

Thesis

**MANAGEMENT OF TOTAL KNEE ARTHROPLASTY IN  
CHONDROGENIC TUMORS**  
**retrospective case series, literature review and  
management recommendation.**

submitted by

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Graz, 13/09/2024

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*I declare on my honor that I have written this thesis independently and without outside help, that I have not used any sources other than those indicated and that I have marked the passages taken from the sources used, either verbatim or in terms of content, as such.*

*Graz, am 13/09/24*

*Judith Maria Kremser m.p.*

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## Zusammenfassung

**Einführung.** Chondrogene Tumoren in der Nähe des Knies, wie beispielsweise gutartige Enchondrome, sind relativ häufige Befunde, die oft zufällig bei Bildgebungen aufgrund anderer Erkrankungen, wie etwa Arthrose, entdeckt werden. Diese Tumoren, die in der Regel asymptomatisch sind, es sei denn, sie werden groß genug, um Schmerzen oder Frakturen zu verursachen, können die Behandlung von Arthrose komplizieren, wenn eine Totalendoprothese (TEP) des Knies erforderlich ist. Die Prävalenz von chondrogenen Tumoren in der Nähe des Knies variiert, wobei einige MRT-Studien eine Häufigkeit zwischen 0,2 % und 2,9 % angeben. Die Herausforderung entsteht, wenn eine K-TEP in Anwesenheit eines chondrogenen Tumors von unklarer Dignität geplant ist, da das Risiko schwerwiegender Komplikationen, einschließlich Amputation, eine zentrale Rolle spielt. Ziel dieser Studie war es daher, die notwendigen diagnostischen, präoperativen und intraoperativen Schritte zu ermitteln, um die bestmöglichen Ergebnisse für Patientinnen und Patienten zu erzielen, die sich einer K-EP in Anwesenheit dieser Tumoren unterziehen.

**Hintergrund.** Chondromatöse oder chondrogene Tumoren sind eine vielfältige Gruppe von knorpelbildenden Tumoren, von denen die meisten gutartig sind, einige jedoch auch intermediäre oder bösartige Merkmale aufweisen können. Die Behandlung dieser Tumoren ist besonders herausfordernd, wenn sie gleichzeitig mit einer schweren Kniegelenksarthrose auftreten, was eine sorgfältige Planung erfordert, um Komplikationen während und nach der K-TEP zu vermeiden. Regelmäßige Nachkontrollen werden empfohlen, um diese Tumoren auf Anzeichen einer Malignität oder eines Wachstums zu überwachen, das möglicherweise einen chirurgischen Eingriff erfordert.

**Material und Methoden.** Diese Studie basiert auf einer retrospektiven Fallserienanalyse und fokussierte sich auf Patientinnen und Patienten, die sich einer K-TEP unterzogen haben, während gleichzeitig chondrogene Tumoren in der Nähe des Knies gefunden worden waren. Eingeschlossen wurden Patientinnen und Patienten, die detaillierte präoperative Bildgebung und eine anschließende K-TEP

erhalten hatten und bei denen Nachbeobachtungsdaten zur Beurteilung der Ergebnisse vorlagen. Sowohl Frauen als auch Männer waren in der Studienpopulation vertreten. Die Studie hielt sich an ethische Richtlinien, wobei die Genehmigung von der zuständigen Kommission eingeholt wurde. Eine umfassende Literaturübersicht wurde ebenfalls durchgeführt, um die Ergebnisse mit bestehenden Forschungen zu vergleichen und die Empfehlungen der Studie zu formulieren.

**Ergebnisse.** Die Studie ergab, dass eine detaillierte präoperative Bildgebung, einschließlich MRT und gegebenenfalls Biopsie, entscheidend für die Bestimmung des geeigneten chirurgischen Vorgehens war. Bei gutartigen Tumoren, die kein unmittelbares Risiko darstellten, war ein konservativer "no touch"-Ansatz mit regelmäßiger Überwachung oft ausreichend. In Fällen, die intermediäre oder bösartige Tumoren betrafen, waren jedoch aggressivere chirurgische Strategien erforderlich, die unter anderem auch ein mehrzeitiges Therapievorgehen erforderlich machten. Die Bedeutung eines multidisziplinären Teams für das Management dieser komplexen Fälle wurde ebenfalls hervorgehoben, um sicherzustellen, dass alle Aspekte des Zustands der Patientinnen und Patienten berücksichtigt wurden.

**Fazit.** Die Studie kommt zu dem Schluss, dass die Durchführung einer K-TEP in Anwesenheit chondrogener Tumoren machbar ist, aber einen hochgradig individualisierten Ansatz erfordert. Die Ergebnisse unterstreichen die Bedeutung einer gründlichen präoperativen Bewertung und einer sorgfältigen chirurgischen Planung, um das Risiko schwerwiegender Komplikationen, einschließlich Infektionen und der potenziellen Notwendigkeit einer Amputation, zu minimieren. Diese Studie liefert wertvolle Erkenntnisse für das Management von Patienten mit gleichzeitiger Arthrose und chondrogenen Tumoren und bietet Empfehlungen zur Orientierung in der klinischen Praxis.

## Abstract

**Introduction.** Chondrogenic tumors near the knee, such as benign enchondromas, are relatively common findings, often detected incidentally during imaging for other conditions like osteoarthritis. These tumors, which are typically asymptomatic unless they become large enough to cause pain or fractures, can complicate the management of osteoarthritis when Total Knee Arthroplasty (TKA) is required. The prevalence of chondrogenic tumors near the knee varies, with some MRI studies indicating a frequency between 0.2% and 2.9%. The challenge arises when a TKA is planned in the presence of a chondrogenic tumor of uncertain dignity, as the risk of severe complications, including amputation, becomes a critical concern. The aim of this study was to determine the necessary diagnostic, preoperative, and intraoperative steps to achieve the best possible outcomes for patients undergoing TKA in the presence of these tumors.

