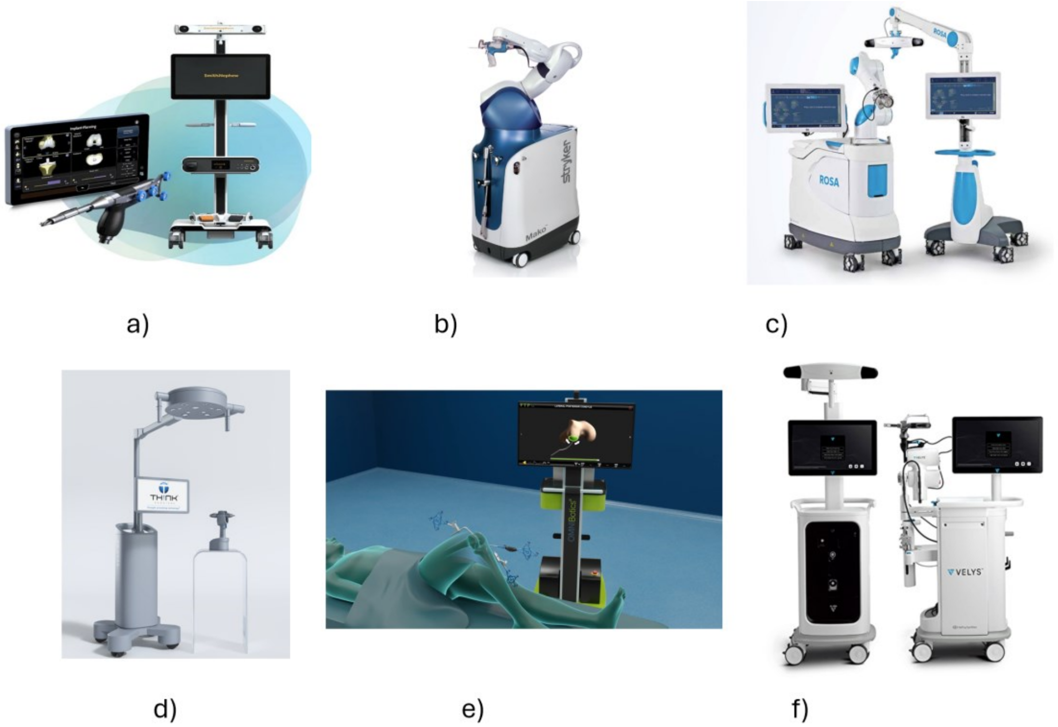


Figure 4-7 a) Smith+Nephew's CORI b) Stryker's Mako Total Knee 2.0 c) Zimmer Biomet's ROSA d) Corin Robotics' OMNIBotics e) Think Surgical's TMINI f) DePuy Synthes' (J&J) Velys surgical systems. Credit Smith +Nephew, Stryker, Zimmer Biomet, Think Surgical and DePuy Synthes(J&J)

Modern TKA robots, such as MAKO (Stryker), ROSA (Zimmer Biomet), OMNIBOT (Corin), TSolution One (Think Surgical), and Velys (Depuy Synthes, Johnson & Johnson), have all improved surgeons' ability to have better bone preparation accuracy and implant positioning. Many of these robots use a 3-dimensional model (either created by preoperative imaging or intraoperative mapping), can provide the haptic interface, and stop the procedure if the bone resection starts to deviate from the planned angle by a certain error margin. Others provide means to control the exposure and speed of the burr used by the surgeon and can incorporate a variety of prosthetic brands [6], [11], [20]. Table 4-1 incorporates technology differences between some of these surgical robots.

Variable	Mako™	CORI™	ROSA™	Tsolution One™	TMINI™	OMNIBotics®	Velys™
Manufacturer	Stryker	Smith+Nephew	Zimmer Biomet	Think Surgical	Think Surgical	Corin Robotics	DePuy Synthes (Johnson & Johnson)
Mapping	CT+ mapping	Imageless mapping	Plain film radiographs using 2D x-rays producing 3D replication	CT + mapping	CT + mapping	Imageless mapping	Imageless mapping
Planning	Preoperative	Only intraoperative	Pre- and intraoperative	Preoperative	Preoperative	Only intraoperative	Only intraoperative
Implant	Brand restricted	Brand restricted	Brand restricted	Implant database	Implant database	Brand restricted	Brand restricted
Measured resection	yes	yes	yes	yes	yes	yes	yes
Functional Alignment	yes	yes	yes	N/A	N/A	Yes, using Balancebot™	yes
Footprint	> 1 m^2	0.5 to 1 m^2	> 1 m^2	> 1 m^2	< 0.5 m^2	0.5 to 1 m^2	< 0.5 m^2

Table 4-1 Summary of Robotic-Assisted Systems. Core resource: [21], other resources credited to the manufacturers' website.

One of the benefits of robotic TKA is its ability to achieve more precise implant placement. By utilizing preoperative imaging data, robotic systems can create individualized surgical plans that account for the patient's unique anatomy [128], leading to better alignment of the implant components, improved joint stability, and reduced risk of complications [129]. The robotic system guides the surgeon in making precise bone cuts and ligament adjustments, ensuring that the soft tissues around the knee joint are correctly balanced [128]. This delicate balance is important for maintaining optimal joint function and minimizing postoperative pain [131]. However, there are still opportunities to improve these features further by incorporating additional technologies. As data has shown improvement in the alignment and functionality of outcomes [13], more studies are required to assess the effect of TKA robotic surgery on the long-term survival and longevity of the implant for the patient [18].

The substantial costs for acquiring and maintaining robotic systems for robotic-assisted TKA and initial longer surgery times for new users pose challenges [192]. However, (as seen in Figure 4-8), with experience, the efficiency of robotic-assisted TKA can match conventional methods [193], [202].

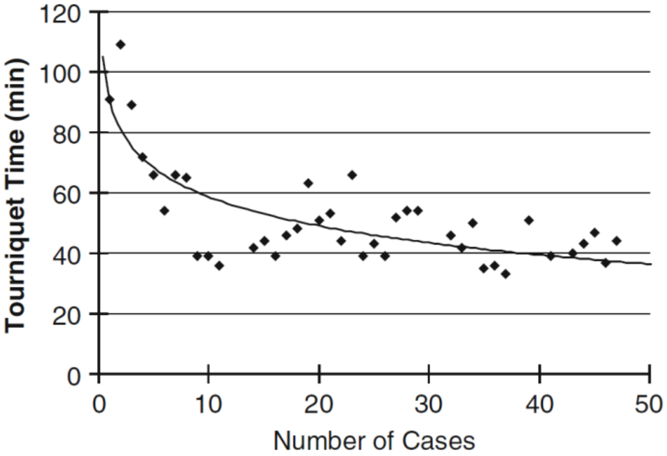


Figure 4-8 New-user learning curve using MAKOplasty [202]

Economic factors may limit RTKA's adoption in many hospitals or ASCs, yet advancements and integration of technology could offer solutions for more cost-effective and widespread use.

