Diploma thesis

Impact of Titanium nitride coating in TKA on the clinical outcome in allergic patients

submitted by

Marc Christoph Ackerl

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Doktor(in) der gesamten Heilkunde

(Dr. med. univ.)

at the

Medical University of Graz

Department for Orthopaedics and Orthopaedic Surgery

1st Supervisor
Dr. med. Lukas Leitner, Ph.D.

2nd Supervisor
Assoz. Prof. Dr. Patrick Sadoghi

3rd Supervisor
Priv. Doz. Dr. Norbert Kastner

Graz, 08.05.2018

Affidavit

I, hereby, declare that the following diploma thesis has been written only by the undersigned and without any assistance from third parties. Furthermore, I confirm that no sources have been used in the preparation of this thesis other than those indicated in the thesis itself.

Graz, 08.05.2018 Marc Ackerl eh

Preface

Since my first clinical internship in July 2014, it was clear for me, that I want to become an orthopaedic surgeon after graduation. From the first day on, I was really impressed of the working methods in orthopaedics, the huge amount of information you can get out of a physical examination or the clinical effort of a total knee arthroplasty and the patients´ quick return to normal life and sports.

As time went by and it was about getting hold of a good topic for the diploma thesis, I browsed through the mug-thesis list of topics and decided to write an email to Assoz. Prof. Dr. Patrick Sadoghi and Dr. Lukas Leitner, Ph.D., which are my supervisors now.

This thesis is my first experience in the world of science and until now, I am very happy that I got the opportunity to work on this topic with these great doctors.

Acknowledgement

It would not have been possible to write and complete this diploma thesis without many people that always stood behind me, in good and bad times.

At first, I want to point out that the biggest piece of the pie is regarded to my family, my parents, Manfred and Doris, and my sister Katharina. There have been many weekends I spent at home in Salzburg writing on the thesis, some also with a lack of motivation and ideas. Nevertheless, in every case someone provided a good hint or motivating words for me, which really helped me a lot to proceed during this time.

Next, I want to thank my friends in Graz for everything, concerning university as well as spare time. The last years here have really been a pleasure and I enjoyed every moment.

Also I want to point out my gratitude to my friends at home in Salzburg, who are on my side for many years now and always get me down to earth when necessary. Thank you for the great friendship notwithstanding the lack of time we spent together since I moved to Graz.

Last, but not least, I want to seize the opportunity to thank my supervisors, Dr. Lukas Leitner, Ph.D., Assoz. Prof. Dr. Patrick Sadoghi and Priv. Doz. Dr. Norbert Kastner for all the support in the data acquisition and writing phase and for the chance to work on a topic I am very enthusiastic about.

Abstract (English)

Background. Up to 20% of patients receiving total knee arthroplasty (TKA) complain about some degree of sustained knee pain. The impact of allergy reaction on the metal components is still controversial in this context. To address this difficulty in allergic patients titanium nitride coating (TNC), considered to have superior biocompatible properties, is available for some knee systems. Clinical impact of the theoretic concept of TNC in longtime follow-up is still discussed controversially and therefore the focus of our study was on clinical outcome with special interest on allergies and related chronic complaints.

Material and Methods. In this retrospective observational study, the clinically approved low contact stress system (LCS) TKA with conventional cobalt-chromium-molybdenum alloy was compared to the advanced coated system (ACS) TKA, using the TNC-system. Allergic status and clinical scores, including Tegner activity scale, WOMAC-score, Knee Society Score Pain/Function (KSS), and the visual analogue scale (VAS) were measured before and 10 years after surgery. Additionally, specific information about subjective sensitivity to weather changes, as well as swelling and redness of the treated knee was included after surgery.

Results. 260 patients (age: 65.95 ± 10.97) receiving LCS and 484 patients (age: 65.87 ± 8.35) receiving ACS were included, of which 19% had a documented allergy. The main follow-up was 11.92 ± 3.05 years. Rate of meteorosensitivity was significantly higher in allergic patients with ACS (ACS: 76.5%, LCS: 18.5%; $p<0.001$), which was also found for the total sample size. Postoperative clinical scores after 10 years revealed statistically significantly better results for overall population of LCS concerning VAS-score without clinical relevance (ACS: 1.95 ± 2.01, LCS: 1.42 ± 1.83; $p=0.003$). Among allergics VAS (ACS: 2.72 ± 2.51, LCS: 1.79 ± 1.88; $p=0.031$) and KSS function (ACS: 59.96 ± 23.5, LCS: 75.32 ± 21.94; $p=0.003$) showed significantly better results in the LCS group without clinical relevance either. Tegner activity scale (ACS: 2.78 ± 1.21, LCS: 2.18 ± 1.47; $p<0.001$) and KSS Pain (ACS: 83.21 ± 15.69, LCS: 70.82 ± 21.87; $p<0.001$) revealed better results for the ACS overall population, without reaching clinical relevance. KSS Pain among allergics was statistically superior in the ACS population (ACS: 78.82 ± 17.75, LCS: 69.23 ± 19.15; $p=0.017$) without clinical relevance. No

significant differences were found for WOMAC-score, KSS Function (overall) and Tegner activity scale (allergics) between the two systems 10 years after operation. All statistically significant differences reached no value of clinical relevance comparing the two different knee systems.

Discussion. The data revealed no clinically relevant difference in the outcome of ACS compared to LCS 10 years after operation for the overall group and allergic patients. Sensitivity to weather changes, an indicator for chronic local inflammatory reaction, was statistically found in correlation with ACS implants more often, but the difference is not considered to be clinically significant either. According to our findings, the concept of TNC reducing local reactivity could not be approved in longtime follow-up in the clinical setting.

Abstract (Deutsch)

Hintergrund. Persistierende, diskrete Knieschmerzen werden von bis zu 20% der Patienten nach Implantation einer Knie-Totalendoprothese (KTEP) beschrieben und allergische Implantat-Unverträglichkeiten könnten eine mögliche Ursache darstellen. Eine Titaniumnitrid-Beschichtung, welcher eine höhere Biokompatibilität zugesprochen wird, soll diesem Problem entgegenwirken. Der klinische Nutzen dieses Konzeptes im Hinblick auf Langzeitbeschwerden nach KTEP wird kontrovers diskutiert. Ziel der Studie war die klinische Evaluierung dieser Beschichtung, anhand der retrospektiven Nachuntersuchung eines großen PatientInnenkollektives, mit einem speziellen Augenmerk auf Allergiker.

Material und Methoden. Wir führten einen retrospektiven Vergleich des low contact stress system (LCS) KTEP-Systems mit konventioneller Kobalt-Chrom-Molybdän-Metalllegierung mit dem advanced coated system (ACS), welches eine Titaniumnitridbeschichtung aufweist, durch. Verglichen wurden Allergiestatus und klinische Scores, darunter Tegner Aktivitätsskala, WOMAC-Score, Knee Society Score Schmerz/Funktion (KSS) sowie die visuelle Analogskala (VAS) präoperativ und 10 Jahre postoperativ. Zusätzlich wurden spezifische Informationen bezüglich Wetterfühligkeit, Schwellneigung und Rötung des operierten Knies postoperativ erhoben.

Ergebnisse. 260 PatientInnen (Alter: 65.95 ± 10.97) mit implantiertem LCS-System und 484 ACS-PatientInnen (Alter: 65.87 ± 8.35) wurden durchschnittlich 11.92 ± 3.05 Jahre nach Implantation in die Studie eingeschlossen, wovon 19% sich als Allergiker deklarierten. Die Rate für Wetterfühligkeit war in der ACS-Gesamtgruppe als auch bei den Allergikern signifikant höher (ACS: 76.5%, LCS: 18.5%; $p<0.001$). Die 10 Jahre postoperativ erhobenen klinischen Scores zeigten statistisch signifikant bessere Werte für die LCS-Gesamtpopulation betreffend VAS (ACS: 1.95 ± 2.01, LCS: 1.42 ± 1.83; $p=0.003$). Unter den Allergikern zeigten sich bei VAS (ACS: 2.72 ± 2.51, LCS: 1.79 ± 1.88; $p=0.031$) und KSS Funktion (ACS: 59.96 ± 23.5, LCS: 75.32 ± 21.94; $p=0.003$) statistisch signifikant bessere Werte in der LCS-Gruppe. Die Werte der Tegner Aktivitätsskala (ACS: 2.78 ± 1.21, LCS: 2.18 ± 1.47; $p<0.001$) sowie von KSS Schmerz (ACS: 83.21 ± 15.69, LCS: 70.82 ± 21.87; $p<0.001$) zeigten in der ACS-Gesamtgruppe statistisch signifikant bessere Werte als in der LCS-Gruppe. Auch die ACS-Allergiker erzielten bei KSS Schmerz (ACS: 78.82 ± 17.75, LCS: 69.23 ± 19.15; $p=0.017$) statistisch

signifikant bessere Ergebnisse. Keine statistisch signifikanten Unterschiede wurden für KSS Funktion in der Gesamtpopulation, Tegner Aktivitätsskala unter Allergikern sowie WOMAC-Score in beiden Auswertungen gefunden. In der gesamten ACS Gruppe als auch bei den Allergikern mit ACS wurde statistisch signifikant häufiger Wetterfühligkeit angegeben. Keiner der statistisch signifikanten Unterschiede erreichte jedoch einen klinisch relevanten Wert.

Diskussion. Es konnten einige statistisch signifikante Unterschiede in den klinischen Resultaten 10 Jahre nach Implantation der beiden Prothesenmodelle gezeigt werden welche jedoch klinisch keine Relevanz aufweisen. Unsere Langzeit-Daten ergaben keinen klinisch relevanten Vorteil durch die ACS-Beschichtung verglichen mit der herkömmlichen Oberflächenbeschaffenheit anhand der von uns erhobenen klinischen Scores.

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Glossary and Abbreviations

ACL	Anterior cruciate ligament
ACS	Advanced coated system
APL	Arcuate popliteal ligament
DTH	Delayed type hypersensitivity
GM-CSF	Granulocyte macrophage colony-stimulating factor
IFN-alpha	Interferon alpha
JSN	Joint space narrowing
KSS	Knee Society Score
KTEP	Knietotalendoprothese
LCL	Lateral collateral ligament
LCS	Low contact stress system
LTT	Lymphocyte transformation test
MCF	Macrophage cytotoxicity factor
MCL	Medial collateral ligament
MH	Metal Hypersensitivity
MIF	Migration inhibitory factor
OA	Osteoarthritis
OPL	Oblique popliteal ligament
PCL	Posterior cruciate ligament
PE	Physical examination
PJI	Periprosthetic joint infections
ROM	Range of motion
TAS	Tegner Activity Scale
THA	Total hip arthroplasty
TiN	Titanium nitride
TKA	Total knee arthroplasty

TNC	Titanium nitride coating
TOP	Tenderness on palpation
VAS	Visual analogue scale
WOMAC	Western Ontario and McMaster Universities Osteoarthritis Index

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A General Part

This first part of the thesis should give a quick overview of the content as well as basic anatomy of the knee, the pathomechanism of osteoarthrosis, the main indications, complications and contraindications for total knee arthroplasty (TKA) implementation, preoperative diagnostics, the advanced coated system (ACS) and low contact stress (LCS) system and in the end some facts about allergies and a concept for allergic patients.

1 Introduction

As life expectancy continuously increases these days, presumably also triggered by improvements in modern medicine, still the main concern is to stay active and healthy in older days.

This diploma thesis focuses on the human knee, the biggest joint of the human body, and especially its surgical replacement, the well-known TKA. Many different types and concepts of TKA were made available by several providers, but the aim of the study was to compare the LCS model, which is commonly used at the Department of Orthopaedic Surgery, Medical University of Graz, with the more recently introduced ACS model, which provides tibial and femoral components coated with titanium nitride (TiN). This special coating may have some advantages regarding the clinical outcome when it is about side effects concerning allergies. The experimental part of this diploma thesis focusses on comparison of these two TKA systems concerning allergies, meteorosensitivity, and clinical outcome.

1.1 Organisation

This thesis is part of a project conducted at the Department of Orthopaedic Surgery of the Medical University of Graz. It is set up in compliance with the IMRD-scheme (Introduction, Methods, Results, Discussion).

Clinical scores including the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), Visual Analogue Scale (VAS) or Tegner Activity Scale (TAS) will be explained, since they are commonly used in the clinical setting and have been evaluated in our patients.

Other points to cover in the thesis contain results found in the study e.g. if there is a difference concerning meteorosensitivity between the ACS and LCS group after implantation, the discussion of the main findings of the study, where the results will be questioned and compared to the already published literature. Finally, the last chapter is to point out whether there were some serious findings in the study and to give a short outlook for following research that could be done about this topic.