**Background.** Chondromatous or chondrogenic tumors are a diverse group of cartilage-forming tumors, most of which are benign, but some can present intermediate or malignant characteristics. The management of these tumors is particularly challenging when they coexist with severe osteoarthritis, requiring careful planning to avoid complications during and after TKA. Regular follow-up is recommended for these tumors to monitor for any signs of malignancy or growth that might necessitate surgical intervention.

**Material and Methods.** This study involved a retrospective case series analysis, focusing on patients who underwent TKA in the presence of chondrogenic tumors near the knee. The patients included were those who had undergone detailed preoperative imaging and subsequent TKA, with available follow-up data to assess outcomes. Both male and female patients were represented in the study population. The study adhered to ethical guidelines, with approval obtained from the relevant committee. A thorough literature review was also conducted to compare the findings with existing research and to frame the study's recommendations.

**Results.** The study found that detailed preoperative imaging, including MRI and biopsy, when necessary, was crucial for determining the appropriate surgical approach. For benign tumors that did not pose an immediate risk, a conservative "no touch" approach with regular monitoring was often sufficient. However, in cases involving intermediate or malignant tumors, more aggressive surgical strategies were required, sometimes involving staged procedures. The importance of a multidisciplinary team in managing these complex cases was also emphasized, ensuring that all aspects of the patient's condition were considered.

**Conclusion.** The study concludes that performing TKA in the presence of chondrogenic tumors is feasible but requires a highly individualized approach. The findings underscore the importance of thorough preoperative assessment and careful surgical planning to minimize the risk of severe complications, including infection and the potential need for amputation. This study contributes valuable insights into the management of patients with concurrent osteoarthritis and chondrogenic tumors, offering recommendations to guide clinical practice.

## Information on previous Publications

### Enchondroma and atypical cartilaginous tumor of the knee and osteoarthritis – case series, literature review and management recommendation

Christine Wibmer, MD, Marko Bergovec, MD, Ines Vielgut, MD, Magdalena M Gilg, MD, Norbert Kastner, MD, Patrick Sadoghi, MD, Andreas Leithner, MD.  
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#### Introduction and Purposes

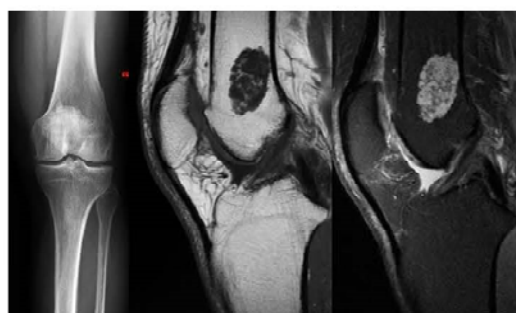
Enchondromas (EC) of the knee are prevalent in 2-3% of the population in MRI-studies. For solitary EC the risk of malignant transformation is reported between 1-4%. Radiologic signs accompanying increased risk of malignant transformation are cortical thickening, deep endosteal scalloping (>2/3 of the cortex) or permeative growth, peritumoral marrow edema and large size (more than 5-7 cm). Specific reports on risk of malignant transformation for this location and management recommendations for EC or atypical cartilaginous tumors (ACT) of the knee and osteoarthritis are lacking; we performed a retrospective case series to analyse treatment and outcome of patients with EC/ACT of the knee and osteoarthritis and a literature review.

#### Materials and Methods

We searched our database for patients with the diagnoses EC/ACT and osteoarthritis of the knee between 2005 and 2018. Diagnosis was confirmed by histopathologic investigation or typical radiologic findings.

#### Results

We retrieved 21 patients, f:m 15:6 with EC/ACT of the knee and osteoarthritis. In all but four total knee arthroplasty (TKA) was performed, whereof one navigated. EC/ACT were treated with curettage alone (n=5), or curettage plus bone cement (n=6), tricalciumphosphate (n=3), autologous spongiosa (n=1) or allograft (n=1). Five enchondromas were not touched surgically. At last follow-up no progression in size or recurrent tumor was found.



50y, m, chondrogenous tumor dist femur, osteoarthritis, X-ray and MRI



67y, f, chondrogenous tumor prox tibia, osteoarthritis, rheumatoid arthritis. Th: TKA no touch of EC

#### Conclusions

Our results reflect the heterogeneous treatment procedures due to missing guidelines. To avoid intraarticular contamination in case of malignancy we recommend TKA without touching the lesion (navigated or standard implantation of TKA) for EC without radiologic signs of malignancy and radiologic follow-up; for EC/ACT with radiologic signs of malignancy we recommend biopsy according to tumororthopedic standards, histopathologic work-up and upon histologic result TKA +/- curettage of the EC/ACT.

**Bibliography** Stomp 2015, Altay 2007

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## List of Abbreviations

$\alpha$	alpha
ACS	advanced coated system
ACT	atypical cartilaginous tumor
AMO	Anti-miRNA-Oligonucleotides
AP	ante-posterior
BMPs	bone morphogenetic proteins
CR	posterior-cruciate retaining
CS	chondrosarcoma grade
DOB	Date of Birth
EC	enchondroma
FB	fixed-bearing
FGFs	fibroblast growth factors
GMRS	Global Modular Replacement System
IGF	insulin-like growth factor
IL-1 $\beta$	interleukin-1 $\beta$
KLC	Kellgren-Lawrence-Classification
K-L stage	Kellgren-Lawrence-stage
LCS	Low Contact Stress
LFU	last follow up
LPS	Limb Preservation System
MB	mobile-bearing
MRI	magnetic resonance imaging

MRT	Magnetresonanztomographie
NP	nanopiece-delivery-platform
OA	Osteoarthritis
PCL	posterior cruciate ligament
PMH	past medical history
PS	posterior-cruciate substituting
PSI	patient specific instruments
ROM	range of motion
TGF- $\beta$	transforming growth factor beta
TKA	total knee arthroplasty
TKR	total knee replacement
WHO	World Health Organization
YOB	Year of Birth
X	Chi

# Glossary

## B

“**Benign**” refers to a disease process without tendency to aggressively spread (metastasize). It is used primarily in the classification of tumors and describes slow, non-invasive growth with gradual displacement of the surrounding structures.