4.4 Artificial Intelligence, Augmented Reality, and Virtual Reality Assistance

AI holds the potential for automating tasks and forecasting outcomes beyond human capabilities. However, the data currently available in healthcare - laden with historical patterns and prejudices - may affect the accuracy and introduce biases into AI algorithms. As AI continues to advance rapidly, it raises concerns about data biases and the necessity of safeguarding information. The lack of detailed insight into the patterns of use for the technologies and methods mentioned in this chapter and their effects in the short, medium, and long term remains a critical gap for using AI algorithms. Despite these challenges, AI's capacity for automation and prediction in TKA offers significant potential for the efficiency of surgeries and the quality of patient outcomes, from implant choice to robotic surgical method and plan adaptation. For example, at AAOS 2024, Smith+Nephew presented its AI-powered Personalized Planning software "as guidance for planning and enables surgeons to set preferences for initial implant starting positions that are customized to patient deformity" [194]. The updates include RI.KNEE software for joint line restoration and the AI-enhanced Cori robotic-assisted solution for image-agnostic surgery personalization are pending further FDA clearance.

The US's first augmented reality knee replacement surgery was performed by Dr Vigdorchik of New York City's Hospital for Special Surgery in 2021 [196]. He used Medacta's NextAR augmented-reality platform, first used in Australia in 2020 [196]. Augmented reality utilizes digital overlays, such as 3D images, through headsets to enhance the surgeon's view. This technology allows surgeons to accurately follow pre-defined operational plans directly within their field of vision. Research is ongoing to study the potential of augmented reality to shorten surgery durations and enhance patient outcomes.

At AAOS 2024, Stryker showcased the myMako app [195], compatible with Apple Vision Pro and iPhone. This app allows surgeons to immerse themselves in reviewing and visualizing Mako surgical plans from anywhere in a dynamic 3D environment. This can potentially enhance surgeons' preoperative planning and intraoperative experience.

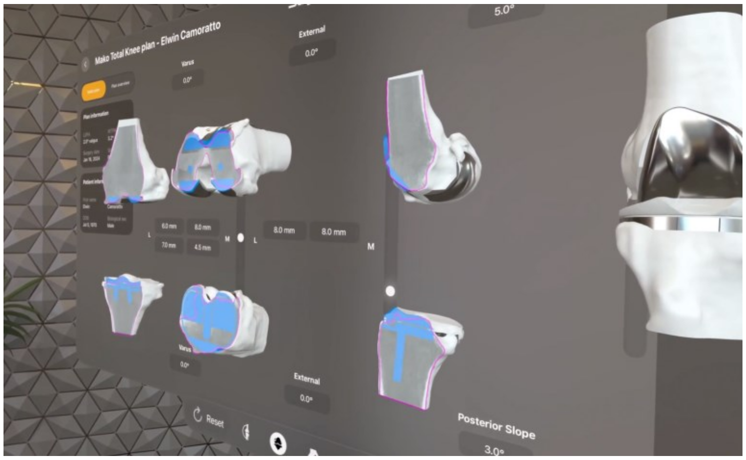


Figure 4-9 "Stryker's myMako app extends a surgeon's experience in and beyond the operating room with Apple Vision Pro and iPhone" [195]

Training with virtual reality (VR) in TKA is becoming increasingly common, offering surgeons a highly immersive environment. VR training systems, such as those developed by Osso VR, allow for precise simulation of surgical procedures, enabling surgeons to refine their skills and techniques in a risk-free setting through interactive, hands-on experience, potentially shortening learning curves and improving surgical outcomes. Osso VR introduced the Hand Control feature, a controller-free feature for its VR surgical training, utilizing headset cameras for hand movement tracking in 2024 [197].

4.5 Knee Alignment

Achieving a stable and functionally aligned knee that would last for long has been a fundamental objective of TKA due to its believed importance in clinical outcomes and implant longevity. Mechanical Alignment (MA) techniques focus on creating a “biomechanically” optimized prosthetic knee rather than restoring original patient-specific anatomy [198]-[200]. Despite MA's contribution to implant survivorship, it has resulted in suboptimal functional outcomes and patient satisfaction [198]. Consequently, there's a growing interest in more anatomical surgical approaches aiming to enhance knee kinematics and improve TKA results, challenging the traditional MA strategy's effectiveness.

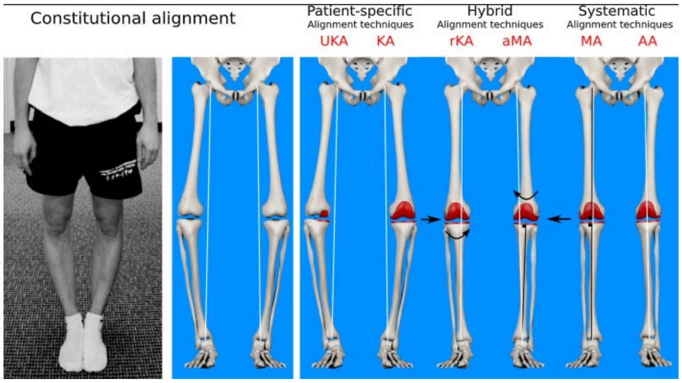


Figure 4-10 To illustrate this classification, a knee with severe constitutional varus deformity has been selected. MA: Mechanical Alignment technique; AA: Anatomical Alignment technique; aMA: adjusted Mechanical Alignment technique; rKA: restricted Kinematic Align

Figure 4-10 depicts the four alternative TKA positioning techniques— Anatomic Alignment (AA), Adjusted Mechanical Alignment (aMA), Kinematic Alignment (KA), and Restricted Kinematic Alignment (rKA) — as alternatives to the traditional MA approach. Rivière st al. show in [198] that the KA technique is noted for promoting quicker recovery and improved functional outcomes compared to MA. However, severe deformity might necessitate the use of the rKA technique or additional interventions for certain patients [198]. Innovations in implant design specific to the KA technique could further enhance TKA results, and future research with extended follow-up is essential to ascertain the comparative effectiveness and appropriate applications of these alternative surgical strategies. We will focus on MA, KA, and rKA methods as the most commonly used methods these days.