1.2 Anatomy of the knee joint

1.2.1 Basics

The knee joint is well known as biggest joint of the human body and is composed of several partial joints. A first one is the patellofemoral joint, consisting of a patellar and a femoral articular surface. The biggest one is the femorotibial joint, made up of medial and lateral femoral as well as tibial condyle. When talking about functional aspects, it is necessary to divide this joint into medial and lateral compartment. (1)

There are additional parts of the knee joint to be mentioned as well, for instance menisci, whose task is to compensate incongruences of the articular surfaces. Another task of the knee joint is to guarantee stability, which is ensured by ligaments, muscles and the articular capsule. (2)

1.2.2 Bony Structures

Bones of the joint mainly include the femur, tibia and patella. With a length of 50-60 centimetres, the femur is the biggest and strongest long bone of the human skeleton.
It is broadly divided into the femoral corpus, the distal and the proximal extremity.
The distal extremity contains more or less of the condyles, which are cylindrically formed and are part of the femorotibial and femoropatellar joint. On the other side, the proximal extremity is part of the hip joint and composes of the trochanters and the femoral head.
The intermediate part of the femur, the corpus, proceeds concave dorsally and serves as insertion for many muscles, e.g. the adductors or parts of the quadriceps muscle. Articular surfaces of the knee joint are limited and just exist of the condyles, where they get in touch with the patella and tibia. (1,3)

Second, the patella or kneecap is the biggest sesamoid bone of the body and part of the patellofemoral joint. From cranial to caudal, there is a basis and an apex and the whole bone is embedded into the quadriceps tendon. The backside is covered with cartilage and works as an articular surface. (1,3)

Last bone to introduce is the tibia, which is part of the femorotibial joint.
Its structuring is similar to the femur. Again, there is a proximal and distal extremity and a corpus, where here just the proximal part articulates with the femoral component. The tibial corpus has the look of a pillar and is constituted triangular in diameter. In fact, there are three margins, an anterior, interosseous and medial one. Like a crown, the tibial head sits on the corpus with its both condyles. The articulating surfaces of a joint have to be as congruent as possible, so the condyles of the tibia nearly fit with their femoral counterparts. Between the superior articulating surfaces of the tibia, the intercondylar eminence with a medial and a lateral intercondylar tubercle is located. In front of and behind these tubercles there is an anterior and a posterior intercondylar area. The distal tibial extremity consists of the mortice and builds the ankle joint together with the calcaneus. (3)

1.2.3 Menisci

The menisci mainly consist of connective tissue with many collagenous fibres and cartilaginous cells embedded. Macroscopically they impress as semilunar panes, which lie between the femoral and tibial articular surfaces and function as mobile joint sockets. (2,3)

When mentioning the medial meniscus, it is to remark that it is connected to the medial collateral ligament (MCL). A difference to the lateral meniscus is the fact, that insertions are more laterally located and therefore the medial meniscus is a bit more fixated, immobile and injury-prone. (2,3)

The lateral meniscus in contrast impresses more circular, because its insertions are located closer to each other. This allows more mobility and leads to less tension stress than on the medial meniscus. (2,3)

Both menisci are linked together through the transverse ligament of the knee on the ventral side. Originating from the posterior horn of the lateral meniscus, there can be an anterior and/or posterior meniscofemoral ligament, inserting on the medial condyle of the femur. (2,3)

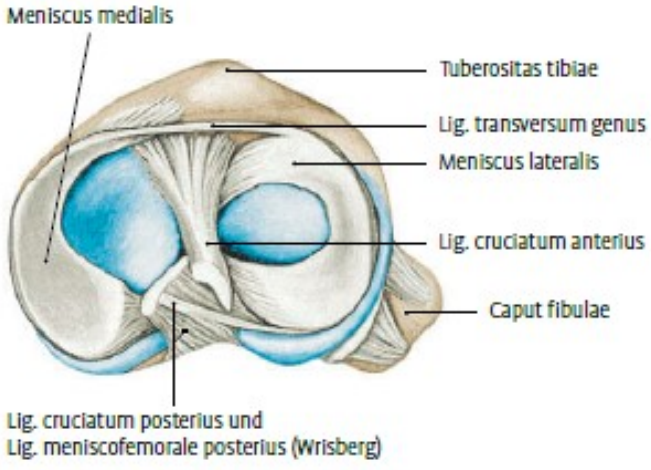

Figure 1: Illustration of a right tibia with menisci and ligaments; cranial view. From: Waldeyer : Anatomie des Menschen : Lehrbuch und Atlas in einem Band. De Gruyter; 2012. p.327 (3)

1.2.4 Ligaments

Several ligaments of the knee joint are working together in order to guarantee stability.
On the ventral side, there is the patella ligament, which continues the quadriceps tendon, representing the part between the apex of the patella and the tuberosity of the tibia.
A patellar retinaculum is located on each side of the patella, which is divided into a lateral and a medial section. The retinaculum consists of fibres of the vastus muscles and its function contains of capsule amplification. (1–3)

Two collateral ligaments, again a lateral (lateral collateral ligament, LCL) and a medial one (MCL), provide horizontal stability of the knee. These two ligaments act as guide ligaments for flexion and extension. (2)

The MCL is a flat triangular ligament and originates on the lateral epicondyle of the femur. It is part of the joint capsule and bears three insertion sites on the tibial region, the first one as the medial tibial margin, the second one inserts on the medial meniscus. The third part originates on the medial meniscus and inserts on the tibia additionally. (1,2)

Counterpart on the lateral side of the knee is the LCL with a much weaker calibre than the MCL and a circular diameter. It connects the femoral lateral epicondyle and the caput fibulae and, in contrast to the MCL is not attached to its neighbouring articular capsule or lateral meniscus. (1,2)

On the dorsal side of the knee joint, there are again two ligaments to mention. Those are the oblique popliteal ligament (OPL) as the lateral end of the semimembranosus muscle, which radiates in lateral and proximal direction, and the arcuate popliteal ligament (APL) between the fibular apex and the tendon of the popliteal muscle. Main Function of these two ligaments is the prohibition of a hyperextension of the knee as well as a limitation of the external rotation, which is the main function of the OPL. (1,2)

The last two ligaments to discuss are the cruciate ligaments. They are located in the centre of the knee, the intercondylar fossa, and in the junction of the rotation axis. (1)

The anterior cruciate ligament (ACL) reaches from the anterior intercondylar area of the tibia to the posterior internal surface of the femoral lateral condyle. The ACL is built of three parts, an anteromedial, a posterolateral and an intermediate bundle, which are twisted together. (3)

The posterior cruciate ligament (PCL) is located vice versa to the ACL, it originates at the posterior intercondylar area and the backside of the tibia and inserts at the anterior internal surface of the femoral medial condyle and has a fan-shaped topography. (3)

Main function of the cruciate ligaments is to stabilize the knee in the sagittal, but also in the horizontal and frontal direction and preventing motion of femur and tibia against each other. (3)

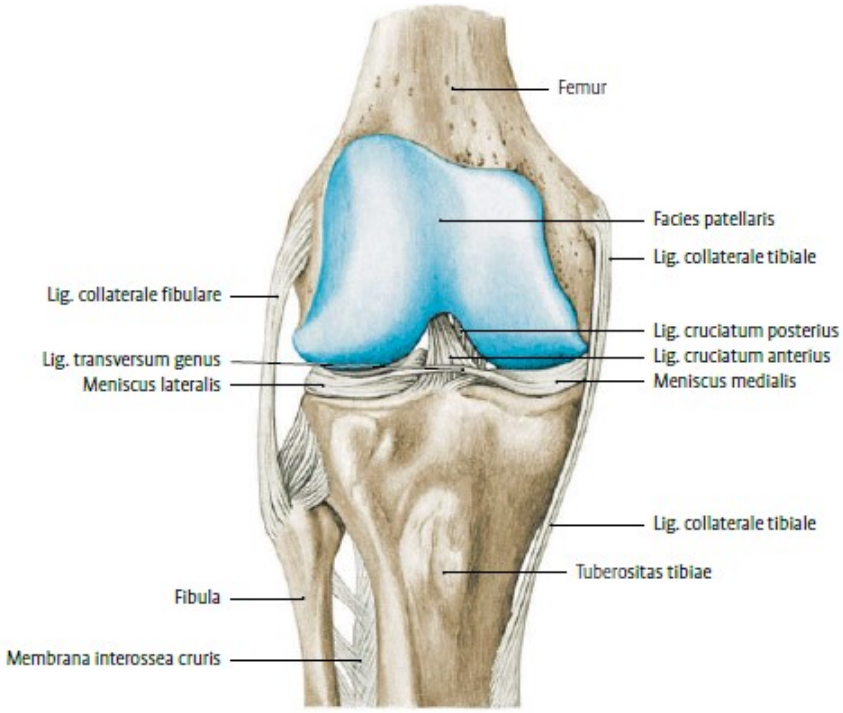

Figure 2: Illustration of a right knee joint; ventral view. From: Waldeyer : Anatomie des Menschen : Lehrbuch und Atlas in einem Band. De Gruyter; 2012. p.321 (3)

1.2.5 Joint Capsule

The articular capsule of the knee joint consists of synovial and fibrous membranes. These two parts are separated by fat depots, which are embedded on the front- and backside.
Of all joints of the human body, the knee has the most complicated construction and this can be seen on the bone cartilage border. (2)

The tibial part of the capsule is fixed just a few millimetres distal of the articular surfaces. (2)

On the femoral condylar, the arrangement is similar, but the suprapatellar bursa, located beyond the quadriceps tendon, extends the bone cartilage border more proximally, building the suprapatellar recess. (1,2)

The constellation, how the cruciate ligaments and the infrapatellar fat pad are arranged, should also be explained here. As the two membranes of the articular capsule do not always fit together, the ACL and PCL lie between the membranous and synovial parts. Moreover, on the ventral side lies Hoffa's fat pad with the same issue, located beyond the patella ligament and the retinacula. (1,2)

In the region around the patella, the synovial membrane is interrupted, where a part of the capsule remains fibrous. (1,2)

1.2.6 Functional Anatomy

First of all, the knee joint bears its stability from the articulating muscles and ligaments. There is no bony guidance available, except in the patellofemoral joint. Due to the fact, that the patella ligament and the retinacula on the ventral side of the knee joint also have the function of a tendon of the quadriceps muscle, those structures work for flexion as well as for extension. As a result, the sagittal range of motion is nearly unlimited. (1,2)

A rotation of the knee is only possible in flexion. This is caused by a tension of the cruciate and collateral ligaments in full extension. (1)

In extension, the condyles of the femur get in a position, where the MCL is entirely unfold, which is then called terminal rotation. The amount of this terminal rotation is about five degrees of external rotation. Other components allowing rotation are tension in the ACL and the shape of the medial femoral condyle. At the same time, there is an external rotation of the tibia and an internal rotation of the femur. In total extension, both collateral and cruciate ligaments are fully strained. (2)

In the bent knee joint in contrast, MCL and LCL are relaxed, but ACL and PCL are still strained. With this constellation, a rotation is possible. It is to remind, that the range of the internal rotation is smaller than in the external rotation, because the cruciate ligaments wrap in each other. (2)

The complete range of motion (ROM) of the knee joint can be seen on Table 1 below.

ROM Knee	Flexion	140 - 160°	[active < passive]
	Extension	0 - 10°	
	Internal Rotation	10°	[90° flexion]
	External Rotation	20°	[90° flexion]

Table 1: Range of motion of the knee joint, Data from: Breusch, Klinikleitfaden Orthopädie Unfallchirurgie. Elsevier; 2009 (4)

The final position of the leg depends mainly on the CCD-angle (Centrum-Collum-Diaphysis) and the proper development of the knee joint. An evaluation of the CCD-angle is maintained through an x-ray of the whole leg and should lie around 125° for adults. Leg deformities cause joint wear and increased incidences of OA at an early age. (2)

In case of a normally developed knee joint, the so-called mikulicz line proceeds along the centre of the femoral head, knee joint and prolongation of the calcaneus.
Deformities of the leg deviate from this definition. A knock-knee, or genu valgum, for instance is characterized by a lateralisation of the mikulicz line, whereas in a bow-leg, or genu varum, the deviation is medially. (2)

Figure 3: Illustrations of a genu varum before (left) and after TKA (right); From: State Hospital Graz, Department of Orthopaedic Surgery

1.3 Osteoarthritis

1.3.1 Background

Osteoarthritis (OA) is a disease, which affects about 15% of the global population with a peak around 65 years. OA can be understood as reaction of the joint to ongoing stress overload over years with a usually progressive development. Depending on various biological and psychosocial factors, there is always a synovial inflammation aspect of OA combined with histological modifications of the subchondral bone. Finally, the joint cartilage is completely destroyed and the result is dysfunction or even failure of the joint. (5,6)

Diagnosis of OA consists of three main factors: clinical presentation, radiological imaging and self-report. OA associated pain is usually more pronounced in the lower extremities. Knee and hips affected by OA tend to have the highest burden regarding physical, psychological and socioeconomic pain. Hence, the need for TKA is often inevitable. (7)

A main risk factor of the degenerative arthritis or OA is the joint wear, mostly due to advanced age or obesity. Obesity is an epidemic in western countries, which might, amongst others, cause the increase in OA incidence. The body mass index is an indicator for the risk of OA development. Up to 25% of new cases of OA and/or knee pain could be prevented by reducing overweight and obesity. (7–9)

Some other risk factors for OA are continuing long-term stress on the knee, high mechanical burden, which also implies trauma history of the joint and endogenous factors. (8,9)

Trauma history of a joint can be another underlying factor leading to OA, there is evidence that more than 30% of patients receiving TKA have a history of trauma before the symptoms of OA appeared. In a recent study, Neuprez et al. (7) published a predictive likelihood of knee OA when there is a history of prevalent traumatic event(s).

In a majority of all cases (up to 95%) OA is caused by primarily unknown aetiology, but with relation to a higher age. The secondary form with just 5% in total, also turning up at a younger age, with congenital joint pathologies, youth obesity, traumatic joint degeneration or systematic diseases, (5) as described above.

End stage OA is the most common cause leading to an indication for TKA with a percentage of 94 up to 97%. In recent years, OA has emerged from a disease affecting only elderly patients to a problem more and more patients at an age of 55 and even below have to deal with. Especially the group between 45 and 55 years are predicted to become the fastest growing group with indications for TKA due to their OA. (10)

Due to the pain and functional limitations of the patients, OA is also an important factor leading to decreased quality of life. (6)

A gender aspect has also been found in the context of OA, the incidence of lower limb arthritis is higher in women with a peak around the age of menopause. Hence, female gender has also been shown as a risk factor for OA of the knee. (7)

1.3.2 Histology

From a histological point of view, the mechanical stress on the joint leads to several changes in the cellular and matrix composition. A significant change of the cartilage is the so-called "osteophytes wrath" on the edges of the join, consisting of proliferating and ossified tissue. Additionally there is an unspecific swelling/effusion and inflammation caused by proliferation of the synovial membrane of the articular capsule. (8)

1.3.3 Pathogenesis

Primary and secondary forms of OA have been introduced already. The pathogenetic course of OA is a multifactorial reaction of joint bodies with two fundamental underlying mechanisms:

At first, there is chondrolysis, a pathological process of chondrocytes producing proinflammatory cytokines. Most important cytokines are TNF-alpha or IL-1, causing a reduction of proteoglycans and type II collagens in the cartilage tissue. Additional acceleration of prostaglandin production leads to inflammation of the synovial membrane. (11)

The second mechanism leading to OA is a loss of chondrocytes, hypothetically caused by apoptosis. This is induced by excessive stress on the cells and further leads to progressive, severe atrophy of the joint cartilage. (11)

Another pathomechanism involved in the development of OA could be a chronic inflammatory state. In this matter, white adipose tissue and its role in the secretion of systemic inflammatory cytokines (so called adipokines in adipose tissue) should be mentioned. (7,12)

Adipose tissue in fact acts as an endocrine, immune regulatory and metabolic organ beside its aesthetic function. Via secretion of adipokines, several processes in the bone and cartilage homeostasis are induced. Adipokines do have an immunomodulatory impact on local and systemic inflammation events. OA affected joints and other cell types like chondrocytes can synthesize adipokines. The most known adipokines are leptin, adiponectin, visfatin and resistin and they are mostly present in the synovial fluid, Hoffa's fat pad and chondrocytes of OA-affected joints. Right now, it is not completely sure, which role every adipokine plays concerning progression of OA. (7,12)

Recent findings in literature describe slow differentiation in adult chondrocytes. Some authors assumed, that adult articular cartilage cells are cycle-arrested without the possibility to proliferate or restore. A recent study of Kozhemyakina et al. (13) found proteoglycan-4 expressing cells in superficial zones of the adult articular cartilage with spreading to the middle zone, which proves kind of slow differentiation. As a consequence, there might be a reference point for further studies to find out more about articular cartilage homeostasis. (14)

1.3.4 Radiological classifications

To assess the severity of the OA radiologically, there is a tried and true classification by Kellgren and Lawrence. Although the classification exists since 1957, it is still common practice and used all over the world.