## C

The **cancellous bone** is a spongy system in the interior of the bone that consists of fine bone trabeculae. The cancellous bone of the bone is surrounded on the outside by the compacta.

**Chondroblasts** are the dividing precursor cells of cartilage cells (chondrocytes). They are a cell stage of chondrogenesis.

The **chondrocyte** is a cell that arises from chondroblasts and resides in cartilage tissue.

**Chondrogen** means “cartilage-forming” or “of cartilaginous origin”. In a broader sense, the term is also used for the cartilaginous (chondrogenic) differentiation of chondroblasts.

A **chondrosarcoma** is a malignant bone tumor that can be primary or secondary and arises from cartilage tissue.

**Computed tomography**, or CT for short, is an X-ray procedure that shows the human body in cross-sectional images (sectional imaging procedure).

## D

**Dignity** is generally understood to mean the biological behavior of tumors (neoplasms) in relation to the entire organism, specifically their "value" with regard to their malignancy.

## E

An **enchondroma** is a cartilaginous tumor (chondroma) that is found primarily in the diaphyses of the phalanges or in the metaphyses of the long bones.

## H

**Histological** means “concerning the histology” or “concerning the tissue”.

## I

"**Intermediate**" often describes spatial location, but can also refer to morphology and other characteristics e.g. a tumor that has the genetic characteristics of two different cell types.

## K

The **knee joint** is the articulated connection between the thigh bone (femur), shinbone (tibia) and kneecap (patella).

## M

**Malignant** usually describes the property of diseases to advance in their development and thereby have a destructive effect on the entire organism.

**Magnetic resonance imaging**, or MRI for short, is an imaging procedure used to display the human body. It belongs to the subgroup of cross-sectional imaging methods.

## N

The term **neoplasia** or neoplasm refers to the new formation of body tissues. In a narrower sense this means an autonomous, pathological tissue proliferation, and in a broader sense it also means a physiological tissue regeneration.

## O

**Osteoarthritis of the knee** is a slowly progressive, non-inflammatory, degenerative change (osteoarthritis) of the knee joint, which leads to progressive destruction of the articular cartilage and other joint structures.

## P

In medicine, a **prosthesis** refers to the replacement of limbs, organs or parts of organs with artificial, functionally similar products.

**Pathological** means “not healthy” or “relating to pathology”. The antonym for “pathological” is “physiological”.

## R

**Radiological** means “concerning X-rays” or “concerning radiology”.

## T

**Total knee joint endoprosthesis** or total knee arthroplasty (TKA) are used as a last resort to treat osteoarthritis when drug therapy is no longer sufficient.

In the narrower sense, a **tumor** is a benign or malignant new formation (neoplasia) of body tissue that arises from a dysregulation of cell growth. Malignant tumors are also colloquially known as cancer.

## X

**X-ray** is a name for an imaging procedure that uses X-rays to produce a representation of pathological changes inside the human body.

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# 1 Introduction

Chondrogenic tumors near the knee, in the vast majority of cases benign enchondromas, are a relatively common finding.[4]

Those tumors are very rarely symptomatic - unless they are very large, which can cause severe pain or even cause fractures - and are therefore almost always diagnosed as an incidental finding on imaging for another cause, e.g. against the background of a osteoarthritis clarification. [4, 5]

Several MRI studies reported a frequency between 2-3%.[6-8] More recent MRI studies with regard to the knee and shoulder joints have shown that the prevalence has probably been overestimated, as it is more likely to obtain values between 0.2 and 2.9% [4, 6, 8-11].

As soon as the diagnosis is made, regular follow-ups should be carried out in any case, as there is a risk of degeneration e.g. a check-up X-ray every year. [6-8] If there is an increase in size, radiological malignancy criteria or symptoms, surgical treatment is indicated, possibly after prior tissue sampling. [6-8] For solitary enchondromas, a risk of malignant transformation between 1-4% has been described, but the literature does not provide precise figures on the risk of malignant transformation in this particular location. [12]

Known factors that increase the risk of malignant transformation are a localization close to the trunk, a size of more than 7 cm in diameter, as well as radiological changes such as thickening or erosion of the cortex. [5] Due to the mentioned epidemiology of chondrogenic tumors near the knee, a coincidence with the very common osteoarthritis (knee joint wear) is also no exception. [5] At the latest when the indication for surgical treatment of osteoarthritis of the knee by implantation of a total knee endoprosthesis arises, the question of the adequate treatment of a cartilage tumor in the operating area arises. [5] To date there are no recommendations for this in the literature that include state-of-the-art tumor-orthopedic management.

With the hypothetical core question of the study, it was asked whether “*Implanting a TKA in a situation with a chondrogenic tumor of uncertain dignity might lead to serious complications including amputation*”.

The aim of this study therefore is not only to shed light on the current situation using a retrospective case series and literature research and, at best, to provide a statement on the management of chondrogenic tumors near the knee in osteoarthritis of the knee but also to show what is necessary to best avoid a transfemoral amputation as an ultima ratio treatment option.