The KA technique for TKA represents a more anatomical approach, akin to hip resurfacing, aimed at preserving individual pre-arthritic limb alignments and knee laxity. This patient-specific, ligament-sparing method does not require complex preoperative planning [198]. It involves precise bone cuts with the facility for intraoperative adjustments, utilizing new landmarks for setting the 3D orientation of implants. Unlike MA, KA focuses on full anatomical positioning, differing in all aspects except the sagittal positioning of the femoral component [198]. The rKA technique offers a balanced approach for TKA, employing computational surgery for precise alignment. It's primarily indicated for minor deformities (≤3° in the limb, <5° in joint line obliquity) to maintain within a "safe alignment zone" [198]. Bone cuts are adjusted accordingly in cases outside this zone, which is roughly one-third to half of all cases. rKA adapts the core principles of KA, prioritizing femoral kinematics and adjusting tibial positioning for alignment correction [198].

4.6 Post-op Sensing and Data Analysis

Postoperative care and rehabilitation exercises following TKA are crucial for successful patient outcomes and enhanced quality of life. Healthcare providers can remotely monitor patients' recovery progress in real-time by employing digital health technologies, such as smartwatches or other wearable devices and mobile applications. Additionally, this capability allows the care team to promptly identify deviations from expected patient mobility patterns, detect complications, and enable interventions for in-person office check-ups.

In 2021 Crawford et al. demonstrated that using smart watches could enhance recovery after TKA [206]. Wearable devices equipped with accelerometer-based sensors gather data on patients' range of motion, walking speed, and daily step counts. This data, combined with other manually entered patient recovery information such as pain scores and surgery site photos, can be periodically sent to care staff or downloaded during office visits to track recovery progress after knee replacement surgery effectively. The information collected helps healthcare providers set benchmarks for recovery following the procedure. MotionSense by Stryker (seen in Figure 4-11) exemplifies such a wearable, providing customized exercises for patients while capturing their data [205].

Figure 4-11 MotionSense by Stryker [205]

This approach facilitates timely interventions personalized rehabilitation plans and enhances patient engagement in their recovery process. Moreover, remote monitoring can potentially reduce the need for in-person visits, making post-operative care more efficient and accessible for patients [203], [204].

In 2021, Zimmer Biomet introduced the first commercially available smart knee implant, Persona IQ® [149], shown in Figure 4-12. The device transfers the patient’s kinematic data to the care team a few days after the surgery. The interval between the data transmission gets longer through the transmitter’s claimed lifetime of at least ten years [149]. The accelerometer data can also provide the movement pattern and potentially predict implant loosening.

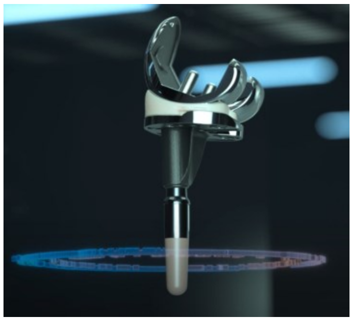


Figure 4-12 Smart knee implant, Persona IQ® by Zimmer Biomet [149]

Many challenges regarding postoperative patient monitoring still need to be addressed. Compared to smart knee implants, wearables offer a greater degree of freedom in terms of technology updating feasibility, ease of battery charging, and lower costs. According to Gartner [134], one in three patients forget to wear their trackers. Moreover, optimal sensor location and variability of the location change have been another challenging issue in extracting meaningful data from these post-op TKA wearable sensors.

The main constraints of smart knee implants include the limited space available to accommodate the sensing circuitry, particularly the battery. This requires the development of more integrated and compact sensors with ultra-low power consumption and advanced battery management systems (e.g., better rechargeable battery solutions or energy harvesting technologies) by the semiconductor industry. Like many wireless medical devices, data security is another critical challenge that must be addressed with wireless data transmission to the cloud.

In [147], Kelmers et al. summarize further enhancements and potential features that could be added to smart knee implants. These enhancements include measuring load [66] and its distribution and initiatives similar to BonTag’s temperature and force sensing [31]. Future developments may also include in-vivo automatic height adjustment of either the medial or lateral tibial compartment [27], detection of implant loosening using temperature measurements [25], magnetic sensors [143], and embedded transducers

[144]. Additionally, the possibility of detecting tibial insert wear through capacitive sensors [145] and optical sensors [146] is discussed.

The field of remote patient monitoring is promising as it offers real-time monitoring, potential early detection, and lowering the overall cost, but it also provides customized care plans and frequent patient feedback and education. In 2023, the Centers for Medicare and Medicaid Services (CMS) allowed New Technology Add-on Payments (NTAP) for the use of Persona IQ® The Smart Knee® for FY 2024.

Chapter 5

Tradespace Analysis

The successful outcome of a TKA operation hinges on many aspects, including the type of prosthesis and its precise positioning, accurate balancing of flexion-extension gaps, ligament tensioning, and soft tissue preservation. Understanding the tradeoffs and coupling between these decisions and evaluating the magnitude of the weight each set of these decisions affects patients' outcomes is important.

5.1 Concept Generation

The architectural decisions chosen here to generate a concept for the tradespace are identified by literature research and interviews with orthopedic surgeons (refer to Appendix), where the current state of TKA and the role of technology in its improvement were discussed. Table 5-1 depicts the Architectural Decisions with the TKA system and the set of currently available attributes in this system.

Architecture Decisions	Option 1	Option 2	Option 3	Option 4
Patient's Age	Adult <~65	Senior		
Implant	Porous Implant Technology and sized	Off-the-Shelf and sized		
Implant Fixation	Cemented	Cementless		
Robotic Assistance	Yes	No		
Computer Assisted Mapping	3D	Xray	Intra-operative	None
Intra-operative Alignment Tools	Bone alignment	Bone and soft-tissue alignment	AR with bone and tissue alignment	None
Surgeon Alignment Method	MA	KA	rKA	

Table 5-5-1 TKA Morphological Matrix

5.2 Limitations and Constraints within TKA System

As mentioned before, the patient’s anatomical and biological factors greatly influence implant size and fixation type. For example, cementless implants are typically preferred for younger, more active patients due to their potential for better bone growth, catering specifically to this demographic's biological needs and lifestyle demands [98], [100], [121], [172]. However, the decision-making process regarding implant selection is influenced by a variety of other constraints within the healthcare system.