In this context, it is important to mention the radiological signs for OA diagnosis: Asymmetrical joint space narrowing (JSN), subchondral sclerosis and osteophytes on the edges of the joint cartilage and scree cysts. (15,16)

Grade 0:	No radiographic features of OA are present
Grade 1:	Doubtful JSN and possible osteophytic lipping
Grade 2:	Definite osteophytes and possible JSN on anteroposterior weight-bearing radiograph
Grade 3:	Multiple osteophytes, definite JSN, sclerosis, possible bony deformity
Grade 4:	Large osteophytes, marked JSN, severe sclerosis and definite bony deformity

Table 2: Radiological classification of Osteoarthritis (Kellgren and Lawrence), Data from: Petersson IF, Radiographic osteoarthritis of the knee classified by the Ahlback and Kellgren &Lawrence systems for the tibiofemoral joint in people aged 35-54 years with chronic knee pain. Annals of the Rheumatic Diseases; 1997 (15)

Another way to diagnose OA radiologically is the Ahlbäck-classification, first proposed in 1968. The focus in this classification also lies on is on bone attrition and JSN once again. (15)

Grade 1:	joint space narrowing (less than 3 mm)
Grade 2:	joint space obliteration
Grade 3:	minor bone attrition (0-5 mm)
Grade 4:	moderate bone attrition (5-10 mm)
Grade 5:	severe bone attrition (more than 10 mm)

Table 3: Radiological classification of Osteoarthritis (Ahlbäck), Data from: Petersson IF, Radiographic osteoarthritis of the knee classified by the Ahlback and Kellgren &Lawrence systems for the tibiofemoral joint in people aged 35-54 years with chronic knee pain. Annals of the Rheumatic Diseases; 1997 (9)

1.3.5 Treatment

As mentioned above, there are psychological and biological factors working together in the pathophysiology of OA. Therefore, a proper treatment has to cover all those factors and should provide individual strategies. (8)

Classic therapy options of treating lower limb OA consist of non-pharmacological and pharmacological methods. TKA is indicated for severe cases without any other possible therapy and will be discussed later in the TKA indication section. (8)

In general, a conservative treatment regimen is always desirable. This includes physiotherapy, lifestyle modification and, of course, an adequate pain management. Lifestyle modification starts with healthy nutrition as well as physical activity. From the physiotherapeutic view, it is necessary to strengthen the muscles and to improve the flexibility, which can be managed by aerobics for instance. These measures are on the one hand preventive for OA and on the other hand, a first step in the therapy of mild OA. (6,8)

Another important point is to carry on doing sports. The only limitation is on high-impact sports with a permanent heavy strain on the knee as it can be present in alpine skiing or in contact sports like soccer or football, especially on a competitive level. (6)

Advanced forms of OA with higher Ahlbäck- or Kellgren/Lawrence-grades require surgical treatment. A wide range of arthroplasty models is available, the focus in this thesis lies on the LCS and ACS systems, which will be described later on. (6)

1.4 Total Knee Arthroplasty

1.4.1 Background

Main indication for a primary total knee arthroplasty is end stage osteoarthritis of the knee joint. Mean age for implantation in Germany was 68.65 years in 2015. The data is very similar compared to the mean age for a total hip arthroplasty (THA) with 68.46 years in Germany. (17)

Numbers of TKAs being performed in OECD-countries nearly doubled and the rate of THA increased by 35% since the year 2000 according to a report of the OECD.
In Austria, the incidence of TKA in 2013 was 215 per 100.000 inhabitants with a rising tendency. (18)

The lifetime risk for a potential TKA in the USA is 9.5% in women and 7% in men according to a study by Weinstein et al. in 2013. (19)

Concerning frequency of arthroplasties, TKA and THA are the most commonly performed surgeries. For example, the ratio between numbers of TKA versus elbow prosthesis implantations is about 50:1 in Germany. (18)

More than 35.000 total arthroplasties are being performed in Austria every year, of which about 14.000 are TKAs with a rising tendency. (20–28)

Recent developments of TKA implantation numbers in Austria are shown in Figure 3.

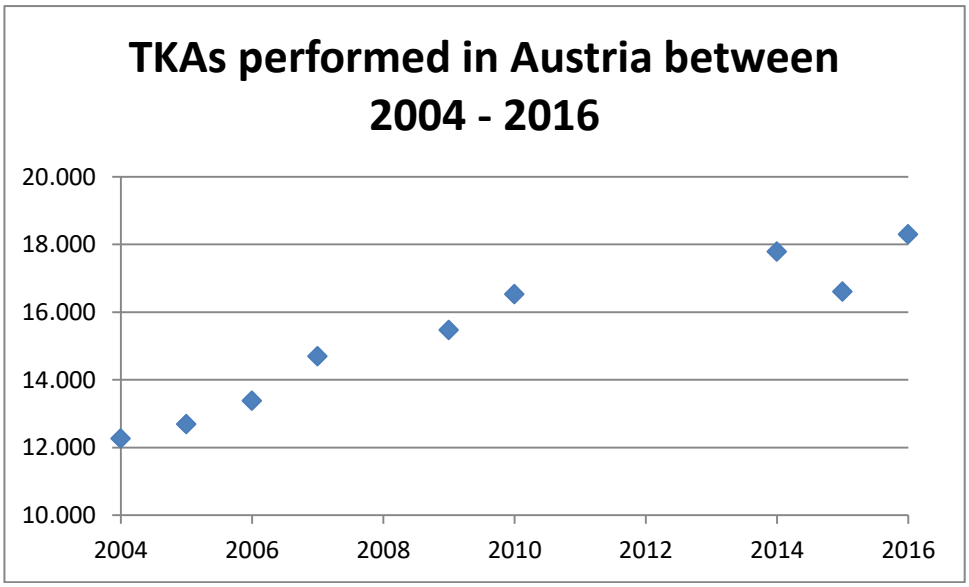

Figure 4: Total amount of TKAs performed in Austria between 2004 - 2016; Data from: Statistik Austria. Jahrbuch der Gesundheitsstatistik 2005-2008, 2010 (20–24); Bundesministerium für Gesundheit und Frauen. 2010, 2014-2016 (25–28)

During the last years and decades there has been a shift in patients' age undergoing TKA. When TKA was almost performed in elderly patients in the past, the age group of 45 to 55 is nowadays rising in TKA numbers. The Australian Joint Register has detected an increase by 40% in this cohort between 2002 and 2007. (10)

A further change in the last few years is the fact, that even surgeons are likely to perform TKA before other therapy methods e.g. unicompartimental knee arthroplasty or tibial osteotomy. A reason therefore might be the decreasing revision rate of TKA, which has become the lowest of all those options in the last years. (27, 28)

A recent study by Aujla et al. (10) performed a closer investigation of relatively young patients receiving TKA (younger than 55 years old). One of the results was, that compared to a group of patients older than 55 years undergone TKA, there was no difference in the incidence of infection or joint wear during the follow up. This hypothesis could be affirmed by a study of Gioe et al. (32).

On the other hand there are studies, e.g. based on the Finnish arthroplasty register (33), claiming that younger age represents a significant risk factor for implant failure. In an example study, Camus et al. (34) postulated a 9% revision rate upon a follow-up of 10 years in this age group. A higher failure rate of active and younger patients <55 years was found especially in THA. (35)

1.4.2 History

Themistocles Gluck performed the first TKA already in 1890. Mr Gluck's prosthesis consisted of ivory and was functionally a constrained hinged joint. The technique being used was revolutionary, but as there had not been aseptic conditions through the implantation, it leaded to implant failure in every case. Since then, there was a straight improvement in the technique of implantation, the used materials and the technique of the procedure. Nowadays, TKA is the gold standard in the therapy of proceeded OA of the knee joint. (29,35)

However, as a consequence of Themistocles Gluck's first results, TKA was not documented some time later on. Mainly because of the success of early-performed THA, the idea of TKA came up again. In the 1940's and 1950's the focus of research was on hinged joint based models. Scientists all over the world wondered about the best material for implantation, ranging from ivory over acrylic resin to vitallium, which is a mix of chrome, cobalt and molybdenum, first used by Walldius from Karolinska-Institute in Sweden around 1960. Another problem on the agenda was the biomechanics of the knee. Due to the material weakness in a biomechanical view and the unequal forces that operate on the knee joint, there was a significant abrasion and the problem of implant failure came up for the first time. Finally, the idea of a reconstruction of the knee joint's surfaces turned up by MacIntosh in Toronto in 1954. The innovation about it was the interposition of materials between the formal and tibial component of the prosthesis led to improvement of stability of the alignment of the system. Over the time the used materials also changed and polyethylene in combination with metal were on the rise. Because of this development, Gunston et al. described the first unconstrained TKA implantation by his group in 1969. (35)

A few years later, in 1977, Büchel and Pappas invented the Low Contact Stress system (LCS), which is still commonly used. The novelty about this system was a mobile, rotating inlay used within bicondylar prostheses. A main thought about this improvement was, to imitate the function of the mobile menisci and therefore to provide a more physiological approach in addition to common TKA models. Back in the present, there are many different types of TKA available like the ACL-conserving surface replacement, posterior-stabilized surface replacement or prosthesis with mobile inlays of many variations. (35)

In the last few years amongst others, a new trend in TKA was the coating of the components with several materials, which might have better biocompatibility characteristics.
As this is a huge part of the main aim of this thesis, it will be discussed in detail in subsection 1.5.3 and the discussion chapter of the special part.

1.4.3 Indications

The main indication for TKA is the primary or secondary OA of the knee joint and is based on three diagnostic columns:

- radiological evidence of a degenerative joint disease
- clinical symptoms
- current health condition (9)

From the radiological view, the procedure is depending on the grade of the OA, classified by Kellgren/Lawrence or Ahlbäck. Amongst others JSN, osteophytes/bone cysts and bone sclerosis are evaluated in this classification. (36)

For the clinical indication of a TKA, specific clinical symptoms to be mentioned are severe recurrent knee pain, especially at night, a limitation of the patient's mobility in common, including difficulties in the daily life and failure of the conservative therapy. (9,35)

Several health conditions should also be given for the indication of primary TKA. These are intact extensor mechanisms, no current evidence of infection, a suitable health condition for the operation and informed consent of the patient. If all these points are covered, implantation of TKA should be considered. (9,35)

Table 4 shown on the next page provides guidance for the indication of TKA.

Symptoms	Radiology	Age	Mobility	Localisation	TKA
Slight or moderate	Ahlbäck I-III				Inappropriate
Slight	Ahlbäck IV-V				Inappropriate
Moderate	Ahlbäck IV-V	<55			Inappropriate
Moderate	Ahlbäck IV-V	≥55		Uni	Inappropriate
Moderate	Ahlbäck IV-V	≥55		Bi-tri	Appropriate
Intense-severe	Ahlbäck I-III	<55		Uni-bi	Inappropriate
Intense-severe	Ahlbäck I-III	<55		Tri	Uncertain
Intense-severe	Ahlbäck I	≥55	Normal		Inappropriate
Intense-severe	Ahlbäck II-III	≥55	Normal		Uncertain
Intense-severe	Ahlbäck I	55-65	Limited		Uncertain
Intense	Ahlbäck I	>65	Limited		Uncertain
Severe	Ahlbäck I	>65	Limited		Appropriate
Intense-severe	Ahlbäck II-III	≥55	Limited		Appropriate
Intense-severe	Ahlbäck IV-V	<55		Uni	Uncertain
Intense-severe	Ahlbäck IV-V	<55		Bi-tri	Appropriate
Intense-severe	Ahlbäck IV-V	≥55			Appropriate
Legend: uni ≙ unicompartimental excluded patello-femoral isolated; bi ≙ unicompartimental plus patello-femoral; tri ≙ trikompartimental					

Table 4: Different scenarios in which TKA is deemed appropriate, uncertain or inappropriate Data from: Escobar, Development of explicit criteria for total knee replacement. IntJ Technol Assess Health Care. 2003;19:57–70 (37)

1.4.4 Contraindications

As many other orthopaedic surgeries TKA is a schedulable intervention and therefore the morbidities and intraoperative risk of the patients should be assessed closely. For instance, the adjustment of cardiopulmonary diseases should be evaluated, since the operation itself is a burden for the patients' system. The medication should be optimized for the scheduled day of surgery. According to some authors, patients suffering from obesity should be advised to lose some weight prior the operation. (35)

In addition, several other comorbidities including diabetes mellitus (correlated with bad wound healing) are risk factors for complications during or following the intervention. (35)

There is clear evidence for some contraindications regarding TKA.
First, there are some common contraindications for surgery of a body region concerning vascular diseases, thrombophlebitis, an acute infection of the joint, crural ulcers or dermatological issues around the knee joint. (29)

Furthermore, it is important to mention specific contraindications for the performance of primary TKA, which can be classified as absolute contraindications. These range from acute or chronic knee infection, muscular weakness because of recurvate knee deformity, a dysfunction of the extensor muscles to the presence of a well-functioning knee arthrodesis. Furthermore, there are several contraindications, classified as relative contraindications for TKA, including circumstances that "preclude safe anaesthesia and the demands of surgery and rehabilitation". Neuropathy or osteomyelitis of the knee joint should be mentioned amongst these relative contraindications. (38)

1.4.5 Preoperative Diagnostics

Preoperative management and diagnostics is still a controversial topic concerning TKA. Focused on the topic of this diploma thesis, there are no clear, published guidelines concerning the impact of preoperative allergy diagnostics. A recent study by Ayers et al., published in 2014, outlined once again that, although every decision for or against TKA is individual, there should be further research on guidelines for decision-making concerning patient selection and TKA timing. (39)

1.4.5.1 Anamnesis

As the TKA is a planned procedure, it is obvious to close out eventual comorbidities to prevent intraoperative complications. During the anamnesis, the observer can also get an impression which compliance can be expected from the patient. (29,35,40)

The anamnesis should contain previous hospital stays including surgeries and diagnostics, accidents, injuries or severe diseases like diabetes, heart failure or hepatitis.
A detailed scheduling of the patient actual medication should be performed. This also includes medication the patient is allergic to. (29,35,40)

If the patient is allergic to any kind of metal, the surgeon should consider thinking about using hypoallergenic TKA implants like the ACS, but this will be discussed later in the special part. (41)

The pain itself, which was leading to the current situation, should also be covered. A scheme to cover all points could be the SOCRATES-scheme, which includes site, onset, character as well as radiation, association, timing, exacerbation and severity of the pain. This builds the bridge to the physical examination, which will be the next preoperative step. (29,35,40)

1.4.5.2 Physical Examination

The physical examination (PE) basically includes inspection, palpation, function testing and observation of the autonomic functions distally from the knee joint.