## **2 Background**

### **2.1 Chondromatous tumors**

The group of chondromatous or chondrogenic tumors includes various growths, all of which are primarily considered benign. [13-15] About 20% of these growths occur in the area of the distal femur. [16] These include osteochondromas (= cartilaginous exostosis with hyaline cartilage cap), which is the most common primary benign bone tumor, *multiple cartilaginous exostoses*, which is an autosomal dominant inherited disease that is characterized by the occurrence of numerous osteochondromas. [17-20]

To the group of chondrogenic tumors also belongs the enchondroma which is a benign intramedullary tumor made of hyaline cartilage tissue, which will be discussed in more detail below. [17-22] There is also an enchondroma disease, enchondromatosis (=Ollier's disease), in which a unilateral or asymmetric distribution of multiple enchondromas is found. [15, 23, 24]

Furthermore, was the chondroblastoma assigned to the group of benign chondrogenic tumors which is a locally aggressively growing bone tumor made up of chondroblasts (despite the locally aggressive growth, the WHO has no longer classified chondroblastoma as an intermediate bone tumor, but as a benign bone tumor since 2020.) with a metastasis potential of less than 1% of cases. [17, 25, 26] Last but not least, synovial chondromatosis (= Reichel syndrome) [27-31] also

belongs to this group, which is a tumor disease of the synovial membrane (here it is exactly the opposite: since 2020, the WHO has no longer classified synovial chondromatosis as benign, but as intermediate Bone tumor a.). [27, 30, 32]

Atypical cartilaginous tumors (ACT) are bone tumors composed of cartilaginous matrix, which were previously referred to as chondrosarcomas G1 [33-35]. Unlike ACT, enchondromas, which are considered to be purely benign lesions, have a low risk of local recurrence and a negligible tendency toward malignant degeneration. Differentiation between enchondromas and ACT is very complex from a clinical, radiological and histopathological point of view.[34]

Malignant bone tumors only make up around 0.5% of all malignant tumors. [21, 36, 37] Given that skeletal metastases occur about 2.5 times more often than primary malignant bone tumors, when adults exhibit symptoms suggestive of tumors, the initial priority is to rule out metastases originating elsewhere before considering primary bone tumors. [21, 36, 37]

If the malignant growth identified within the bone is a primary bone tumor, it typically involves modified skeletal mesenchymal cells with the potential to differentiate into osteo-, chondro-, and/or fibroblastic lineages. [21, 36, 37]

In addition, mixed differentiations also exist. This results in benign and malignant bone-, cartilage- and fiber-forming tumors. [21, 36, 37] Ewing's sarcoma and osteosarcoma are the most common bone sarcomas in childhood, whereas in adults, chondrosarcoma and osteosarcoma are. [36, 38, 39]

Bone tumors exhibit high clinical and biological heterogeneity. [13] The histopathological subtyping is based on the current WHO classification, which provides for division into dignity groups. [13]

This table only shows tumors of the “chondrogenic” category: [13]

<b>Chondrogenic Tumors</b>		
<b>Benigne</b>	<b>Intermediate</b>	<b>Malignant</b>
	This group includes tumors that either grow locally aggressively or, in rare cases, metastasize.	
Enchondroma Osteochondroma Chondroblastoma Subungual exostosis	Atypical cartilaginous tumor Chondromatosis	Chondrosarcoma

Table 1: Chondrogenic Tumors -  
 histo-immuno-morphological classification of bone tumors according to WHO 2020 [13]

All bone tumors and tumor-like lesions are essentially diagnosed with images only. [21] Only in case of suspected high grade malignancy histological assessment is needed. It should always include the X-ray findings (overview X-ray in 2 planes), since a biopsy usually only reflects a small section of a heterogeneously structured tumor, whose biological behavior in relation to the surrounding area can be seen in the X-ray image (serves as a replacement for macroscopy) is often much easier to see. [21] How heterogeneous this group of tumors is, is also illustrated by the fact that the WHO distinguishes between over 60 entities. [21]

As previously mentioned, the chondromatous tumors belong to the group of cartilage-forming tumors and, can be benign, intermediate / mixed differentiated or malignant.[12-14, 17, 19-21, 37, 38, 40-43] In the following the enchondroma and ACT, and chondrosarcoma are discussed in more detail below, as they are the three relevant entities for this retrospective study.

### 2.1.1 Enchondroma

**Definition.** Enchondromas [also called chondromas] are common benign chondrogenic tumors of hyaline cartilage tissue that grow in the medullary cavity and for which a possible origin from epiphyseal remnants is discussed. [5, 6, 17-20, 22] Both enchondromas (EC) and atypical cartilaginous tumors (ACT, also previously known as grade 1 chondrosarcoma) are neoplasms of cartilaginous origin in the bone marrow canal.[4, 6, 44, 45] ACTs represent an intermediate-risk neoplasm that is often difficult to differentiate from enchondromas. [4, 6] Differentiating the two lesions from each other is important but often difficult because atypical cartilaginous tumors (unlike enchondromas) definitely require surgical treatment. [4, 45]

**Epidemiology & etiology.** ECs occur approximately equally in men and women (0.9:1) with a frequency of 3-13% of all benign bone tumors. [5, 6, 17-20, 22] Although this frequency has been assumed up to now, more recent studies with regard to the knee and shoulder joints have shown that the prevalence has probably been overestimated, as it is more likely to obtain values between 0.2 and 2.9% [4, 6, 8-11]. The prevalence of ACT is 0.4% [4], compared to a prevalence of just under 2% (at the shoulder) [11] to 3% (at the knee joint) [10] for enchondromas [4, 46]. Both enchondromas and ACT occur predominantly in long bones – and enchondromas in particular – also in short bones [10, 11, 47].