Firstly, insurance policies and reimbursement models (e.g., bundling) affect hospital protocols and the emphasis placed on certain types of care or technologies. The extent of insurance coverage often dictates which implants and surgical interventions are accessible to patients. Secondly, the training and experience of surgeons with specific implants or surgical robots also play a crucial role. Surgeons, understandably, tend to favor devices with which they are most familiar and skilled as they consider the impact of care delivered to their patients. Furthermore, hospital-vendor relationships are another critical factor. Hospitals typically have contracts with specific vendors based on their variety of tools, services, and prices. The presence and influence of vendor representatives—who are often key sources of support and information to surgeons and care teams—can sway decisions based on their reliability and helpfulness. Lastly, the type of surgeon-assisted robot available in a hospital can also constrain choices, as many robotic systems are designed to be compatible exclusively with their manufacturer’s implants, limiting the range of options for TKA procedures. Figure 5-1 highlights some of the complex interplays in the selection of orthopedic implants and associated technologies.

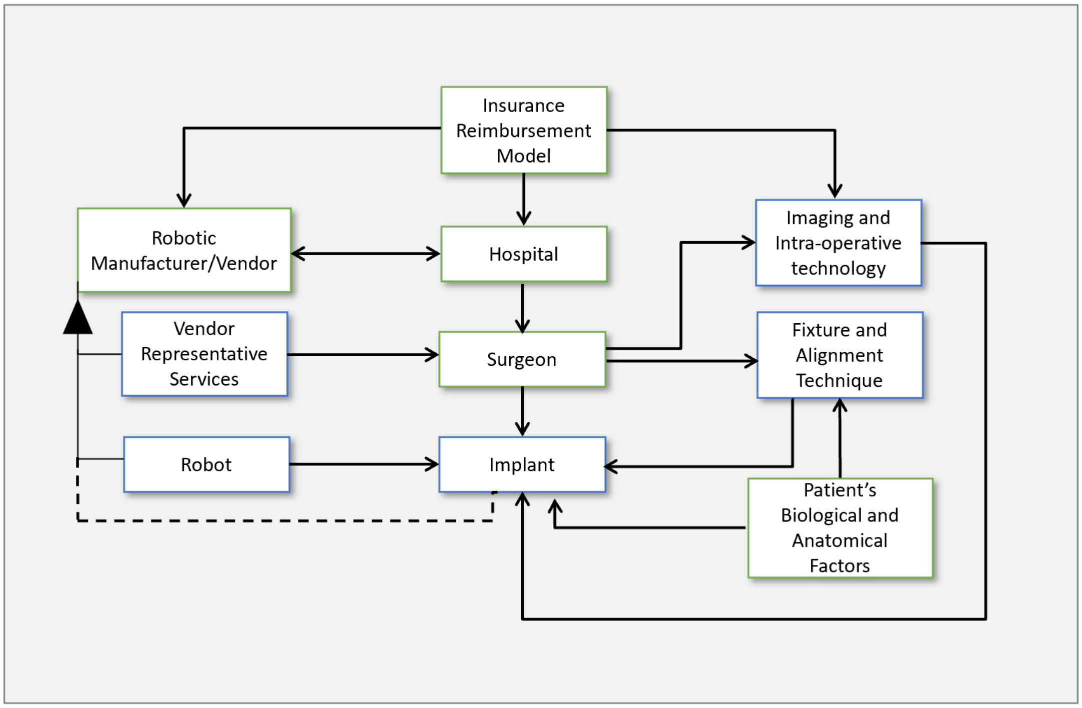


Figure 5-1 Complex interplays in selecting orthopedic implants and associated technologies.

5.3 Understanding TKA FOMs

The metrics by which the performance of the TKA is measured are based on the patient's outcome, where early functionality and longevity are considered the most impactful outcomes in a TKA system. This section analyzes the impact of each decision in the morphological matrix of the TKA on early functionality and longevity.

Age

In general, younger patients have shown better early functional outcomes compared to older patients. For example, big improvements have been seen in the ROM [22], patient-reported outcomes (PROs) [23], walking speed and stair climbing ability [24], and smaller but substantial improvements in the younger demographic's satisfaction [26].

Some studies show evidence that older patients generally have a higher 10-year survival rate, a lower 10-year revision rate, slower improvement in function, and higher patient satisfaction compared to younger patients [32]-[36]. For example, Perdisa et al. mentioned in [32] a higher 15-year survival rate (94.8%) in older patients (≥66 years) compared to younger patients (<50 years) with 78.7%. However, other research indicates no difference in long-term outcomes [37]-[41].

Implant

As discussed in previous chapters, there are many types of implants with various brands, sizes, features, and materials. When selecting implants for their patients, surgeon's personal experience and success with particular implants play a critical role, guiding their decisions based on past outcomes and familiarity with the product. We assigned two attributes to this architectural choice in our system: Off-the-shelf sized implant and Personalized porous implant. The assumption is that the surgeon chooses an anatomically compatible implant (sized) and durable (per patient's age), as ample choices satisfy these assumptions these days for a TKA candidate. However, the personalized implant (currently using additive manufacturing/3D printing) will provide more precision and customization, potentially and theoretically providing more anatomical compatibility on the patient's bone and soft tissue structure and the surgeon's bone resection pre-operation plan.

The research on the benefits of personalized implants using 3D printing shows a mix of evidence of their effect on early functionality. Some studies have reported improved early functionality with these personalized implants, such as shorter hospital stays and faster return to normal activities [82]-[84]. The studies have noted the promotion of osseointegration with their porous structure, where the bone growth improves the implant's stability and reduces the risk of revision surgery [85], making it more beneficial for patients with significant bone defects [86], [87]. However, other research has found no advantageous difference [88]-[95], including short and mid-term functionality [89], [90] or kinematic alignment improvement of the patients [94] compared to off-the-shelf conventional joints. There is a lack of adequate research into the effect of personal implants on TKA patients' longevity. However, controlled porous 3D structures in knee joints have shown a reduction in stress shielding [96] and excellent mid-term ingrowth [97], [98]. On 3D implants, we will focus on the effect of their porous coating and the comparative lack of this option for other sorts of implants.