Inspection mainly contains a quick check of the legs in standing, walking and lying position. Common pathological findings of the gait pattern are protective limping, limping due to a shortening of one leg or a reduced ROM. (35,42)

Palpatory observation gives insight to the muscle tonus, eventual swelling of the joint and temperature of the skin. Joint swelling can be detected through a positive dancing patella sign with an intraarticular effusion of more than 10 millilitres. Tenderness on palpation (TOP) of the tibial tubercle is spotted with Osgood-Schlatter's disease, usually turning up at an age between 8 and 15 years. Palpation of the knee pit is necessary to evaluate a Baker's cyst. In the worst case, the cyst can rupture and cause a compartment syndrome. (4,42)

Another important test is the palpation of the joint line. TOP of the medial or lateral joint line can be caused by each structure of the region. This palpation test allows a relatively precise diagnosis of the pain trigger. (35,42)

The status of autonomic pathways is essential in the PE as well. For this purpose, the examiner palpates the pulse of the arteries of the knee and crural region. (35,42)

Fundamental cornerstones of the functional testing are the following:
Documentation of the ROM actively and passively, as seen in Table 1, is the first thing to do, followed by an evaluation of the menisci. It is to remind that in cases of gonarthrosis, the validity of the meniscus sign is limited. (4,35)

A next step is the stability testing of the ligaments. Beginning with the collateral ligaments, MCL and LCL, the knee is inflected to 30° and varus or valgus stress is put on the joint. In this position, a clinical differentiation between partial or complete ruptures of the ligaments is possible. (4,35,42)

The cruciate ligaments ACL and PCL are evaluated via the drawer test or the Lachman-test. The only difference between the methods is the flexion of the knee, about 10 to 20° when using the Lachman-test and 90° in the drawer test. An optional variant for the ACL would be the Pivot-shift-test (4, 34,41)

It is of advantage to evaluate the Q-angle between quadriceps muscle and the patella tendon. A deviating angle can cause the patella syndrome or a habitual luxation of the patella. The Q-angle should lie around 13° in male patients and 18° in female patients. (35,43)

1.4.5.3 Clinical Scores

Tegner Activity Scale

Evaluation of knee disability is an essential method for planning therapeutic procedures and objectifying further outcomes. The Tegner activity scale (TAS) can be used for this observation. (44)

Basically, TAS is an indicator for the pre- and postoperative limitations of the patients' sports and working activity or participation. It is a numeric scale ranging from zero to 10, where each value stands for a specific subgroup. (44)

A zero value corresponds with "Sick leave or disability pension because of knee problems", a 10 value stands for "Competitive sports Soccer-national and international elite", which can also be used for alpine skiing according to an evaluation of the score conducted by Wirth et al. (45,46). The same study claimed that a clinical difference through surgery must be at least 1.4 points. The common recreational sportsman mostly evaluates himself as 6 on the scale, which complies with "Tennis and badminton, handball, basketball, downhill skiing or jogging, at least five times per week" (45). These recreational and competitive sportsmen are the only population to reach values from 6 to 10 per definition. (47)

The TAS is an internationally used and accepted standard evaluation tool, which was originally been established for anterior cruciate ligament injuries, but is also in use for clinical evaluation of OA and knee injuries in common. There are no floor or ceiling effects reported by several studies, according to a review of Collins et al. (47).

Western Ontario and McMaster Universities Osteoarthritis Index

The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) is another health status questionnaire especially for patients with OA of the lower limbs. It was developed for evaluation of parameters such as physical function, pain and stiffness. (48)

Consisting of four sections, the WOMAC-score assessment starts with seven questions about symptoms in general, followed by two questions about potential stiffness of the concerned body part and nine questions about pain. The last section includes 17 questions to evaluate the function and daily living. Each question can be answered from "None/Never" with a value of 0 points to "Always/Extreme", worth 4 points. In the end, every patient is receiving a score between 0 and 100, where higher scores indicate worse conditions of each section being asked for. (47,49)

When talking about changes of the score from pre- to postoperative status, the minimal clinically important differences are 0.51-1.33 for worsening and 0.67-0.75 for improvement according to a study of Angst et al. (50).

Knee Society Score Pain/Function

The origins of the Knee Society Score (KSS) for pain and function reach back to 1993. The latest version is actually from 2011 and consists of two separate parts. The first part assesses only the knee joint and relevant parameters such as pain, ROM, flexion contracture or extension lag, alignment and stability of the knee. After this, the functional section evaluates the patients' ability to walk and climb stairs and the necessity of using walking aids. Reason for this dual system is that due to this combination, there is no influence of the patients' infirmity and the score remains objective. (51,52)

KSS for pain has a range from 0 to 100 again, where the subjective estimation of pain is already worth 0 to 50 points, followed by ROM with a maximum of 25 points. Extension lag and flexion contracture, if present, are worth negative points between -2 and -15. Scores of 60 and below are interpreted as poor, where scores between 80 and 100 are seen as excellent results. (51,53)

Second part of the KSS, the evaluation of function deficits, moves in a range from -20 to 100, where negative scores are counted as zero. Walking aids can reduce the score from -5 to -20, depending on the aid being used. The sections for walking and stair climbing are both worth 0 to 50 points and the results can be interpreted equally to the KSS pain score. (51,53)

Visual Analogue Scale

This is maybe the simplest variant to evaluate the present level of pain. The Visual Analogue Scale (VAS) is an analogue scale from zero to 10, where the patient has to state his subjective burden of pain. Zero stands for no pain, 10 therefore means maximum pain. (54)

Templates of each assessed clinical score can be found in the "Appendix" section at the end of this work.

1.4.6 LCS-System

1.4.6.1 Background

The LCS system is already in use since 1977. Back then, Büchel and Pappas invented this bicondylar system with an ultra-high-molecular polyethylene mobile bearing inlay. Femoral and tibial component consist of a special cobalt-chrome-molybdenum alloy with a slight nickel additive. Their usual thought was that the architecture of the prosthesis should base on the physiological anatomy of the human knee joint. To imply this, the rotating inlay should orientate on the menisci. (35,55)

The underlying idea is to decrease the incidence of joint wear and aseptic loosening risk due to a close-to physiologic joint architecture. Low contact stress results from congruent articular surfaces. The pressure on the contact surfaces is allocated over the whole area and thus, there is less pressure on each point. (56)

Figure 5: Low Contact Stress TKA system. From: DePuy Synthes. LCS® COMPLETE Knee System [Internet]. 2017. Available from: https://www.depuysynthes.com/hcp/knee/products/qs/LCS-COMPLETE-Knee-System (57)

After 30 years using the LCS system in a clinical setting, the technique itself remains nearly the same. Things that changed are the development of new instrument sets like the MILESTONE instrumentation set, which will be introduced later, and the inception of robot-assisted surgery. The system was actually invented to address the problem of wear due to the high contact stress of fixed bearing TKA systems. When implanting prostheses of the LCS type, it is necessary to find the right size for the tibial and femoral components. (56)

1.4.6.2 Surgical Technique

The following part describes the exact surgical steps to perform a proper TKA with the LCS Total Knee System and the MILESTONE Instruments.

An essential goal in the surgical procedure is to reconstruct the knee's ability to rotate in physiological conditions. This is necessary, because the anterior cruciate ligament is sacrificed during the standard procedure. The goal is to create a ROM similar or even equal to the human knee joint with its usual stability. This is ensured by steady contact pressure of the femoral and tibial component to the inlay. Another advantage here is the protection from subluxations and dislocations. (57)

The size of the femoral component must be nearly equal to the anatomy in sagittal and horizontal plane. On the tibial side, the inclination of the implant has to be similar to the usual conditions. This prevents the implant from shearing and guarantees a better flexion in the end. (57)

Preoperative it is necessary to know the valgus angle of the knee to undergo TKA. This is the angle between anatomic and mechanical axis of the distal femur, which should already be ascertained preoperative and range from 3 to 8 degrees. The valgus angle of the prosthesis has to fit to the body height of the patient and differs from 3 to 5 degrees, with a smaller angle in taller patients and vice versa. (57)

The surgical entrance leads from 7 to 10 centimetres cranial of the patella parapatellar downwards and median forward to the tibial tubercle. At our institute, the parapatellar approach is performed medial from the patella.
When the patella is reflected beside insight to the tibiofemoral joint is possible.
The next steps are the inspection of the tibial and femoral area and the extraction of potential osteophytes, which can interfere in the further procedure. (57)

Using the 'tibia-first technique' as performed at our institute, the proximal tibia is being resected and in the same step, the balance of the soft tissue must be checked in extension. Then, the correct size for the femoral implant has to be found. This is followed by the positioning of an anterior-posterior block and drilling of an intramedullary hole through the longitudinal axis of the femoral bone. After the rotation of the femur is determined, the femoral condyles are resected in horizontal plane and the flexion gap is checked via a spacer. Now the distal femur condyles are resected and the extension gap checked with a spacer again. Afterwards, the other femoral resections are done and the tibial component is getting finished too. If the surgery is a tricompartimental one, the patella is resected and drilled now as the last bone to be prepared for the prosthesis. Then the surgeon has to test several implant components with provisional duplicates. If the parts all fit together properly, they must be fixated in a cemented or non-cemented way followed by a final implant evaluation. The last steps are closure of the surgery area, drainage application and an adequate wound management. (57)

Another point to discuss is the surgical technique, to use cement or not. The cement shall fill out weak points of the bone, interlock with it and therefore act preventive for fractures. According to a study of Fricka et al. (58) , both variants have a similar outcome on a short term follow-up. Rand et al. (59) spoke of a higher survival rate in cemented versions over conventional fixation after a 10 year follow-up.

A review of Franceschetti et al. (60) did not reveal additional benefits of cemented TKA models, although both types could target good outcomes.

The cemented TKA has some advantages and disadvantages to mention. Initial fixation and bone grafting appears better and easier than in the cementless variant. In addition, the technical requirements are lower in using cement. On the other side, the operation time is significantly longer due to the cementing process. The incidence of retained loose fragments and for third body wear is higher in cemented implants. In case of demand for a revision, the cemented prosthesis requires larger bone resection. (58,61,62)

An objecting point might be the fact that cement is another foreign substance in the body besides the prosthesis. Also very important is the correct size and position of the prosthesis. In this case, the proper planning of the procedure is inevitable. The x-ray series required for the TKA planning must be of excellent quality. (29)

1.4.7 Complications

In this section, the focus lies on postoperative complications, such as loosening of the implanted prosthesis, infections or metal hypersensitivity, which will be discussed later in subsection 1.5.
These complications are differentiated into functional and bony causes. The Konsensus-classification (29) describes types of implant failure from I to IV, each type with a specific pathophysiological background. Type I is usually determined by abrasion, type II as an infectious aetiology, a combination of these in type III or the indifferent type IV, characterized by a non-particle induced arthrofibrosis. (29,63,64)

According to a study by Randeep S. Aujla (10), the most common causes for implant failure are joint wear, aseptic loosening, periprosthetic fractures, extensor mechanism failure, arthrofibrosis and instability.

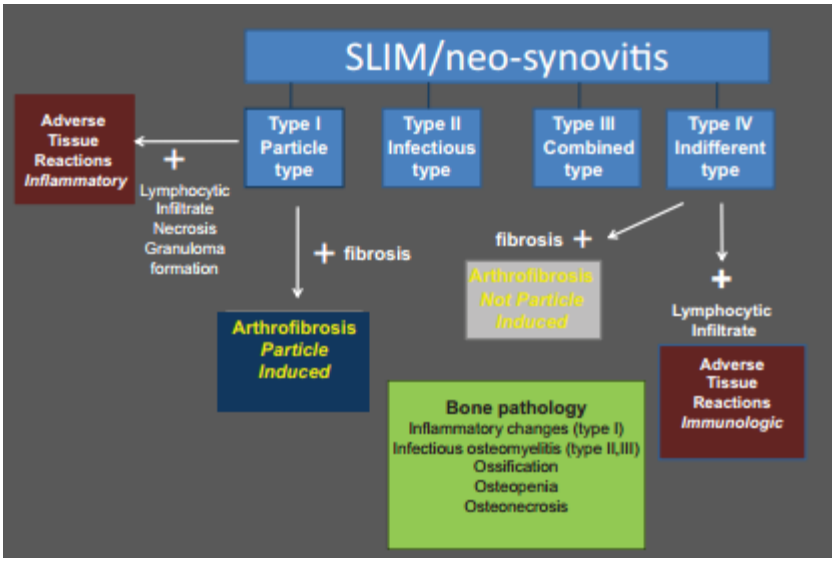

Figure 6: Konsensus-classification of joint implant related pathology; From: Krenn V, Morawietz L, Perino G, Kienapfel H, Ascherl R, Hassenpflug GJ, et al. Revised histopathological consensus classification of joint implant related pathology. Pathol Res Pract (64)

1.4.7.1 Aseptic Loosening

The mechanism of aseptic loosening per se is periprosthetic osteolysis. From an aetiological view, this can be triggered by hypersensitivity, specific particles or biomechanically induced. Osteointegration is being interfered by dynamic micro-movements of 50-150 µm or a high fluid pressure in the interface between bone and prosthesis. An important point according to osteointegration is the amount of initial implant stability, where a lack of it can cause the loosening. The second main factor is the abrasion product, which can stimulate the macrophages and thus subsequently lead to osteolytic processes. The relation between femoral component of the prosthesis and the inlay determines the grade of abrasion. A way to reduce this complication is the use of rotating inlays. (29,35,63)

In general, aseptic loosening is considered the main cause for prosthetic revisions with about 50% of all revision surgeries in total. (35)
About 51% of all cases of aseptic loosening can be counted to type I of the Konsensus-classification, followed by type II with 20% and type IV with 18%. (35,64)

Some risk factors are not related to the implant or the surgery: a high body-mass-index, comorbidities like osteoporosis, a higher activity level especially at a younger age, alcohol or nicotine abuse. An important factor concerning the implant survival rate is the combination of materials being used, further influencing potential abrasion of the inlay, which is the most common indication for a revision in TKA. (29,63)

Diagnostics of the aseptic implant loosening include PE and a radiological assessment. In the PE, it is necessary to test the operated leg for rotation and vertical compression pain. This in combination with an implant movement and seam formation backs up the diagnosis of implant loosening. (29,63)

1.4.7.2 Infections

Basically, the incidence of periprosthetic joint infections (PJI) is extremely rare with 0.8% and 1.9% in comparison to the amount of TKA being performed. It is a foreign body associated process, which affects the surrounding of the prosthesis, not the prosthesis itself. A problem with PJI is the prosthesis functioning as a reservoir for germs. The clinical occurrence of a PJI does not have a specific pattern. In most of the cases, the onset is nearly harmless and therefore difficult to detect in an early stage. Complications of this type of infection can be amputation of the concerned leg and in the worst case septicaemia. In this case, the only therapeutic option is mostly a removal of the prosthesis. (65–67)