On average, patients are 38 years old when they are first diagnosed with enchondromas, as 60% of enchondromas are discovered between the ages of 20 and 50. [5, 6, 17-20, 22] The small long bones of the hands and feet are mentioned as the main location (40-65%), but the long bones like distal femur, proximal tibia and proximal humerus are mentioned as the second most common locations (~25%) for enchondromas. [17-22, 48, 49]

Only a few studies have so far evaluated the prevalence of benign cartilage tumors in the knee area using MRI and obtained values between 0.2 and 2.9% [4, 6, 8-10]. Although the overall prevalence is very low for the incidental finding of an EC in the region near the knee, the distal femur still has the highest prevalence at 2.0%. [6]

Since most of these studies were based on small to medium-sized cohorts [4, 6, 8, 9], another newer study [10] aimed to verify these figures using a study on a larger and uniform cohort of patients with MRI scans of the knee, which had an overall prevalence of 1.45% for cartilage tumors of the knee joint. [10] In addition, a constant increase in prevalence was found for enchondromas over a period of 13.2 years, whereas the prevalence for ACTs remained constant over the same period.[10]

**Histology & Macroscopy.** These benign tumours are typically located in the diaphyses and metaphyses of short tubular bones and, more rarely, of long tubular bones. [17-22] If they occur close to the trunk (e.g. on the pelvis), enchondromas may have a worse prognosis but these bone tumors are classified as benign. [17-22] Macroscopically, enchondromas have a glassy appearance and their histology shows mature cartilage tissue. [17-22] In radiology they appear as lobulated osteolysis with ring-shaped calcifications in the shaft area.[17-22]

**Clinic & Symptoms.** Enchondromas stay stable or grow very slowly and are almost always painless, only large lesions cause pain or - especially in short bones – pathological fractures [4, 17-22, 50, 51] In the short long bones of the extremities, these tumors behave benign despite increased cell count and increased binucleation and therefore have a good prognosis. [17-22, 50] In the long bones, the same histological findings may correspond to a low-grade chondrosarcoma or an entrapment of bone, as it is known from ACTs. [17-22, 50] Since they are usually asymptomatic, they are often incidental findings obtained radiologically, as a result, the true prevalence of enchondromas remains uncertain. [4, 17-22, 49, 50]

**Diagnostic Features.** Basic diagnostics include conventional X-rays, in which possible findings such as intramedullary, rounded, sharply defined lytic lesions without periosteal reaction, possibly calcifications, erosion of the cortex or expansive growth with thinning of the cortex and swelling of the bone can be detected. [17-22, 50]

Computed tomography (CT) can be used to determine the exact size or extent of the enchondromas and, if necessary, whether there are erosions of the cortex. [17-22, 50] The lobulated character of the enchondromas can be detected in magnetic

resonance imaging (MRI), but also whether satellite foci and/or surrounding edema exist. [17-22, 50] Special imaging features allow an assessment of the tumor's dignity to a certain extent: larger lesions, the presence of a periosteal reaction of an endosteal bulge, but also perilesional edema can help to distinguish ACT from enchondroma. [6, 51].

The histopathology report shows evidence of hyaline cartilage and nodular hypocellular avascular lesions. [17-22, 50] In molecular genetics, in some cases, the mutation in the genes of IDH-1 and IDH-2 can be detected. [17-22, 50]

**Differential Diagnosis.** The most important differential diagnoses include chondrosarcoma or bone infarction. [17-22] Currently, the treatment of enchondromas depends on the symptoms and risk of fracture. [17-22] Asymptomatic lesions without a risk of fracture are regularly checked radiologically, while symptomatic lesions or lesions at risk of fracture are resected intralesionally and a biopsy is taken. [17-22] Under certain circumstances, these resection areas may need to be refilled with cancellous bone or bone cement, or osteosynthetic stabilization may be necessary. [17-22] The therapy usually consists of radiological follow-ups, careful curettage or, if necessary, an en bloc resection. [17-22]

Concerning the journal article *The 2020 WHO Classification of Soft Tissue Tumours: news and perspectives*, no new findings have emerged in this tumor group:

*“[...] no new entries have been included. Both [...] chondroma and [...] osteosarcoma represent exceedingly rare lesions. In [...] 50% of soft tissue chondroma FN1 gene rearrangements have been documented. Extraskkeletal osteosarcoma remains an extremely aggressive neoplasms of elderly patients, often presenting with lung metastases at diagnosis.” [43]*

### 2.1.2 ACT – Atypical Cartilaginous Tumors (ACTs)

ACTs are bone tumors composed of cartilaginous matrix, which were previously referred to as chondrosarcomas G1 [33-35]. Unlike ACT, ECs, which are considered to be purely benign lesions, have a low risk of local recurrence and a negligible tendency toward malignant degeneration. Differentiation between ECs and ACT is very complex from a clinical, radiological and histopathological point of view.[34]

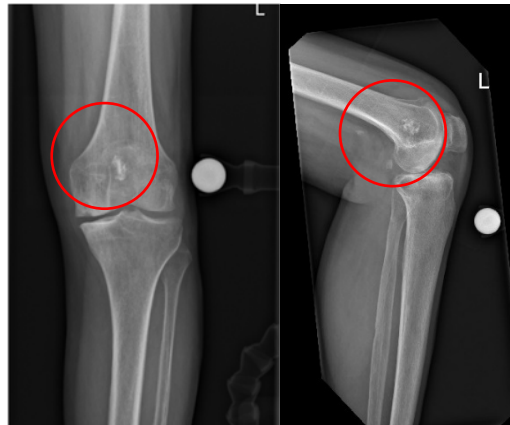


Figure 1: ID018 - preoperative plane X-Ray AP/lateral

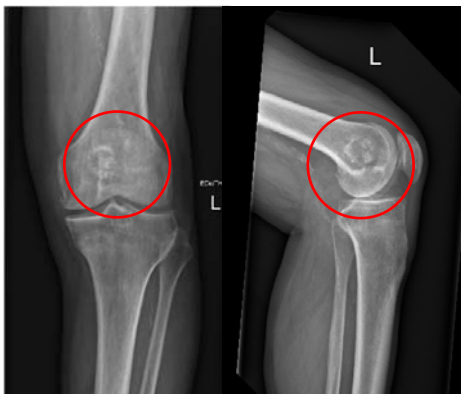


Figure 2: ID019 - preoperative plane X-Ray AP/lateral

**Epidemiology.** In 2013, G1 CSs of the long and short bones were distinguished by the World Health Organization (WHO) from truly malignant G2 and G3 CSs by changing the name to ACT [33-35]. This change states that ACT should be classified as tumors of intermediate dignity, since they behave locally aggressively but only very rarely metastasize.[34] The prevalence of ACT is