Implant Fixation

As the traditional method of fixation in TKA for many decades, cemented bonding provides an early strong and durable fixation between the implant and the bone [cite], where it has a significant effect on patients with poor bone quality and offers compensation for inaccurate resection [100]-[104]. However, there is moderate aseptic loosing and implant debonding of cemented fixtures [100], [105], [108], which particularly increases in the long term. Advancements in implant design and materials have prompted more adoption of cementless fixation, especially among younger, active individuals and patients with higher BMIs [100], [112], [113]. Studies comparing cemented and cementless fixation have shown comparable outcomes in terms of in-hospital pain scores, opioid use, and early postoperative PROMs [7]. Additionally, recent research in [110] indicates similar revision rates for cemented and cementless TKA, with cementless TKA demonstrating significantly more long-term functional recovery. Recently, Gibon et al. demonstrated that within 389 randomized clinical trials, the cementless TKA had an excellent outcome at a 10-year checkpoint [121].

Computer Assisted Systems

Jones and Jerabek conclude in [182] that numerous well-conducted studies support the conclusion that the use of both traditional large-console CAS and more recent handheld navigation systems enhances the precision and accuracy of component alignment in TKA.

Despite this technological advancement, the literature lacks definitive evidence showcasing their clinical benefits, such as enhancements in patient-reported outcomes or a reduction in long-term revision rates.

While the importance of precise alignment is widely acknowledged, the significant costs associated with large-console CAS systems remain a major barrier to their widespread adoption [182]. In contrast, the advent of more affordable handheld CAS navigation tools offers a potential solution to this challenge, promising to fill this critical gap. In [5], Batailler et al. provided an overview of using bone alignment tools and their functional outcome till early 2021, from revealing inconsistency and no significant improvement in [115] by Budhiparama et al. to questioning its impact on short-term functional outcomes [116], to their significant value in challenging and complex TKA in [117], [118]. As mentioned in [5], the accuracy of the current bone alignment system is tied directly to the position of reference points (set by the surgeon or staff) and the type of alignment performed. In [119], Swamy et al. indicated that there was a reduction in coronal and sagittal alignment outliers yet not in rotational alignment of their subject TKA patients in their study. Similarly, Treu et al. indicate no significant improvement in patient-reported outcomes in [120].

Soft tissue releases in TKA are performed to correct the imbalance in the femoral and tibial gaps during flexion and extension. Improper soft tissue balancing can lead to instability issues and residual pain. While intraoperative soft tissue balancing pressure sensor tools have been shown to provide more accuracy and better guidance to surgeons [122], [123], their relatively new technology and compatibility with only a few implants have led to a lack of data on their short- and long-term effectiveness [124]. Adding to this complexity is the variety of alignment methods surgeons use and their impact on short- and long-term outcomes. In 2022, MacDessi et al. reported no significant improvement in clinical and functional outcomes at the two-year mark [125] when surgeons used tissue balancing tools compared to conventional methods. Similarly, Sava et al. did not see a significant difference in the range of motion and early functionality between both methods [126]. However, Sah et al. [127] recently observed less reported pain and better early functionality within the first six weeks following surgery.

Robotic Assistance

Overall, robotic surgery has assisted surgeons in achieving better soft tissue balancing, accuracy in implant placement, and enhanced alignment, which has provided promising results in improving alignment and functionality outcomes compared to traditional TKA techniques [132], [133] and functionality of outcomes [13], yet there are still opportunities to improve these features further by incorporating additional technologies. Moreover, advancements in robotic technology could further enhance its effectiveness in TKA. The integration of haptic feedback systems, for instance, could provide surgeons with real-time tactile feedback during the procedure, allowing for better precision and control [135], [136]. Robotic surgery has shown to be a valuable tool in the armamentarium of a TKA surgeon.

However, more studies are required to assess the effect of TKA robotic surgery on long-term survival, the longevity of the implant for the patient [18], [137], and its comparison to other technologies utilized for TKA.

Surgeon Alignment Method

Although fairly new, many studies have compared the outcomes of different alignment methods in TKA. While the results are somewhat mixed, a general trend suggests that KA and rKA may offer certain advantages over mechanical alignment in terms of early functionality and pain reduction.

Studies have consistently demonstrated that kinematic alignment and rKA lead to an improved early range of motion and walking ability compared to mechanical alignment

[138]-[142]. This enhanced early functionality is attributed to the restoration of natural knee motion and improved joint congruence. In [143], Risitano et al. indicate that rKA provides equivalent or slightly better PROMs than MA.

5.4 Cost

The cost of a TKA surgery depends on many aspects, including but not limited to location, implant, facility setting (in-patient or out-patient), the new technology utilized for the surgery, sterilization, number of trays used, and operating room time. The price of readmission is not included in this thesis analysis. According to [153], "total costs per case for robotic-assisted TKA were $92,823 (low volume), $29,261 (mid volume), and $25,730 (high volume) compared with $25,113 for conventional". We consider TKA in a mid-volume setting as most hospitals do not opt for low-volume robotic TKA surgery. As the cost of cementless implants has decreased and gotten closer to the implants used with cement fixtures [100], [108], [109], and cementless TKA requires less operating room time and less material, the total cost of these two procedures has come closer to each other than before [100], [107], [108]. In [154], Christen et al. summarize the additional cost of image-based and imageless robotic surgery into $2600 and $1530, respectively.

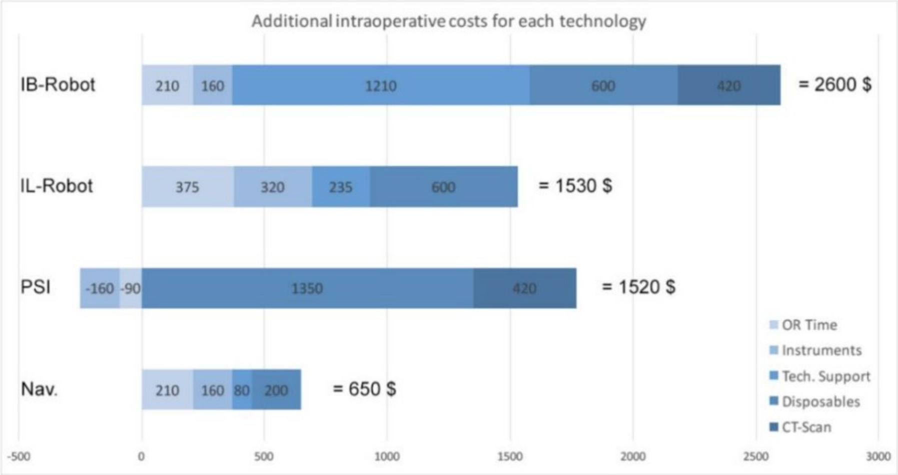


Table 5-5-2 Additional costs per TKA technology [154]

5.5 Tradespace Observations

Figure 5-3 depicts a single-attribute tradespace plot where the throughput of Early functionality is represented on the y-axis and cost is represented on the x-axis. The ideal scenario (as marked with the utopia point) would hypothetically produce the greatest throughput at the least cost. The Pareto frontier depicts scenarios with the best value at cost.