An early first stage of the PJI is determined by a macrophage-induced granuloma formation and the building of a bacterial biofilm. This biofilm enables the survival of bacteria on the implant surface, where it is protected from the innate immune response. An infectious disease occurs, when the germs induce an infection of the implant surrounding bone and soft tissue, which is the definition of a PJI.
The germs are protected from the innate immune system and antibiotics, when located on the biofilm of the implant, but not at the location of the PJI. Therefore, the biofilm serves as a reservoir for the bacteria, which can make the infection reoccur, even if it has been eliminated before. In the end, the only way to eliminate the germs is to eliminate the implant with its biofilm. (65,68,69)

Germs that induce periprosthetic infections are restricted to several bacteria, ranging from Staphylococcus epidermidis, Staphylococcus aureus, Propionibacterium, and Staphylococcus spp. and some gram-negative germs. About 20% of all PJIs are caused by Streptococcus strains, such as Streptococcus pneumoniae or group A, B, G or D streptococci. Various Salmonella species count to potential PJI germs as well. (29,68,69)

There are several risk factors, which are relevant for the development of a PJI. Systemic factors are for instance obesity, alcohol or nicotine abuse, the human immunodeficiency virus, renal insufficiency, diabetes, age, chronic inflammatory processes or immune suppression. Some local risk factors are to mention as well. Some are scars, soft tissue defects, local fistulation, circulation disorders or prior surgery in the body region. (65,68)

All these risk factors can again be divided into a pre-, intra- and postoperative section. Beginning with the preoperative setting, eventual comorbidities must be treated, which could affect the TKA. Some of these are intraarticular cortisone therapy, infections of the urinary tract and even nasal colonisation with Staphylococcus aureus, especially the resistant ones like MRSA or VRSA. (65,68,69)

A proper perioperative management for prevention of PJI includes aseptic conditions in the theatre, an antibiotic prophylaxis as well as the lavage of the surgery area with chlorhexidine. Postoperative measures are mainly the prevention of infections via appropriate wound management. (65,68)

The clinical appearance of PJI mainly consists of three different types, each of them with the incidence of about one-third. These are classic inflammation signs as swelling, reddening and pain, local signs with fistulation or soft tissue changes or inconspicuous soft tissue findings. Specific symptoms are especially pain, less common night sweat and fever. A problem, when there is none of these symptoms present, can be the differentiation of PJI and aseptic loosening. (29,65,69)

Blood parameter changes according to PJI are an increased C-reactive protein, erythrocyte sedimentation rate and procalcitonin. To clarify the diagnosis, the synovial fluid has to be analysed via sterile punction as well. The opportunity to use apparative diagnostics should be maintained as well. An x-ray can display osteolytic lesions or periosteal reactions. Sonography is an elegant way to check for fluid surrounding the implant. Another option can be three-phase bone scintigraphy, CT scan or even positron emission tomography with fluor. (29,65,69)

Evaluation of a specific germ and the pathogenesis itself determine the definitive therapy of the PJI. In most cases, the removal of the implant is indicated, because it is the only way to getting rid of the bacterial biofilm around the prosthesis. In the course of this, it is also necessary to debride the tissue thoroughly. Antibiotic therapy can be applied adjuvant to support the surgical treatment. Antibiotics without surgery can alleviate the symptoms of the infection, but there cannot be a complete remission. (29,65,68,69)

1.4.7.3 Arthrofibrosis

The problem about arthrofibrosis is mainly a limitation in ROM of the concerned joint, caused by excessive proliferation of scar tissue. Arthrofibrosis is mostly associated with pain as well. As mentioned in subsection 1.2.6, there is normally a flexion of about 130 to 150° and an extension of 0 to 5° in the sagittal plain of the knee joint. Rotation is just possible at a flexion of 90° due to tension of the collateral and cruciate ligaments in full extension. (29,70)

A potential motion deficit caused by surgery can be promoted by factors mentioned before, during the operation and post-operative. Examples are a possible motion deficit, which has been present even before surgery, bad positioning of the prosthesis or insufficient removal of osteophytes intraoperative and infections or bad analgesia afterwards. A problem concerning the diagnosis of arthrofibrosis is, that there is no consensus on diagnostic criteria as a result the prevalence is more or less unknown. The incidence lies between 1% and 13%, which was observed in the USA, performing about 700.000 TKAs per year. (29,70)

Ways to treat a motion deficit after surgery can be a continuous passive motion splint, a closed narcotic mobilisation or the open revision of the affected joint. Very important in this case is physiotherapy as a first line therapy option combined with adequate analgesia and use of the REST- scheme to accomplish an improvement of the ROM. (29,70)

1.5 Concept for allergic patients

1.5.1 Allergies

An allergy can be defined as a specific overreaction of the immune system, or atopy, to an antigen, what is then called allergen. (71)

Referring to published data by Carr et al. in 2012 (72), there is a very high rate of sensitivity to metal in TKA patients, of around 20 in total. Of this percentage, just a few people really exhibit symptoms, but this will be discussed later. (71,73)

The secondary immune reaction or immunization, boosted through repeated antigen contact, is normally a protective mechanism for the foreign tissue. However, in case of a present allergy, it leads to destruction of the foreign tissue. Hypersensitivity reactions are divided into types from I to V. An overreaction due to metal sensitivity is ascribable to type IV, also known as delayed type hypersensitivity (DTH). (71)

Type I is a reaction determined by a prior allergisation. The second contact will cause an anaphylactic reaction with a characteristic exhibition of inflammatory mediators. The type II allergic reaction is also known as cytotoxic hypersensitivity. Again, after the allergisation, the next antigen contact will cause a severe reaction through activation of the complement system. Reactions of type III are triggered by antigen-antibody-complexes. Autoantibodies against hormone or transmitter receptors function as trigger for type V reactions. (71)

Most essential for the study is the type IV reaction, or DTH. The name has its origin in the fact that the peak of the reaction is reached after a latent time of 2-4 days. Additional, the sensitisation phase after the first contact has duration of about 5 days. Central contributors to this reaction are CD4-helper cells, T-killer-cells and macrophages, triggered by germs as viral proteins, or tuberculosis, other foreign proteins like gliadin or haptens like certain types of metal. This will build the bridge to our metal hypersensitivity (MH) later in this context. From a pathophysiological view, the antigen first is prepared by antigen-presenting cells like macrophages and later presented to the TH1-cells, which are a central aspect of the DTH reaction. The second contact or effector phase begins with a transformation of TH1-cells to CD4-helper cells, what leads to a production of monocytes in the bone marrow. This is caused by IL-3 and granulocyte macrophage colony-stimulating factor (GM-CSF). (71,73,74)

In addition, the TH1-cells emit macrophage migration inhibitory factor (MIF) and macrophage cytotoxicity factor (MCF) to lure macrophages and monocytes. In turn, these are activated by interferon alpha (IFN-alpha). The result is a severe inflammatory reaction with a potential to destroy the body's own and foreign, implanted tissue. (71,73,74)

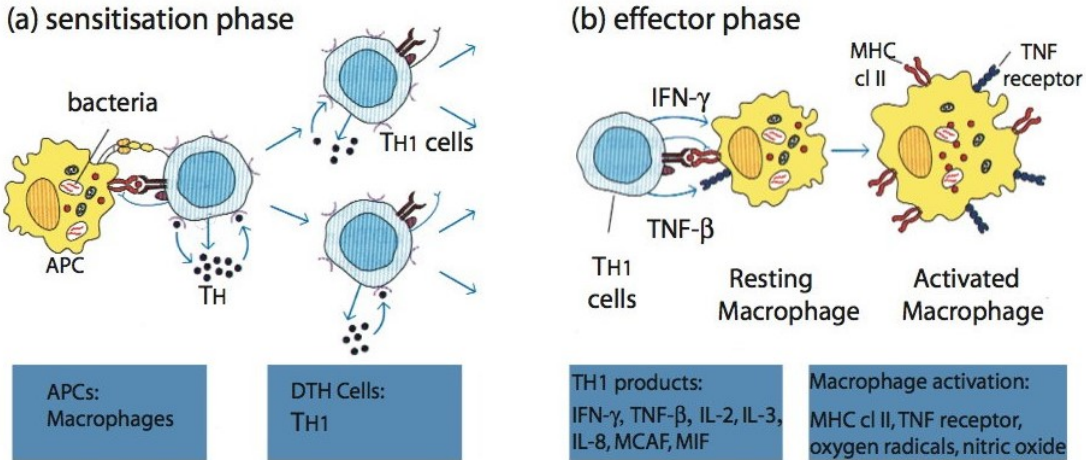

Figure 7: Pathogenesis of type IV hypersensitivity; From: Goldsby et al. Immunology 5th Ed, 2003, p.384 (75)

DTH can also cause cutaneous symptoms. Specific haptens, like nickel in a watch for example, can induce a contact dermatitis. Basically, the ions of the nickel are transferred to the skin, where it is bound to special proteins and finally identified as an antigen and processed by cutaneous macrophages. The macrophages gather in the regional lymphatic nodes and present the antigen to the specific T-cells. These immediately differentiate into a huge amount of T-killer cells or CD4-helper cells and get to the region of antigen exposure (71,73).

1.5.2 Metal Hypersensitivity and TKA

Approximately 10 to 15% of the world's population is affected by MH (76). The main problem about MH in TKA is corrosion. A specific process in the development of MH after TKA is the forming of complexes with proteins because of immune system activation, mediated by metal ions. Allergens to be considered as causing factor for MH could be those complexes. TKA models used today combine several types of metal, which leads to a mix of different metal ions that the human body is exposed to. Free ions are the main cause for corrosion in the TKA system. The most recently used metals that are related to MH are nickel, chromium and cobalt. Also, a cross-reactivity of cobalt and nickel can turn up in some cases. Other potential metals to cause MH reactions are titanium, tantalum or vanadium. (76,77)

Thienpont and Berger (74) pointed out that three factors are still unknown in this context:

- The specific metal to mediate implant-related MH
- The real prevalence of MH
- The clinical impact of MH on TKA

A manifest metal allergy impresses with cutaneous symptoms like redness, itching and eczema. To confirm the diagnosis contact dermatitis, caused by an orthopaedic implant, the eczema must radiate around the incision or cranial of the operated joint. Main criteria for the diagnosis are the postoperative occurrence, a chronic process, the fading of the eczema within 2 months after removal and exclusion of other aetiologies or deep implant infection. A generalised eczema is very unlikely to occur, because the load of metal ions is low enough due to avoidance of metal-metal contact in TKA. (74,77)

A huge problem regarding the diagnosis of MH is the lack of an adequate test to safely detect the pathology. Also, the relation between deep implant associated tissue reactions and a positive skin test still displays a problem here. (74,77)

Several in-vitro and in-vivo tests are available in the clinical routine nowadays. Due to the complexity and the costs of in-vitro tests, the in-vivo tests are more commonly used clinical setting. (74,77)

A first test in most cases is the epicutaneous testing or patch test, because of the easy use and relative low costs. The very high sensitivity of 100% speaks for itself, but with a specificity of 64% it is important not to diagnose overhasty, because a prediction of failure cannot be granted by a positive test. Nevertheless, a negative test can exclude MH. (74,77)

Lymphocyte transformation tests belong to the group of in-vitro tests and detect proliferative response of lymphocytes after activation. In the algorithm for the diagnosis of a MH, this test is to confirm or deny a positive patch test. Another possibility is to test the leukocyte MIF to impose the limitation of their migration. (73,74,77,78)

In order to provide a clinical insight to the problem of implant failure caused by MH, Table 5 describes the different haptens to turn an allergic reaction up. The data is used from a study performed by Granchi et al. (77).

	No Implant (n=20)	Aseptic Loosening (n=21)	Septic Loosening (n=17)	Mechanical Failure (n=9)
At least one hapten	15 %	61,9	58,8	44,4
Nickel sulphate	10	23,8	35,3	0
Chromium	5	28,6	11,8	11,1
Cobalt Chloride	5	19	5,9	11,1
Manganese chloride	5	19	23,5	33,3
Vanadium trichloride	5	23,8	17,6	11,1
Follow-up median months	-	24	24	24

Table 5: Frequency of positive skin reactions to metal haptens in case of TKA failure; Data from: Granchi D et al. Sensitivity to implant materials in patients with total knee arthroplasties. Biomaterials. 2008;29(10):1494–500. (77)

Summing up the data, the diagnosis of MH is still critical and in order to decrease the number of affected people, it was and still is a point in research, to find ways to fight against MH in TKA-systems. A possible, relatively new starting point will be discussed within the next chapters.

1.5.3 Advanced Coated System

1.5.3.1 Background

The ACS type TKA system (Implantcast, Buxtehude, Germany), is available in a mobile or fixed bearing variant and for primary or revision surgery with a special titanium nitride coating (TNC). It is currently available in cemented and non-cemented variants. (79)

Through the TNC, particularities of the implant surface are changed, but not the biomechanical functionality or the material itself. TNC is considered to reduce wear, have a better biocompatibility and a preventive function concerning DTH reactions. From the geometry and implanting procedure, there is no difference to other TKA systems, for example the LCS system, to which it is compared in the special part of this thesis. (79)

Figure 8: ACS-Prosthesis, From: Implantcast. ACS® Kniesystem. Available from: http://implantcast.info/index.php?option=com_content&view=article&id=75%3Aacsr-und-acsr-sc-kniesystem&catid=925%3Aprimaerversorgung&Itemid=67&lang=de (79)

1.5.3.2 Biocompatibility

TKA belongs to the most expensive medical procedures with lifetime costs ranging from $37.100 to $57.900 per patient in the USA. (80)

Regarding to these numbers, the need for improvement and cost-reduction is high in this issue. A promising approach lies in improving the biocompatibility of TKA. The theoretical effort here would be less third body wear and a lower risk of implant failure, which should also result in lower lifetime costs per treated person. (81)

Today's prostheses of knees and hips survive more than 15 years in about 90% of all cases (82,83). The topic of biocompatibility is very essential in this context, because it can reduce costs and prevalence of revision surgery. Biocompatibility is a terminus present for decades now and regarding to B.D. Ratner (84), there is a necessity for a new definition: "Biocompatibility is the ability of materials to locally trigger and guide normal wound healing, reconstruction, and tissue integration".

An innovation is the term of biotolerability, also publicized by Ratner, which describes "the ability of materials to reside in the body for long periods of time with only low degrees of inflammatory reaction. In other words, the body can tolerate them, but they're not always compatible." (85) Concerning biocompatibility and TKA, there are three main issues to be enlightened by further basic and clinical research:

- The primary integration of the prosthesis into the bone
- Outgrowth of wear with secondary aseptic loosening and osteolysis
- Development of new bearing surfaces for an improvement of implant lifetime (82)

The last point addresses the main topic of our study in the special part, the question whether TNC has the biocompatible characteristics to improve complains and the lifespan of knee prostheses.