0.4% [4], compared to a prevalence of just under 2% (at the shoulder) [11] to 3% (at the knee joint) [10] for ECs [4, 46]. Both ECs and ACT occur predominantly in long bones – and ECs in particular – also in short bones [10, 11, 47]. The term “ACT” should only be used in the area of the extremities, while the histologically low-grade chondrogenic tumors of the axial skeleton (e.g. pelvis, scapula) should be referred to as “CS G1” and treated differently (i.e. further resection) [52].

#### **Clinic, symptoms & diagnostic features.**

Appropriate radiological markers (e.g., large lesion size, periosteal reaction, perilesional edema, and endosteal scalloping) help to differentiate ACTs from ECs [6, 10, 11, 33, 51]. ECs are mostly found in small bones of the hand and foot (40–65%) [10, 11, 48, 49, 53], followed by femur, humerus, tibia and ribs.[10, 11]. Figure 2 & Figure 1 each show preoperative images of patients with an ACT/G1 CS.

### 2.1.3 Chondrosarcoma

**Definition.** CS are chondroid matrix-producing mesenchymal tumors which typically show slowly infiltrating growth and whose primary genesis is [10, 11] unclear with sporadic mutations, but whose secondary genesis almost invariably arises from malignant transformations of previously benign forms. [21, 36, 37, 54, 55]

**Subtypes.** Essentially, there are two main subtypes of CS: the conventional and the non-conventional type, with conventional CS accounting for approximately 85-90% of all cases and being divided into central, peripheral and periosteal subgroups. [41] In contrast, non-conventional CS includes the following three types: mesenchymal, clear cell and dedifferentiated CS.[41] As with many other tumors, the etiology here is largely unknown. [21]

**Epidemiology & Etiology.** Although CS are generally rare tumors, with an incidence of around 15%, they are the second most common malignant tumor from the group of bone tumors in adult patients with a mean age of onset of 60 years. [21, 36, 37, 54, 55] It occurs slightly more often in males than in females, and the frequency of cases increases steadily, although slowly, until the age of sixty. [21, 36, 37, 54, 55] The preferred locations are the pelvis, the extremities near the trunk (femur, humerus) and the ribs. [10, 11, 36, 37, 54, 55]. Significant differences regarding metastasis can be found in the literature, particularly depending on the grading and location of the tumor. [36, 37, 54, 55]

**Clinic & Symptoms.** They often appear symptomatically with local swelling and other non-specific complaints. [36, 37, 54, 55] On average, metastasis occurs in approximately 23% of cases, usually pulmonary.[36, 37, 54, 55]

**Diagnostic features** in conventional x-rays include calcifications, osteolysis (e.g. “moth-eaten”: the higher the grading, the more lytic areas), and thinning (= scalloping) or breaking through of the cortex. [36, 37, 54, 55] In MRI, contrast medium accumulates in the areas discussed previously (MRI is particularly helpful in distinguishing between benign and malignant cartilage-forming tumors). [36, 37, 54, 55]

**Histology & Macroscopy.** The histological result of the biopsy shows lobular structure with possibly fibrous septa, tumor cells of different differentiation and a chondroid matrix. [36, 37, 54, 55] In molecular pathology, for example, an EWSR1-CREB1 gene fusion can be detected in myxoid CS.[36, 37, 54, 55] An expansion of the medullary cavity with thinning and erosion, sometimes also exfoliation of the cortex due to tumor infiltration, can be found in the long bones. [4, 21] Macroscopically, the picture corresponds to that of an EC with grey-bluish cartilage tissue, which can also occur within the cortex. [4, 21]

In histology, the CS is in sections more cell-dense than it would be the case with an EC and also grows in an osteodestructive manner. [4, 21] Clear cell atypia with isolated mitoses is shown, although direct osteoid or bone formation by the CS cells is not detectable. [4, 21] Based on nuclear size, nuclear hyperchromasia and cellularity, 3 grades of malignancy are distinguished (G1: 60%, G2: 35%, G3: 5%). [4, 21] Metastasis rarely occurs in G1 CSs. [4, 21] Well-differentiated CSs are often only recognized late due to the lack of pain. [4, 21] In addition, these tumors only metastasize very late. [4, 21]

**Treatment.** The treatment of choice is usually wide resection, including the biopsy channel (due to the risk of so-called implantation metastases). [4, 21] CSs are classified based on the WHO classification for chondrogenic tumors (conventional (grade G1-G3), dedifferentiated (grade 4), mesenchymal, clear cell and extraskeletal chondrosarcoma), and staged according to the TNM classification (system for classifying malignant tumors: “T “ (Tumor) describes the extent and behavior of the primary tumor, “N” (Nodus) the involvement status of regional lymph nodes and “M” (Metastasis) the presence of distant metastases). [36, 37, 54, 55] CSs are not very chemo- and radiosensitive, which is why a so-called R0 resection is usually carried out and the extent of the operation depends on location and grading. [36, 37, 54, 55] Intralesional resections are associated with an almost 100% risk of local recurrence. [36, 37, 54, 55]

Targeted tumor therapy (immunotherapy) is currently not a standard of care. [36, 37, 54, 55] Nevertheless, a study published in 2019 [56] showed that the treatment of chondrosarcomas by systemic delivery of NPs carrying AMO (anti-miRNA

oligonucleotides) may be promising (VEGF and MMP1 expression, MMP activity and tumor volume decreased by 32% in 38 days and the individual survival rate increased from 23 to 45%). [56]