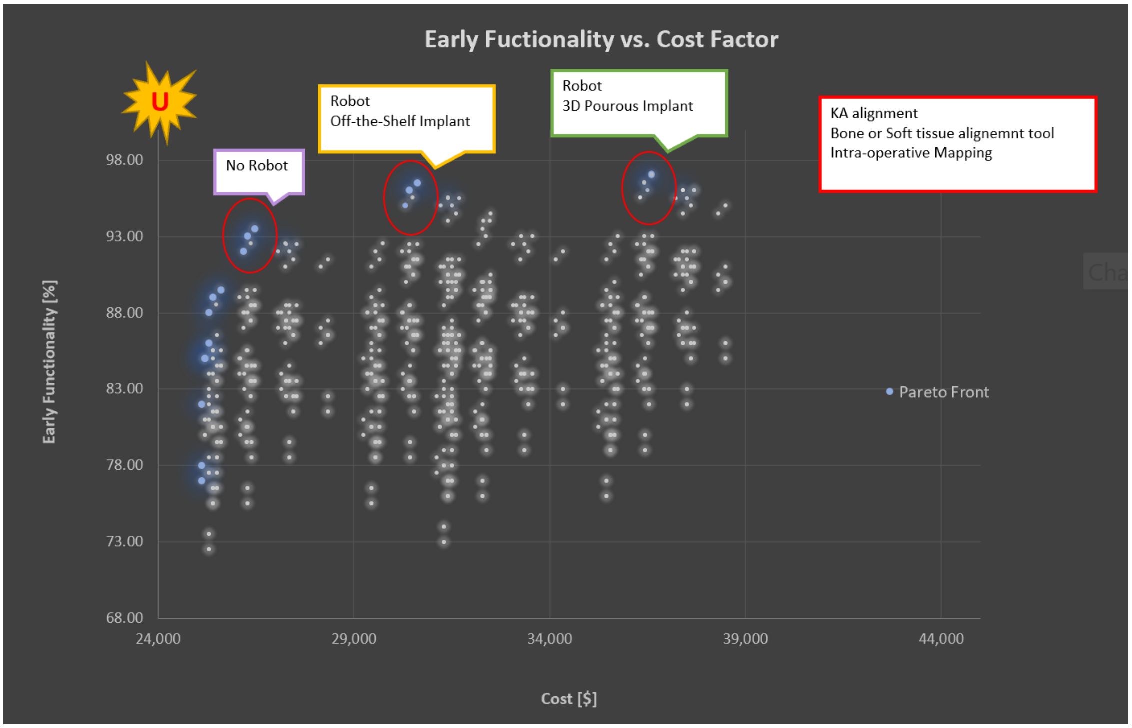


Table 5-3 Single-attribute trade space, Early Functionality vs Cost

Scenarios below the Pareto Frontier points are considered dominant scenarios. These scenarios offer less benefit at the same relative cost as scenarios on the Pareto Frontier [53]. The points belonging to the Pareto Frontier are marked blue. Some of the architectural decisions in this TKA analysis have created a clear cluster in this tradespace and are marked below.

Variables such as KA alignment, utilizing bone and tissue alignment tools, intraoperative mapping, and robotic assistance show positive outcomes in this tradespace. Even though there are opportunities to improve robotic-assisted surgery, it emerges as a precise tool in complex TKA operations, saving operating time, improving outcomes, and decreasing revision rates. While data limitations persist in identifying conclusive factors impacting TKA longevity, evidence points towards specific elements that can significantly contribute. High cross-linked polyethylene, durable metal bearings, and strong fixation techniques, particularly cementless bonding for younger, active patients, all play crucial roles in extending implant lifespan.