1.5.3.3 Titanium nitride coating

Titanium nitride is in surgical use since 1972, where Steinemenan patented the "use of titanium or a titanium alloy implants for the surgical treatment of bones" (86) and is basically a ceramic that impresses through its gold-yellow colour.

Titanium nitride is the result of a reaction of titanium hydrogen powder or simple titanium with nitrogen at a temperature of about 1200° (87).
A method to imply TNC is the use of this nitrogen ion implantation, physical vapor deposition and plasma ion nitriding (88).

In the last few years some other methods, including powder immersion reaction assisted coating, nitrogen plasma immersion ion implantation or the Hardion+ nitrogen implantation technique have been established as well. These methods might lead to a better adhesion of TNC to the prosthesis (89–91).

TNC is further used in other medical treatments such as pacemakers, ventricular assist devices for heart failure patients, neurological electrodes and even in dental implants, also due to the aesthetic aspect of a golden tooth. (92–96)

The most important fact to keep in mind concerning the special issue of implant failure is that every metal getting in contact with human tissue undergoes corrosion and MH might accelerate this in a negative way. (96,97)

TNC is a potential way to reduce the burden of patients with MH after implantation of knee prosthesis. A hypersensitivity to metal is tested via patch skin test and according to a study of Ajwani et al. (98) the prevalence is between 10 and 17% in total. The TNC variant of knee systems is indicated for patients, which complain of sustained local or systemic symptoms. The application of titanium nitride onto the prosthesis is ensured by "physical vapour deposition in a layer of 3–4 μm". (96,97)
Besides that, TNC is said to have corrosion-protective characteristics, according to a study of Wisbey et al. (84).

The advantages of this coating is considered to be decreased joint wear, increased hardness (2000 kg/mm^2) of the implant components, less adhesion to polyethylene and a low friction coefficient (81,95,99).

Furthermore, TNC also has a barrier function for ions including cobalt and chrome, which derive from the metal substrate. These ions can cause allergic reactions, just as described in the allergy section below (100,101).

1.5.3.4 TNC and recent Evidence

A hot topic in the decision of using TNC or not is the question, if metal allergy really exists (102) and if there can be a causal relationship between cutaneous symptoms and deep-tissue reactions (103). Although a high percentage of the world's population is sensitive to metal with values between 10 and 48% (74,104,105), just a few, Thienpont et al. (74) spoke of less than 1%, really develop symptoms.

A second issue here is the lack of universally accepted diagnostic algorithms to confirm a metal allergy. Thienpont et al. (74) here pointed out that a first step should always be the self-report of a patient regarding to potential existing allergies. If the patient confirms an allergy, the next thing to do would be skin patch-testing. The advantage here lies in 100% sensitivity, which implies a perfect negative predictive value. If the test is positive, the last test to confirm or deny a metal allergy will be the lymphocyte transformation test (LTT) and the indication for the use of hypoallergenic implants like TNC should be given or not.

Kitagawa et al. (106) argues against this algorithm for some reasons: They claim that a self-reported allergy is enough justification for the use of TNC implants. The value of patch-testing and LTT is not doubtless in diagnosing metal allergy not only because of the high price of LTT.

A recent review of van Hove et al. (81) discussed the effect of TNC on the biocompatibility. Altogether, a positive effect has been found, but on the contrary, there is currently no proof of clinical improvement on a long term basis. This will be discussed later in the special part.

Other reasons to question the use of TNC is the amount of published studies, which describe third body wear due to delamination, cohesive failure of the coating or higher levels of polyethylene wear. This might be dependent on which processes is used for the coating procedure, what Harman et al. also pointed out (107). It should be mentioned that these complications mainly occurred after total hip arthroplasty. Knee implants were affected to a lower content, here the problem more often was a periprosthetic fracture, which was confirmed with two studies by Mohammed et al. and Park et al. (108,109).

TNC per se is a common issue of today's scientific research in many fields of dental and human medicine and the results are varying widely therefore too. In a recent study of Cui et al. (110), the authors proposed a special graded nano-TiN coating of implants, which is said to improve wear resistance. As there are some contraries to TNC, this new technique should "significantly improve adhesion strength, hardness and anti-wear performance". Also the biocompatibility was approved in-vitro and could target good results. (110)

In a study of Ratner et al. (85), it was criticised that there is no adequate measuring method for biocompatibility available at the moment, what results in wild speculations about the effort of new findings in this topic. The goal here, according to the author, should be a kind of an instrument to estimate the effect of new materials concerning their biocompatible characteristics.

1.5.3.5 Problems about TNC

Anyway, there are also comparative studies with less favourable results for TNC.

For instance, in studies conducted by van Hove et al. (81) or Galetz et al. (114), blistering of the coating was observed. This might be caused by differences in the stiffness between implant and coating.

Furthermore, third body wear could be detected in some studies, for example in Harman et al. (107) or Lappalainen et al. (111). This is due to delamination of the TNC. Results like this were found in studies concerning total hip arthroplasty, but not TKAs yet.

Underlining the current problematics, Li et al. (112) postulated the mechanisms that lead to aseptic loosening or osteolytic loosening in titanium alloy implants. Basically, the problem lies in the poor tribological performance of the commonly used titanium alloy. The consequence after some time is a cumulating amount of fine wear debris, which leads to a toxicity reaction of the periimplant tissue and further to loosening and/or osteolysis.

B Special Part

2 Materials and Methods

2.1 Ethics

A votum of the local ethics board was available for the clinical evaluation of patients who had received ACS type knee prosthesis. The number was 26-527 ex13/14.

2.2 Hypothesis

This thesis is part of a study performed at the Department for Orthopaedics and Trauma of the Medical University of Graz with a special focus on the differences between the allergic and non-allergic subgroup of our patient sample. Special emphasis was on allergies and potential chronical symptoms, which might turn up due to local or systemic allergic reactions.

The main hypothesis was if there are significant differences between our two therapy groups, the clinically approved low contact stress system with conventional cobalt-chromium-molybdenum alloy on the one hand and the advanced coated system, a relatively new TNC-system, on the other hand concerning clinical outcome and chronical inflammatory processes. All relevant parameters were analysed for an overall patient group and a separate group including patients, who declared themselves as allergic or were identified as allergic in our medical database.

2.3 Study Design

All patients, who received TKA of the ACS model at the Department of Hospital Bad Radkersburg between 2004 and 2006, were invited to attend this study with an invitation letter. Non-responders were contacted by phone. Of 669 patients, 432 patients (484 prostheses) could be included in this crossover survey between 2015 and 2016 at our department. This led to a mean follow-up of 11.92 ± 3.05 of all included patients; the intended follow-up examination time point was 10 years after surgery.

Within the study data was collected by anamnesis and physical and radiological examination of the patients. Common clinical scores were used for the standardized clinical evaluation of the outcome after ten years.

For the control group, a historic cohort of patients receiving a TKA of the LCS model at the Department for Orthopaedics and Trauma, of the Medical University of Graz and received a follow-up after a similar time point was used (n=474).

Furthermore, there was a special focus on symptoms, which might be induced by an allergic reaction caused by the metal components of the knee prosthesis. The following descriptions cover all relevant parameters that were used in the study.

2.4 Study Population

2.4.1 Background

Based on the fact, that there is currently no long-term study evaluating the clinical benefit of TNC on allergic TKA patients with an adequate population published, the aim of this study was to deliver first clinical data on this interesting topic.

The study population contained 744 patients, of who 484 received TKA of the ACS model and 260 patients where an LCS system was implanted. The LCS subgroup got treated in Graz between 1986 and 2002, whereas the ACS implantations were performed in Bad Radkersburg between 2004 and 2006.

2.4.2 Inclusion Criteria

- For the LCS subgroup, the only inclusion criterion was an implantation between 1986 and 2002 at the State Hospital of Graz
- The ACS population had to get their prosthesis received between 2004 and 2006 at the State Hospital of Bad Radkersburg

2.4.3 Exclusion Criteria

- None

2.5 Data Acquisition

2.5.1 Allergic Status

As the central parameter of this study, every patient had to determine himself as allergic or not. In the case of the patient not knowing his status, it was evaluated through the patients' medical records. It was documented with "yes" or "no". In addition, specific details on substances the patient is allergic to was recorded in our study database.

2.5.2 Sensitivity to Changes in the Weather

The second important parameter evaluated for this project was subjective meteorosensitivity regarding to implanted knee prosthesis. This value was also recorded as “yes” or “no” by the patient. Further specification concerning sensitivity to warm or cold weather and approaching storms was evaluated too, but not analysed.

2.5.3 Swelling and Reddening

Another parameter to indicate a chronic local inflammatory process of the surgically treated knee is swelling and reddening, two cardinal symptoms of inflammation. This information could only be raised for the LCS subgroup and therefore is just mentioned shortly. Again, the value here was either “yes” or “no” and specific information was noted too, but also not analysed.

2.5.4 Tegner Activity Scale

As described in subsection 1.4.5.3, the TAS got used to objectify the patients’ sport and working limitations and abilities prior and after surgery.

2.5.5 Western Ontario and McMaster Universities Osteoarthritis Index

The WOMAC-Index was also mentioned in subsection 1.4.5.3 and estimates the function, pain and stiffness of OA affected hips, knees and ankles. This score was used in all patients within this study.

2.5.6 Knee Society Score Pain/Function

KSS is a score divided into two parts and evaluates pain relevant parameters as well as functional abilities. More information got already provided in subsection 1.4.5.3. This score was used in all patients within this study too.

2.5.7 Visual Analog Scale

The last clinical score used in this study is the VAS score, which describes the current pain level of the patient. In subsection 1.4.5.3 again, more specific insight to the score was already given.

2.6 Statistical Methods

For the initial data collection, Excel (Microsoft, Redmont, WA), was used. All data was collected here for each patient without initial analysis. Measures and evaluations of clinical scores as described below were included as well as patient data, follow-up, data on surgery, the prosthesis itself and complications that occurred.

After the process of data acquisition was completed, all data was put into an IBM SPSS Statistics Software version 23 database (IBM, Armonk, NY), where statistical calculations were performed. Graphical portrayals were created via GraphPad Prism Version 7.04 (GraphPad, La Jolla, CA).

Statistical analysis was performed using chi-squared-test for comparison of categorical parameters, t-test for comparison of continuous normally distributed parameters and Spearmen's correlation coefficient for calculation of correlations. In addition, we set values for clinical relevance according to each measured score.

The statistical analysis was done with a defined significance level, or P-value, of $p \leq 0.05$. Regarding diagrams, * corresponds with $p \leq 0.05$, ** with $p \leq 0.01$ and *** with $p < 0.001$.

3 Results

3.1 Population Overview

This section should give a quick overview on the general analysis of the relevant parameters for the overall study population and the allergic subgroup.

3.1.1 Overall Population

Altogether 744 patients took part in the study, of which 484 (65.87 ± 8.35 years) received an ACS prosthesis and 260 (65.95 ± 10.97 years) got treated with the LCS system.
Table 6 below provides all relevant information concerning the whole patient sample.

Overall Population (n=744)	ACS	LCS	p-value
Age (years)	65.87 ± 8.35	65.95 ± 10.97	0.919
Type (ACS/Scorpio/LCS)	405/71/0	0/0/260	**<0.001**
Side (l/r)	269/215	103/121	**0.017**
Sex (f/m)	341/143	209/51	**0.003**
Allergy (n/y)	411/70	163/70	**<0.001**
Meteorosensitivity (n/y)	206/268	170/52	**<0.001**
Tegner preoperative	3 ± 1.26	3.04 ± 1.46	0.772
Tegner postoperative	2.78 ± 1.21	2.18 ± 1.47	**<0.001**
VAS preoperative	7.61 ± 1.39	6.93 ± 1.84	**<0.001**
VAS postoperative	1.95 ± 2.01	1.42 ± 1.83	**0.003**
KSS Pain	83.21 ± 15.69	70.82 ± 21.87	**<0.001**
KSS Function	65.71 ± 25.89	71.1 ± 29.08	0.085
WOMAC	81.16 ± 15.47	81.31 ± 14.58	0.933
Swelling/Reddening (n/y)	-	171/60	-

Table 6: Overall population (n=744) analysis of demographic data and clinical scores after a follow-up of 11.92 ± 3.05 years

The ACS group patients were clinically and radiologically examined shortly after surgery and after a main follow-up of 11.92 ± 3.05 years. Usual date of the follow-up evaluation was the 10-year routine examination, to which an invitation letter was sent.

Among the ACS overall population, there were 29.5% male and 70.5% female patients, whereas in the LCS group 19.6% were male and 80.4% female in total. There was no significant (p=0.919) difference between the two groups concerning mean age. The allocation of allergic people amidst the two therapy groups revealed 14.6% allergics in the ACS group and 28.8% in LCS treated patients. There was a significant higher (p<0.001) amount of allergic patients in the LCS group.

Regarding to Table 6, the rate of sensitivity to weather changes was significantly higher in ACS patients ($p<0.001$) with 56.5%, compared to 23.4% in the LCS subgroup. The last self-determined parameter to mention, swelling and reddening of the treated knee, revealed 26% answers with "yes" in the LCS group. The ACS complement was not evaluated.

3.1.2 Allergic Subgroup

Exactly 19% of the overall population, or 140 patients, were declared allergics. As shown in Table 6, the mean patients' age is different between the two subgroups. LCS allergics, with a mean age of 60.72 ± 12.79 years, are significantly older ($p=0.021$) than their ACS counterpart with 65.07 ± 8.47. Among the allergic subgroup, the allocation of prosthesis types was 70 against 70 in total. The ACS population included 54 ACS and 16 Scorpio prostheses.

An analyzation of the gender distribution showed, that 77.1% of our ACS allergics were female and 22.9% male, which was quite similar in the LCS sample with 84.3% female and 15.7% male patients.

Allergics (n=140)	ACS	LCS	p-value
Age (years)	65.07 ± 8.47	60.72 ± 12.79	**0.021**
Type (ACS/Scorpio/LCS)	54/16/0	0/0/70	**<0.001**
Sex (f/m)	54/16	59/11	0.284
Meteorosensitivity (n/y)	16/52	53/12	**<0.001**
Tegner preoperative	3.12 ± 1.32	3.27 ± 1.28	0.564
Tegner postoperative	2.49 ± 1.01	2.9 ± 1.51	0.128
VAS preoperative	7.88 ± 1.18	7.74 ± 1.07	0.554
VAS postoperative	2.72 ± 2.51	1.79 ± 1.88	**0.031**
KSS Pain	78.82 ± 17.75	69.23 ± 19.15	**0.017**
KSS Function	59.96 ± 23.5	75.32 ± 21.94	**0.003**
WOMAC	78.16 ± 14.83	81.17 ± 11.51	0.319
Swelling/Reddening (n/y)	-	55/15	-

Table 7: Allergic subpopulation (n=140) analysis of demographic data and clinical scores

As already discussed in subsection 3.1.1 for the overall population, the rate of sensitivity to changes in the weather among allergic patients was also significantly higher in our ACS group ($p<0.001$) with 76.5% compared to 18.5% in LCS patients. A comparison between allergic and non-allergic population is illustrated in Figure 9.