With regard to the prognosis, it should be mentioned that the 5-year survival rate between 10-80% does not actually allow any meaningful conclusions, but it is known that there is a tendency to recurrence, especially if the resection is incomplete.[36, 37, 54, 55]

#### **2.1.4 Radiological Differential Diagnoses of another histological Nature**

**Baker's Cyst.** The Baker cyst is a hygroma (cystic accumulation of fluid) of the knee joint. [21] It is caused by repeated trauma, usually on the inside of the popliteal fossa. [21] The Baker cyst is connected to the knee joint cavity and is filled with synovial fluid. [21] It can be a complication of osteoarthritis of the knee joint but also of chronic polyarthritis. [21] Treatment consists of excision. [21]

**Ganglion.** Ganglia are pseudocystic changes in joints and tendon sheaths, the etiology and pathogenesis of which is not yet clear. [21] It is assumed that degenerative processes (myxoid degeneration) of the synovial connective tissue, supported by trauma, play a role. [21] Macroscopically, one can find single- and multi-chambered pseudocysts that adhere to the tendon sheaths and are filled with viscous (stringy) fluid. [21]

**Bone Infarction.** Bone marrow necrosis occurs in various neoplastic (e.g. acute myeloid or lymphatic leukemia, metastatic carcinomas) and non-neoplastic diseases (e.g. infections, sickle cell anemia). [21] Ischemia or the formation of tumor necrosis factors (TNFs) by neoplastic cells are discussed as causes. [21]

**Osteochondrom.** Osteochondroma is the most common benign new formation of bone, accounting for about 40% of cases. [21] It usually occurs as a solitary lesion, but rarely multiple lesions in the context of autosomal dominant exostosis disease. [21] Osteochondromas occur primarily in the first three decades of life, mostly in males. [21]

## 2.2 Osteoarthritis of the Knee Joint

Osteoarthritis refers to all degenerative diseases of the knee joint (femoro-tibial and femoropatellar), which are characterized by progressive destruction of the articular cartilage with involvement of joint structures such as ligaments, bones, synovial and fibrous joint capsules and periarticular muscles. [21] Osteoarthritis, also known as arthrosis deformans, is characterized by progressive degeneration and eventual loss of articular cartilage. [21] This disease primarily occurs in joints that are subject to greater stress which subsequently leads to compaction (sclerosis) of the subchondral bone and thus to the formation of bone outgrowths (osteophytes) on the edges of the joint. [21] A basic distinction is made between primary (without a clearly identifiable cause) and secondary (with a known cause) form of osteoarthritis. [21] Clinically, the disease presents with inflammatory and non-inflammatory phases. Only a proportion of patients with radiological changes have functional disorders or pain. [57]

As previously mentioned, primary osteoarthritis involves cartilage degeneration without a clearly identifiable cause. [21] With this form, there is the assumption that the degeneration could be due to an endogenous cartilage formation defect and that the increasing age of the affected person further promotes this. [21] In contrast, mechanical influences play a key role in secondary osteoarthritis as it develops with excessive strain (e.g. in obese people), in a traumatically damaged joint (st.p. accident), with poor "fit" of the joint components (e.g. congenital hip dysplasia), with infections, crystal deposits (e.g. gout) or through joint bleeding. [21]

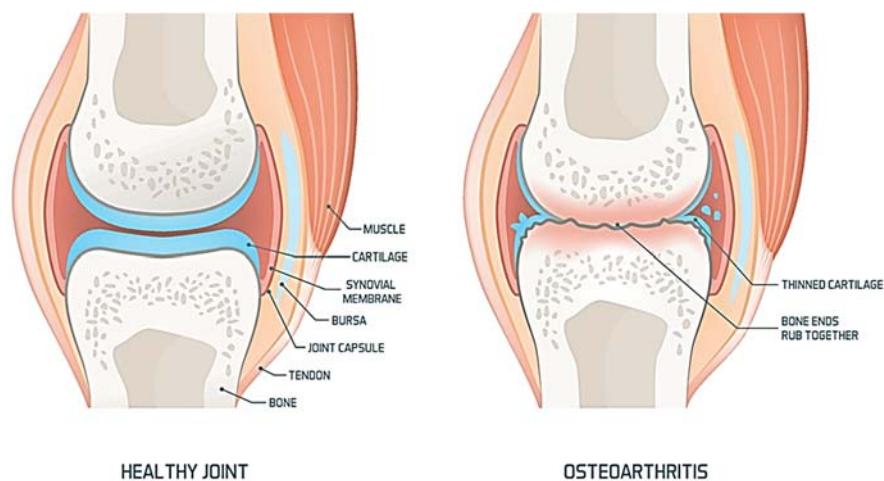


Figure 3: Healthy Joint vs Osteoarthritis Joint [58]

It has been found that clinical and radiological signs of osteoarthritis occur in approximately 24% of all people over 60 years of age.[59]

Clinical Features	Clinical and Laboratory Characteristics	Clinical and Radiological Features
Knee pain + at least 3 additional criteria:	Knee pain + at least 5 additional criteria:	Knee pain + at least 1 additional criteria:
age >50 years	age >50 years	age >50 years
Crepitations	Crepitations	Crepitations
Joint stiffness <30 minutes	Joint stiffness <30 minutes	Joint stiffness <30 minutes
Local tenderness	Local tenderness	Local tenderness
Bone enlargement at the edges of the joint	Bone enlargement at the edges of the joint	Osteophytes
no overheating of the joint	no overheating of the joint	
	BSG <40 mm/h	
	Rheumatoid factor <1:40	
	Synovial fluid: clear, viscous or leukocytes <2000/mm <sup>3</sup>	