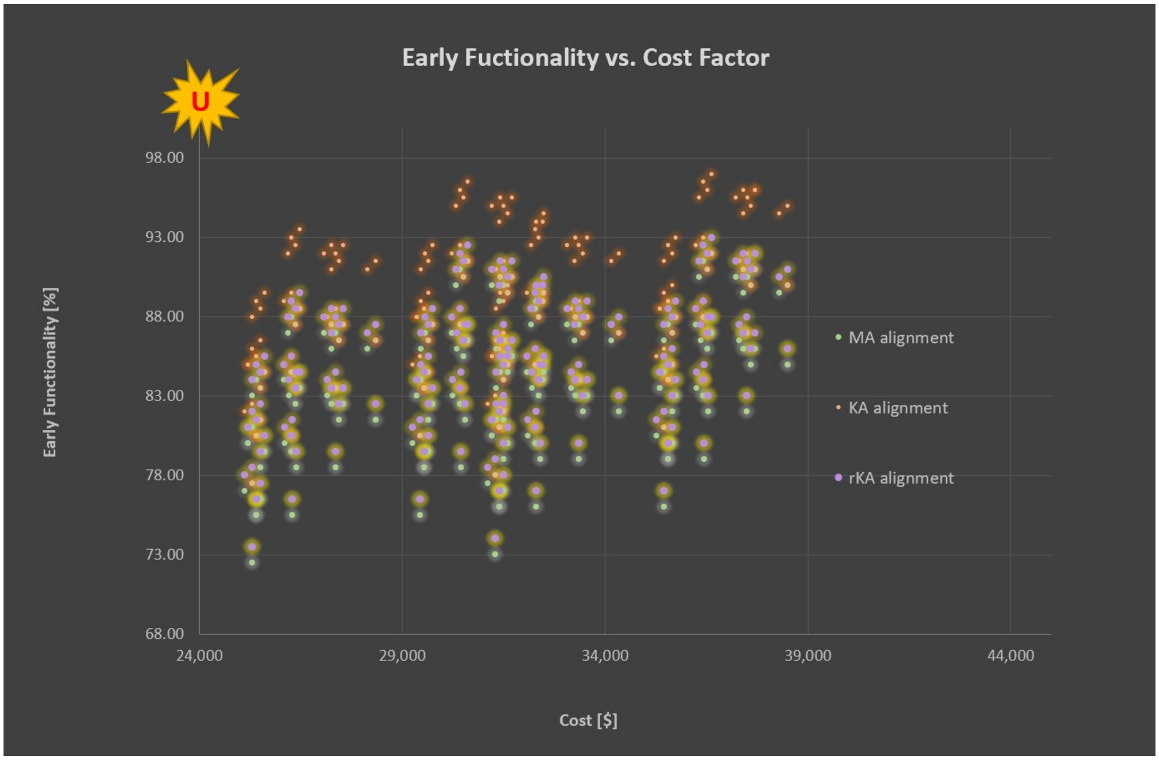


Figure 5-4 Alignment Distribution Demonstration: Single-attribute trade space, Early Functionality vs Cost.

Individualized alignment, tailored to each patient's anatomy, has demonstrably improved initial knee function. However, its long-term impact on longevity remains unclear. Further research and extended follow-up are crucial to definitively ascertain the effectiveness of kinematic alignment strategies like rKA compared to conventional KA alignment in promoting TKA longevity. Understanding these nuanced relationships between surgical techniques, implant design, and patient-specific factors requires continued and rigorous investigation.

Chapter 6

Discussion on the Opportunities and Limitations of TKAs

This chapter explores both the advancements and challenges within TKA, delving into innovation opportunities that can potentially enhance outcomes and address the limitations that currently affect the efficacy and accessibility of TKA procedures. Below are the key points discussed:

Ceiling Effect in Functionality Measurement: While significant advancements have been made in the development of tools for measuring TKA outcomes, a critical limitation remains: they often hit a ceiling effect at the high end of functionality, making it difficult to differentiate between patients with excellent knee function [Surgeon #1]. This problem is particularly relevant for younger, active individuals who naturally have higher demands on their knees than the majority of TKA recipients, who are typically older patients with lower functional needs. Consequently, current outcome measures struggle to detect subtle but potentially significant differences in functional capacity within this high-demand population. This presents a clear gap that technology can be bridged by developing more sensitive and nuanced outcome measures tailored to capture the full spectrum of functional demands in younger, active TKA patients.

Advances on Additive Manufacturing: While porous structures offer a promising avenue for improving knee implant performance by promoting bone growth and longevity, further research and technological advancements are crucial. Optimizing pore characteristics, developing fabrication methods that eliminate the residual of a fine powder, and optimizing the electrolyte composition are some of the key challenges to unlocking the full potential of this approach [177].

Soft-tissue Balancing Limitations: Soft-tissue balancing in TKA remains a critical yet subjective skill heavily dependent on the surgeon's technical expertise and experience. This lack of objective quantification often leads to inconsistent outcomes, particularly for less skilled surgeons. The need for better tools with more precision ability to assess the patient’s soft tissue highlights the need for more sophisticated technology to quantify soft-tissue properties and address inconsistent outcomes. One example would be measuring force and tension on medial-lateral tissue. While the theoretical potential of sensor-guided soft-tissue balancing in TKA is promising, its clinical efficacy remains unclear. Concerns surround the lack of direct translation between improved intraoperative measurements and demonstrably better long-term patient outcomes. Furthermore, given the increased complexity (operating room time) and cost associated with this technology - as highlighted in Figure 5-4 tradespace analysis - its implementation might be more advantageous within the context of robotic-assisted surgery rather than as a standalone soft-tissue alignment tool as the cost associated with one-time use, setup time and training of an independent tool would be saved within the incorporation of the soft-tissue balancing into a bone alignment tool. The integration of this tool could manifest as a robot in settings with the financial capacity and high volume of TKA procedures, offering a comprehensive solution. Alternatively, incorporating it into a handheld accelerometer-based bone-alignment tool would present a globally accessible and cost-effective option for soft-tissue balancing, catering to a broader range of healthcare environments.

Utilization of Artificial Intelligence: Artificial intelligence has emerged as an important tool for personalizing healthcare in recent years. JARR is a valuable database with information about patient demographics, medical history, implant details, surgical techniques, patient assessments, and outcomes. Leveraging AI to mine this database not only can identify the patterns and insights into what combination of tools and methods would contribute to the improvement of early functionality and longevity for the patient, but it could potentially unlock the optimal balancing between early functionality, longevity, and cost. As Batailler et al. highlight in their comprehensive literature review [155], AI holds immense potential across the entire TKA journey. It can optimize pre-operative steps like patient eligibility assessment, implant selection, personalized bone and soft tissue planning through advanced image processing, and even guide during surgery through closed-loop feedback in robotic-assisted procedures or augmented reality enhancements. However, despite this vast potential, actual implementations of AI in TKA surgical care remain limited [156]. Therefore, a crucial analysis is needed to assess AI's true role within the operating room: how effectively it can assist surgeons and healthcare staff, and at what cost? Unfortunately, the lack of long-term assessment data also limits the use of AI for longevity predictions.

Implant Selection Limitations: Despite the availability of over 150 implant types [1], surgeons often base their selection on a limited scope, influenced by their institutional training, early career experiences, or their hospital's preferred supplier contracts [Surgeon #1-3]. This reliance on limited options hinders optimal patient care. A deeper understanding of how individualized implant selection can affect early functionality and long-term outcomes (by analyzing the data stored in AJRR) is crucial to push for a shift towards empowering surgeons to move beyond pre-determined options. Moreover, equipping surgeons with comprehensive knowledge about the distinct advantages and predictive modeling of patient-specific outcomes associated with various implants can significantly ease the need for a learning curve related to adopting new implant types.

Healthcare Ecosystem Challenges: While pre-determined implant options and the limited availability of long-term data for new technologies pose significant obstacles to conventional TKA system evaluation, the broader healthcare ecosystem also plays a role. Reimbursement models (e.g., bundling) and authorization processes can introduce complexities that need to be considered and present significant hurdles in evaluating the TKA system within traditional frameworks.