The issue of swelling and reddening amongst the allergic population was analysed for the LCS group. In fact, 21.4% of the patient sample complained about these symptoms, which is slightly less than in the overall population.

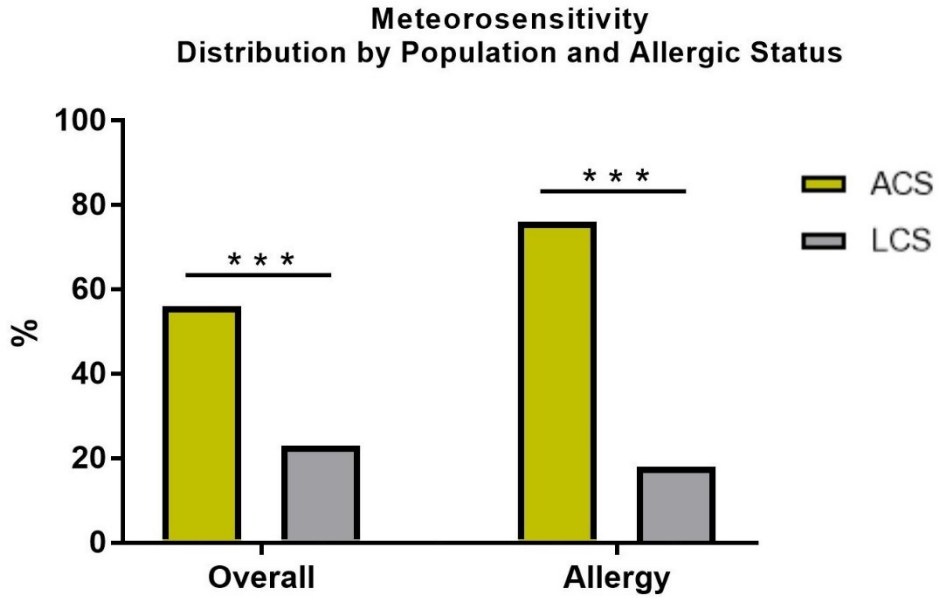

Figure 9: Box-Plots pointing up significantly higher rates of subjective meteorosensitivity among overall and allergic ACS-patients (p<0.001 each)

3.2 Analysis of Clinical Parameters

All relevant clinical scores have been introduced in the background part of the thesis already. We analysed both therapeutic subgroups independently and received the following results:

The Tegner activity score preoperative revealed no significant differences between the overall or allergic population with values close to 3, which is defined as "work – light labour (e.g. swimming, hiking)". In addition, the different therapy groups could not reveal differences.

After surgery, the values indeed varied. We found statistically significantly higher TAS scores regarding the overall ACS population than in LCS patients (p<0.001), without clinical relevance though.
On the allergic side, this result was turned upside down with statistically significantly better results for the LCS allergic patients (p=0.128) with the highest postoperative scores in this calculation. Again, we could not detect a clinically relevant difference either.

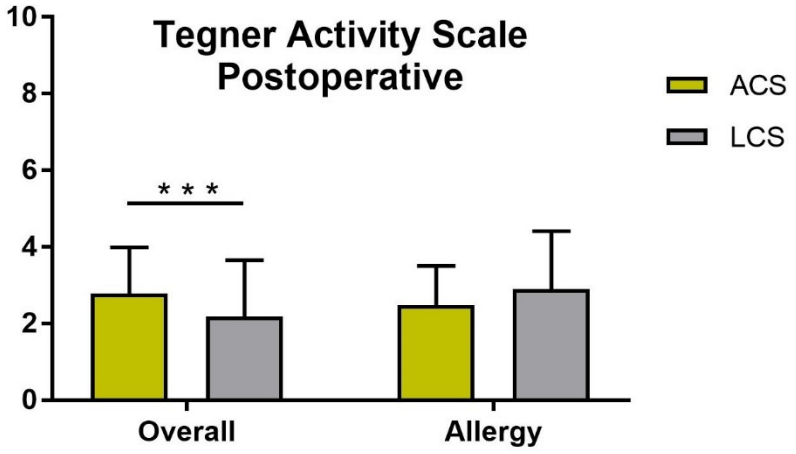

Figure 10: Tegner Activity Scale postoperative scores for overall and allergic population with a significantly better outcome for the overall ACS population without clinical relevance

The next analysis was about the VAS, in which, objectively seen, all groups and subgroups could improve ten years after TKA had been implanted. This can be seen in reductions of VAS values from 7.88 ± 1.18 to 2.72 ± 2.51 in allergic ACS patients and 7.74 ± 1.07 to 1.79 ± 1.88 in the associated LCS group. The same could be found for the overall population, where the LCS group improved from 6.93 ± 1.84 to 1.42 ± 1.83 and the ACS group from 7.61 ± 1.39 to 1.95 ± 2.01

Preoperative VAS scores revealed significantly better results without clinical relevance for the overall LCS group ($p<0.001$), where in the allergic population no significant difference could be found. After surgery, the LCS group revealed statistically significantly better results than in the ACS population, for overall population ($p=0.003$) as well as for the allergic patient subgroup ($p=0.031$). However, these results could not implement clinical relevance.

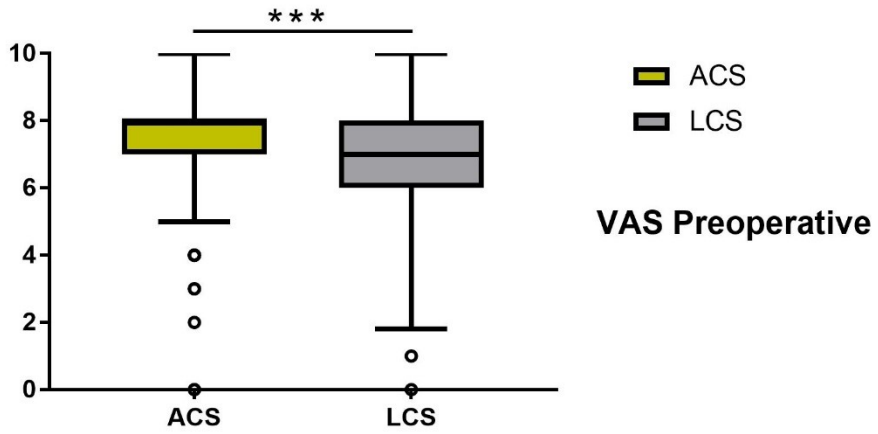

Figure 11: Preoperative VAS of the overall population showing significantly higher scores in ACS (golden) than in LCS (silver) patients; without clinical relevance

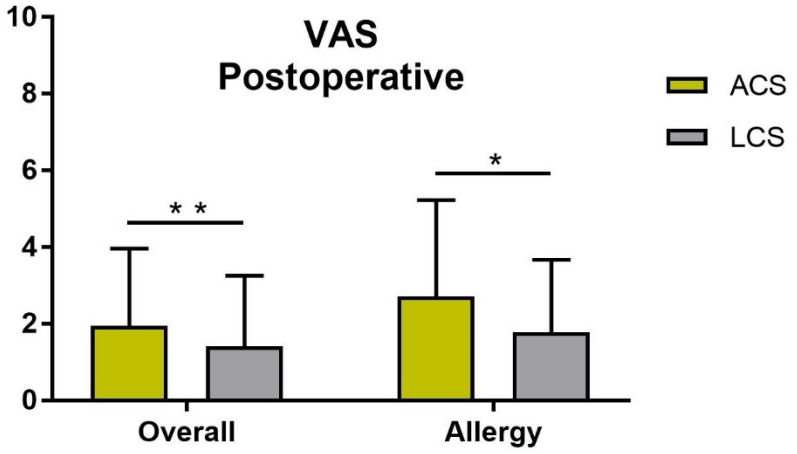

Figure 12: Box-Plots showing postoperative VAS scores for the overall and allergic ACS and LCS population.

As described in subsection 1.4.5.3, the Knee Society Score objectifies the pain level on the one hand and functional aspects on the other hand. KSS for Pain and Function were only evaluated at the postoperative follow-up.

Beginning with KSS Pain, in the overall population statistically significantly better scores without clinical relevance ($p<0.001$) for the ACS system were explored. The mean values were 83.21 ± 15.69 compared to the LCS group targeting values of 70.82 ± 21.87. This statistically significant difference in favour of the ACS group was also detected for the allergic subgroup ($p=0.017$), also here without clinical relevance. The ACS values of 78.82 ± 17.75 approved upon them of the LCS group with 69.23 ± 19.15.

Figure 13: Analysis of postoperative KSS Pain Scores for overall (left) and allergic (right) population displaying significantly higher scores in ACS patients with clinical relevance

KSS Function, a score to estimate functional deficits, also revealed significant differences within the subgroups. Among the overall population, the LCS group had statistically significantly better results than in ACS patients (p=0.085). Hence, for the allergic subgroup, the difference was statistically significant better (p=0.003) in patients, treated with the LCS system with higher scores of 70 and above. As before, these differences did not contain clinical relevance.

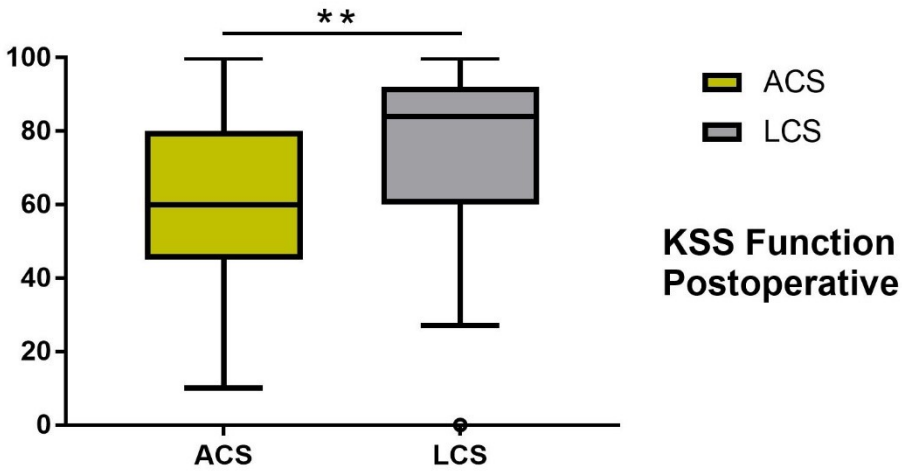

Figure 14: Box-and-Whisker Plots for KSS Function among allergic patients showing significantly higher scores in the LCS population, clinically relevant

The last clinical score to discuss is the WOMAC score, an OA specific measuring instrument, which was also evaluated after surgery. In all populations and subpopulations, there could be found a homogeny pattern of results with relatively high scores around 80.
No significant differences could be found here.

Although many statistically significant differences could be observed comparing the LCS with the ACS prosthesis, none of these differences reached a clinically meaningful value of over 20% change in the measured scores. Therefore, we present no clinically meaningful difference between the LCS and the ACS prosthesis after ten years of follow-up in the overall population or the subpopulation of patients with allergies.

4 Discussion

4.1 General

Main goal of this project was to evaluate potential clinical differences in allergic patients regarding to their different TKA treatment, so the discussion will be focussing on the allergic subgroup of the patient sample.

Intention of the TNC in ACS prostheses is to find a way to prevent hypersensitive patients and patients with metal hypersensitivity from devastating complications like loosening, periprosthetic infections or arthrofibrosis. As the problem with MH is, that there is currently no universally approved diagnostic algorithm, it is a difficulty to objectively estimate the real number of affected patients. A potential key to solve the MH related issues is the use of prosthesis models with a higher biocompatibility, which are proposed to have improved characteristics when interacting with the human tissue after implantation.

When TNC was invented, a main hypothesis was that it will improve clinical scores after a long time follow-up as well as subjectively perceived parameters like meteorosensitivity, which can be interpreted as an indicator for chronic local inflammatory reaction.

4.2 Result Interpretation & Comparison

The biometrical analysis did not reveal gravid differences at all except of a significantly younger patient collective among allergics in the LCS therapy group. However, there was no clinical relevance detected.

More than two thirds of the patients were female, which also matches the gender distribution in earlier published cohorts with OA of the knee. The age distribution correlates with similar results of specific studies published by Pennington et al. (113) and Sims et al. (114).

Analysis of subjective sensitivity to weather changes resulted in significantly better results for the LCS subgroup, which would be contradictory the intention of TNC. It is to remark that, since the measured difference was very small, this statistically significant difference does not seem to be clinically relevant. Meteorosensitivity, which can be interpreted as kind of an indicator for a chronic local inflammatory reaction, should hypothetically be reduced by the protecting effect of TNC.

Just 23.5% of allergic patients with a TKA system of the ACS type did not report meteorosensitivity over the whole follow-up. As there are no long-term studies on meteorosensitivity as a possible complication following TKA, there is a lack of studies to compare with.
Nevertheless, in fact this is an important point to question a positive effect of TNC, because on the other hand only 18.5% of the LCS sample reported meteorosensitivity at all.

Evaluation of results for clinical scores revealed a similar tendency as described above for meteorosensitivity. It should be mentioned that the preoperative scores for TAS and VAS revealed no significant difference, so the initial situation was homogeneous among the allergic subpopulation.

After the 10-year follow-up interval, all measured function scores revealed improvement for both groups in general, but with significantly better results for VAS and KSS function in the LCS subgroup. Just the KSS for pain was better in the ACS group. All these findings did not imply clinical relevance at all.
These facts underline the assumption from our meteorosensitivity results, that TNC may not have a positive or even protective long-term effect in allergic patients receiving TKA.

One step further, it seems that the outcome compared to the generally approved LCS prosthesis system tends to be slightly inferior, although concept underlying the LCS system does not deal with allergic patients in particular.

In this context, some other studies could also reveal interesting results.

Van Hove et al. (115) also compared a therapy group treated with LCS prosthesis to an ACS provided group and ascertained VAS, KSS score, revision rate, ROM and other parameters like temperature of the knee. After a follow-up of five years, no significant differences between the two groups could be explored either. The conclusion from the study was that there is no benefit on the outcome of ACS implants, but the system is also not inferior to the common LCS prosthesis. Advantages of the coated version can only be justified, as the authors state, in-vitro. Our opinion is that an advantage of a specific anti-allergic coating should also be measurable with clinical endpoints, for example a specific group of allergic patients. Otherwise the effect of a novel implant coating might be questionable.