Early Bonding of Cementless Fixture: While cementless technology holds promise for enhanced longevity and durability, particularly in younger and healthier patients, this potential benefit may come at the cost of a slightly higher early failure rate. Technologies that can enhance the early bonding of the cementless implant to the bone would tremendously revolutionize TKA for active individuals by ensuring a secure and durable implant fixation from the outset, maximizing their long-term mobility and functional outcomes.

Ergonomic Advancements in Surgical Tools: Orthopedic procedures have significant impacts on a surgeon's musculoskeletal health due to the physical demands and prolonged periods of standing often required [111]. Total hip and knee are among the most physically demanding (e.g., heavy-duty tools) and are associated with a higher risk of injuries [40]. Implementing solutions that feature more compact designs and low-power wireless tools while promoting ergonomic settings can further alleviate these physical strains. This approach reduces fatigue and stress on surgeons' bodies and enhances efficiency and freedom in movement/manipulations during surgical procedures. Moreover, incorporating ergonomic, compact, and portable solutions in outpatient facilities and ambulatory surgical centers (ASCs) optimizes the use of space and improves functionality within sterile surgical areas. For example, orthopedic surgeon-assisted robots, traditionally space-consuming, present opportunities for redesign into more compact form factors. The use of such compact and portable equipment in these settings is especially advantageous, as it expands the work area, creating a safer and more streamlined environment for surgical procedures.

Economic Evaluation of New Technologies: Lastly, further research is crucial to comprehensively evaluate cost-saving potentials beyond incorporating technologies. This includes analyzing the impact of shorter hospital stays and faster rehabilitation while adopting the technology combinations, tools, and techniques.

Chapter 7

Conclusion

Total Knee Arthroplasty (TKA) offers significant quality-of-life improvements for countless patients suffering from chronic knee pain and mobility issues. Even with the remarkable advancements in TKA technology, there are existing challenges and limitations that still impact patient satisfaction and healthcare costs. This thesis aimed to shed light on the complexities of the TKA ecosystem, identifying critical gaps and opportunities for technological innovation to enhance patient outcomes.

Emerging research in the field of TKA technology shows promise in areas such as personalized implants, advanced surgical navigation systems, and smart sensor technologies for post-operative monitoring. These developments can potentially offer more precise, patient-specific treatments and data-driven rehabilitation strategies. As these innovations continue to evolve, fostering collaboration among researchers, clinicians, and industry partners is crucial to ensure their successful translation into clinical practice.

The analysis began by mapping the network of processes and stakeholders involved in a patient's TKA journey, from pre-operative planning to post-operative rehabilitation. This analysis pinpoints the critical junctions where technology impacts the success of the procedure and the patient's recovery. Understanding these key intersections helps focus efforts on developing and implementing impactful technological solutions.

The current state-of-the-art technologies employed in TKA were evaluated, exploring their functionalities, limitations, and impacts on patient outcomes throughout the surgical procedure: The research explored various knee implant aspects, including materials, fixed and mobile bearings, and different implant fixation techniques such as cemented, cementless, and hybrid methods. Innovations in bicruciate-retaining and gender-specific implants and the trend towards personalized knee implants were also examined. Advancements in surgeon-assisting tools and methods, such as imaging, computer-assisted surgery (CAS), and robotic-assisted surgery, were assessed. This review provided insights into the strengths and weaknesses of existing technologies, highlighting areas such as developing more sensitive outcome measures to address the ceiling effect in high-functioning patients, especially younger or active individuals.

The study further discussed the promise of porous structures and advanced manufacturing techniques in enhancing implant integration and longevity. However, challenges such as optimizing pore characteristics and developing cleaner fabrication methods remain. Similarly, the subjectivity in soft-tissue balancing underlines the need for further research. This research should focus on analyzing data stored in the American Joint Replacement Registry (AJRR) database and incorporating bias-mitigated artificial intelligence (AI) as a transformative tool to personalize TKA procedures. Furthermore, post-operative care and rehabilitation exercises are essential for successful patient outcomes and enhanced quality of life after TKA. The key to better outcomes is influencing patient behavior by encouraging patients to engage in more frequent and appropriate exercise routines. Providing tailored feedback to patients (either via the care team or through automated means) depends not only on analyzing the captured post-operation relevant gait data and patient-specific factors such as age, health conditions (e.g., BMI, diabetes), and activity level but also on understanding how to provide feedback to change the patient's behavior effectively. Developing strategies to deliver targeted feedback that effectively guides patients and their physical therapists seems a promising avenue for enhancing patient recovery.

The tradespace analysis explored various combinations of technologies in TKA, seeking to identify the most value-generating solutions regarding patient outcomes and cost-effectiveness. By comparing different technology combinations, this research aimed to provide guidance for innovators in making informed decisions about the adoption and development of TKA technologies that maximize patient benefits while considering economic constraints.

Lastly, this thesis identified areas where investment in technology, innovation, and collaboration is most crucial within the TKA field. By exposing these limitations and challenges, this work aims to catalyze further research and development efforts, encouraging stakeholders to join forces in pursuit of novel solutions that address the unmet needs in TKA. For example, institutional and economic barriers impact the evolution and adoption of new TKA technologies. Reimbursement models, authorization processes, and reliance on limited implant options due to institutional preference hinder optimal and personalized patient care. Understanding these gaps is the first step towards driving meaningful advancements that will ultimately benefit patients and the healthcare system holistically.

In conclusion, the comprehensive exploration of the TKA ecosystem presented in this thesis sheds light on its complexities, limitations, and opportunities for technological advancement. By serving as a decision-making guide, the research empowers innovators to channel their resources toward impactful solutions that elevate both short- and long-term patient outcomes in TKA surgery.

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Appendix A List of Interviewed Orthopedic Surgeons

1. **Name:** Dr. Mark J. Spangehl, MD

   Title and Affiliation: Orthopedic Surgeon; Professor and Program Director of Orthopedic Residency Program at Mayo Clinic, Phoenix, AZ.

2. **Name:** Dr. Javad Parvizi, MD

   Title and Affiliation: Orthopedic Surgeon; James Edwards Professor of Orthopedic Surgery and Vice Chairman of Research at Rothman Orthopaedic Institute, Thomas Jefferson University, Philadelphia, PA.

3. **Name:** Dr. Richard Iorio, MD

   Title and Affiliation: Orthopedic Surgeon; Professor of Orthopedic Surgery, Harvard Medical School; Vice Chairman, Clinical Effectiveness and Chief, Adult Reconstruction and Total Joint Arthroplasty Service Brigham and Women's Hospital, Boston, MA.