Thienpont (73), another expert in this field, underlines these findings:
He conducted a study, where TNC prostheses were compared to conventional cobalt chrome implants. No statistically significant or clinically relevant outcomes after a 2-year follow-up period could be found at all: There were no significant differences in clinical or radiological outcome at all and the author pointed out that TNC implants are not inferior in comparison with conventional arthroplasty systems. Our results after a 10-year follow-up could in some way confirm these findings, because the TNC implants reached similar clinical results in most of the parameters included in our study. It is just to remark, that both outcomes were clinically satisfying and the statistical differences were not clinically relevant.

In a study with a longer follow-up of 4 years by Beyer et al. (41), the authors described nearly identical clinical outcomes when comparing a cohort with coated TKA treatment to a conventional implant group. There were no adverse effects in the coated group during any time point of the follow-up. The authors claimed excellent results in both therapy groups. A negative point here could be that an exclusion criteria for the study was MH in the patient's history, which is in general considered a major indication for the use of a coated prosthesis. Altogether, the results of this mid-term follow-up study really come close to our data.

Breugem et al. (116) evaluated the outcome of over 1000 implanted TNC prostheses of the ACS type in a recent study with a mean follow-up of 46 months. Their findings could reveal "good to excellent patient satisfaction and function of the arthroplasty". VAS-scores were even lower than in our study. This can be seen in values between 0 and 1 on a 0-100 scale compared to our ACS-allergics outcome with values of 2.72 ± 2.51 on a 0-10 scale. In addition, our LCS allergic subgroup could come closer to that with values of 1.79 ± 1.88. The authors refer to the importance of long-term studies in this field, because of two reasons:

- The current unsureness about the effect of TNC on polyethylene wear on a long-term basis is still a big point to discover
- Their results were truly satisfying at all

We could approve with these statements in some points, but also object to them, as we explored no improvement of TNC after our 10 to 13 years follow-up compared to conventional TKA systems. The importance of further investigation is unneglectable in this context.

Also worth mentioning concerning the effects of TNC is the different outcome in preclinical studies and in-vitro testing. Regarding biocompatibility, the coating revealed good results in a study conducted by van Hove et al. (95). On the other hand, they could just deliver insufficient evidence for advantages of TNC in the clinical setting or signs of an improved life spawn, since there were no long-term results available. Based on our findings we could not proof these hypotheses with our study either, since the outcome of our ACS group was not superior to the conventional LCS group. Especially the statistically higher rate of subjective meteorosensitivity in the TNC therapy group clinically contradicts the in-vitro described improvement of biocompatibility for in-vivo conditions.

Summing up, based on the results from our study we think that prospective, randomized long-term studies with special focus on metal sensitivity, and hypersensitivity or allergy in general, have to be conducted to clarify the current uncertainty concerning TNC, related implant failure and coating technique. Until then, according to my opinion, a specific benefit of TNC for patients with metal sensitivity, and hypersensitivity or/and allergy in general cannot be drawn from our results.

4.3 Limitations

As there are limitations in every scientific paper, our work contains some as well.
First, the retrospective approach is somewhat suboptimal, because it can appear as if the results were led into the wanted direction. A better variant would be the prospective study design, which is said to be free from bias in this way. In addition, a randomization of the patient sample would be a more unbiased option than our version, where just the ACS patients from Bad Radkersburg and the LCS patients from Graz were differentiated. Therefore, the perfect alternative design would be a prospective randomized multi-centre study.

The decision to invite the patients via post way in fact presents a limitation of this study. It is obvious that the rate of replies lies way beyond the maximum here due to several reasons. Patients may not respond to the invitation because the journey to Graz is difficult or there is no subjective need to have one’s wellbeing checked.

Due to the design of the study it is possible that especially very unpleased patients do not respond since they wish no further treatment at our institution or, on the other hand, mainly unpleased patients respond, since they wish an improvement of their clinical situation. An optimal solution would be the setting of a prospective and randomized study.

Our two therapeutic subgroups were treated in two separate hospitals by different surgeons, which could have biased the outcome as well.

Dead patients were not registered and analysed in our study, which could present a selection bias. Since significantly increased mortality of a study group, caused by the type of prosthesis used, seems unlikely I do not consider this bias as relevant for the outcome of our study.

5 Conclusion

Based on our statistical analysis and recent scientific findings, this study underlines the uncertainness of a positive impact of TNC compared to uncoated conventional TKA implants in the clinical setting in allergic patients. Different than what we would have expected from the in-vitro data the results of the hypoallergenic implant could not target improved clinical results among allergic patients in a long-term observation. This was determined through clinical scores, which were equal to the conventional implant model, and worse rates of meteorosensitivity. It is also to remark that the results of both implant models were satisfying after evaluation of ten years. According to our findings, we would recommend to use the ACS system in patients with multiple allergies or on individual patients´ request in case of concerns regarding allergies.

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Appendix

VAS

Wie würden Sie ihre Schmerzen im Moment einschätzen:

1	2	3	4	5	6	7	8	9	10

keine vorstellbare Schmerzen — **stärkste Schmerzen**

WOMAC

Symptome

Diese Fragen beziehen sich auf Beschwerden von Seiten Ihres Kniegelenkes in der **vergangenen Woche**.

S1. Haben Sie Schwellungen an Ihrem Knie?

niemals ☐ selten ☐ manchmal ☐ oft ☐ immer ☐

S2. Fühlen Sie manchmal ein Mahlen, hören Sie manchmal ein Klicken oder irgendein Geräusch, wenn Sie Ihr Knie bewegen?

niemals ☐ selten ☐ manchmal ☐ oft ☐ immer ☐

S3. Bleibt Ihr Knie manchmal hängen, oder blockiert es, wenn Sie es bewegen?

niemals ☐ selten ☐ manchmal ☐ oft ☐ immer ☐

S4. Können Sie Ihr Knie ganz ausstrecken?

immer ☐ oft ☐ manchmal ☐ selten ☐ nie ☐

S5. Können Sie Ihr Knie ganz beugen?

immer ☐ oft ☐ manchmal ☐ selten ☐ nie ☐

Steifigkeit

Die nachfolgenden Fragen betreffen die Steifigkeit Ihres Kniegelenkes während der **letzten Woche**. Unter Steifigkeit versteht man ein Gefühl der Einschränkung oder Verlangsamung der Fähigkeit Ihr Kniegelenk zu bewegen.
Für jede der nachfolgenden Aktivitäten sollen Sie das Ausmaß der Schwierigkeiten angeben, welche Sie durch Ihr Kniegelenk innerhalb der letzten Woche erfahren haben.

S6. Wie stark ist Ihre Kniesteifigkeit morgens direkt nach dem Aufstehen?

keine	schwach	mäßig	stark	sehr stark
☐	☐	☐	☐	☐

S7. Wie stark ist Ihre Kniesteifigkeit nach dem Sie saßen, lagen, oder sich ausruhten im **Verlauf des Tages**?

keine	schwach	mäßig	stark	sehr stark
☐	☐	☐	☐	☐

Schmerzen

P1. Wie oft tut Ihnen Ihr Knie weh?

niemals	monatlich	wöchentlich	täglich	immer
☐	☐	☐	☐	☐

Wie ausgeprägt waren Ihre Schmerzen in der **vergangenen Woche** als Sie z.B:

P2. sich im Knie drehten?

keine	schwach	mäßig	stark	sehr stark
☐	☐	☐	☐	☐

P3. Ihr Knie ganz ausstreckten?

keine	schwach	mäßig	stark	sehr stark
☐	☐	☐	☐	☐

P4. Ihr Knie ganz beugten?

keine	schwach	mäßig	stark	sehr stark
☐	☐	☐	☐	☐

P5. auf ebenem Boden gingen?

keine	schwach	mäßig	stark	sehr stark
☐	☐	☐	☐	☐

P6. Treppen herauf oder heruntergingen?

keine	schwach	mäßig	stark	sehr stark
☐	☐	☐	☐	☐

P7. nachts im Bett lagen?

keine	schwach	mäßig	stark	sehr stark
☐	☐	☐	☐	☐

P8. saßen oder lagen, z.B. auf der Couch?

keine	schwach	mäßig	stark	sehr stark
☐	☐	☐	☐	☐

P9. aufrecht standen?

keine	schwach	mäßig	stark	sehr stark
☐	☐	☐	☐	☐

Aktivitäten des täglichen Lebens

Die nachfolgenden Fragen beziehen sich auf Ihre körperliche Leistungsfähigkeit. Hierunter verstehen wir Ihre Fähigkeit sich selbständig zu bewegen bzw. sich selbst zu versorgen.

Für jede der nachfolgenden Aktivitäten sollen Sie das Ausmaß der Schwierigkeiten angeben, welche Sie durch Ihr Kniegelenk innerhalb der **letzten Woche** erfahren haben.

Welche Schwierigkeiten hatten Sie **letzte Woche** als Sie z.B.:

A1. Treppen herunterstiegen?

keine	wenig	einige	große	sehr große
☐	☐	☐	☐	☐

A2. Treppen heraufstiegen?

keine	wenig	einige	große	sehr große
☐	☐	☐	☐	☐

A3. vom Sitzen aufstanden?

keine	wenig	einige	große	sehr große
☐	☐	☐	☐	☐

A4. standen?

keine	wenig	einige	große	sehr große
☐	☐	☐	☐	☐

A5. sich bückten um z.B. etwas vom Boden aufzuheben?

keine	wenig	einige	große	sehr große
☐	☐	☐	☐	☐

A6. auf ebenen Boden gingen?

keine	wenig	einige	große	sehr große
☐	☐	☐	☐	☐

A7. ins Auto ein- oder ausstiegen?

keine	wenig	einige	große	sehr große
☐	☐	☐	☐	☐

A8. einkaufen gingen?

keine	wenig	einige	große	sehr große
☐	☐	☐	☐	☐

A9. Strümpfe/Socken anzogen?

keine	wenig	einige	große	sehr große
☐	☐	☐	☐	☐

A10. vom Bett aufstanden?

keine	wenig	einige	große	sehr große
☐	☐	☐	☐	☐

A11. Strümpfe/Socken auszogen?

keine	wenig	einige	große	sehr große
☐	☐	☐	☐	☐

A12. im Bett lagen und sich drehten, ohne das Knie dabei zu beugen?

keine	wenig	einige	große	sehr große
☐	☐	☐	☐	☐

A13. in oder aus der Badewanne kamen?

keine	wenig	einige	große	sehr große
☐	☐	☐	☐	☐

A14. saßen?

keine	wenig	einige	große	sehr große
☐	☐	☐	☐	☐

A15. sich auf die Toilette setzten oder aufstanden?

keine	wenig	einige	große	sehr große
☐	☐	☐	☐	☐

A16. schwere Hausarbeit verrichteten (schrubben, Garten umgraben, ...)?

keine	wenig	einige	große	sehr große
☐	☐	☐	☐	☐

A17. leichte Hausarbeit verrichteten (Staub wischen, kochen, ...)?

keine	wenig	einige	große	sehr große
☐	☐	☐	☐	☐

KNEE SOCIETY SCORE-PART 1

Part 1 - Knee Score (max. 100)

Pain	Points	Mild (Walking and Stairs)	30
None	50	Moderate – Occasional	20
Mild / Occasional	45	Moderate – Continual	10
Mild (Stairs only)	40	Severe	0

Total Range of Flexion	Points	61-65	13
0-5	1	66-70	14
6-10	2	71-75	15
11-15	3	76-80	16
16-20	4	81-85	17
21-25	5	86-90	18
26-30	6	91-95	19
31-35	7	96-100	20
36-40	8	101-105	21
41-45	9	106-110	22
46-50	10	111-115	23
51-55	11	116-120	24
56-60	12	121-125	25

Stability (Maximum movement in any position)	Points	Mediolateral	
Antero-posterior		<5°	15
<5mm	10	6-9°	10
5-10mm	5	10-14°	5
>10mm	0	15°	0

Flexion Contracture (deduction)	Points	Extension Lag (deduction)	Points
5°-10°	2	<10°	5
10°-15°	5	10°-20°	10
16°-20°	10	>20°	20
>20°	15		

Tibiofemoral Angle (deduction)	Points
5°-10° (valgus)	0
0°-4° (varus, max.15 pts [3 pts/°])	
11°-15° (valgus, max.15 pts [3 pts/°])	

Total	

KNEE SOCIETY SCORE-PART 2

Part 2 - Function Score (max. 100)

Walking	Points	Staires	Points
Unlimited	50	Normal up and down	50
> 2 km	40	Normal up and down with rail	40
1-2 km	30	Up and down with rail	30
< 1 km	20	Up with rail, down unable	15
Household	10	Unable	0
Unable	0		

Walking aids used (deduction)	Points
None used	0
Use of cane/Walking stick deduct	5
Two canes/sticks	10
Crutches or frame	20

Total	

Grading for the Knee Society Score	
100-80	Excellent
70-79	Good
69-60	Fair
below 60	Poor

Tegner Activity Scale

Aktivitätsgrad	Tätigkeit	Wertung
Wettkampfsport – auf nationalen und internationalem Niveau	• Fußball, Ski alpin (auf nationalem oder internationalem Niveau)	10
Wettkampfsport	• Eishockey, Ringen, Turnen, Fußball, Ski alpin (auf regionalem Niveau)	9
Wettkampfsport	• Snowboard, Badminton, Squash, Leichtathletik (Sprungdisziplinen)	8
Wettkampfsport Freizeitsport	• Tennis, Leichtathletik, (Lauf- und Wurfdisziplinen), Geräteturnen, Handball, Basketball, Orientierungslauf, Crosslauf • Eishockey, Fußball, Ski alpin	7
Freizeitsport	• Badminton, Tennis, Squash, Basketball, Handball, Volleyball, Orientierungslauf, Crosslauf, Snowboard, Aerobic (high impact), Joggen (mindestens 5x die Woche)	6
Wettkampfsport Freizeitsport Arbeit	• Radfahren, Skilanglauf, Eiskunstlauf • Turnen, Gymnastik, In-line-skating, Klettern, Bergsteigen, Skitouren, Schneeschuhlaufen, Joggen auf unebenem Boden (mindestens. 2x die Woche) • Schwere körperliche Arbeit (Bauarbeit, Waldarbeit)	5
Freizeitsport Arbeit	• Skilanglauf, Radfahren, Tanzen, Aerobic (low impact), , Bergwandern (abwärts), Joggen auf ebenem Boden (mind. 2x die Woche) • Mittelschwere körperliche Arbeit (schwere Hausarbeit)	4
Wettkampf- und Freizeitsport Arbeit Gehen	• Schwimmen, Wandern, Walking, Kegeln, Bowling • Leichte körperliche Arbeit • Querfeldein ist möglich	3
Arbeit Gehen	• Vorwiegend sitzende Tätigkeit • Auf unebenem Boden möglich	2
Arbeit Gehen	• Sitzende Tätigkeit • Nur auf ebenem Boden möglich	1
Arbeit Gehen	• Arbeitsunfähig oder berentet aufgrund von Knieproblemen • Nur eingeschränkt möglich	0