Figure 4: Osteoarthritis of the knee [60]

### 2.2.1 Pathogenesis of Osteoarthritis

Osteoarthritis is a multifactorial, degenerative disease of joints that leads to a progressive remodeling of the joint structures and is associated with painful functional restrictions and even extensive loss of function of the affected joints. [57] Due to the heterogeneous etiology of osteoarthritis, a simple / uniform description of the resulting pathogenetic processes is not possible. [57] Central etiological factors are genetic components, age-related changes in regenerative capacity, (bio)mechanical changes or stresses, metabolic influences and mechanisms of local inflammation. [57] In principle, osteoarthritis affects all tissues and structures of a joint, but the structural structure of the hyaline articular cartilage and the changes that occur in it represent a central key to understanding osteoarthritis.[57]

Healthy articular cartilage consists of 95% extracellular matrix with a proportion of 5% chondrocytes and is a layer of tissue measuring a few millimeters. [57] The structure of the extracellular matrix is formed by a collagen network (especially

proteoglycans: determine turgid properties of the cartilage tissue), in which other structure-forming molecules are embedded. [57] Proteoglycans are able to initiate signaling cascades themselves or to bind other signaling molecules (e.g. GFs / chemokines) and thus function in the sense of a bioactive matrix. [57] (Bio)Mechanical changes, damage to the cartilage or other biological 'stress factors' for chondrocytes lead to a change in the composition of the cartilage matrix, which can lead to a continuously progressive loss of cartilage when the regenerative capacity of the cartilage is exceeded or exhausted. [57]

The morphological stages range from softening of the cartilage, to cartilage tears (which can later extend to the bone) to finally a complete loss of the cartilage layer are accompanied by increased new bone formation both in peripheral parts of the joint (there appearing as osteophytes) and subchondral (with manifestation as sclerosis). [57] Ultimately, all of these are primarily expressions of biochemical and molecular biological changes in the articular chondrocytes, which contain distinct phenotypic reactions (death of the cartilage cell, hypertrophic proliferation / differentiation) in the osteoarthritic degeneration process. [57] It is sometimes unclear whether specific mediators of pathological chondrocyte activation or differentiation exist.[57]

In recent years, a number of growth factors (e.g. TGF $\beta$ , BMPs, FGFs, IGF) and (inflammatory) cytokines (e.g. IL-1 $\beta$ ) have been identified that are found to a different extent in osteoarthritis and whose disturbed expression pattern at least partially aspects of the phenotypic change in chondrocytes. [57] In inflammatory joint diseases, the synovial membrane is not involved as a result of cartilage degeneration, but it is in osteoarthritis. [57] The destruction of the integrity of the cartilage matrix results in the detachment of cartilage components, which can lead to (reactive) synovitis. [57] Not only the non-specific stimulation of synovial cells by cartilage wear products (detritus) plays a role here, but also the specific and receptor-mediated stimulation of synovial fibroblasts and macrophages by individual molecules from the cartilage (previously associated with the extracellular matrix). [57] The synovial membrane then responds by producing inflammatory cytokines and this reaction pattern increases the degradative metabolic process in the cartilage, so that we can speak of a vicious circle of osteoarthritis.[57]

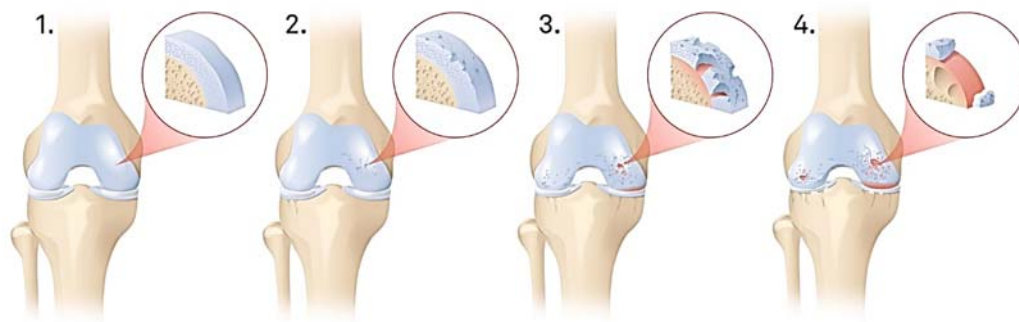


Figure 5: Stages of Osteoarthritis [61]

## 2.2.2 Morphology of Osteoarthritis

OA primarily affects large joints, such as the knees, the hips and the shoulders, but also the cervical and lumbar vertebral joints. [21] With the exception of Heberden nodules in the phalangeal joints, all other smaller joints are not affected by arthrosis deformans. [21] Macroscopically and radiologically, cartilage loss (presented as a reduced joint space), sclerotherapy (shown as widening / densification of the subchondral bone with pseudocyst formation) and osteophytes (as a result of increased new bone formation in the border region between the joint cap and cartilage with fibrocartilage-covered marginal exostoses) are found. [21] Changes show a gradual progression, with characteristic expressions (table below):

### Morphological changes according to the gradual progression

Stage I	Superficial loss of proteoglycan in cartilage and superficial cartilage tears (= fissures).
Stage II	Fissures deepen and extend to zone of radial cartilage. Cartilage cells perish. At the same time, surviving chondrocytes proliferate to form "brood capsules" → are surrounded by proteoglycan-rich halos → foreign body stimulus → development of synovitis → activation of synoviocytes → lymphoplasmacellular inflammatory (rare)
Stage III	Cracks become deeper → reach deep layers of cartilage → larger pieces of cartilage break off → cause further irritation of synovial membrane → can lie freely in joint space (rare)
Stage IV	Loss of articular cartilage exposes the bony cover plate. Vessels sprouted into defect from the epiphysis and subchondral bone. Chain reaction → osteoclastic bone loss, increased reflex osteoblast activity, sclerotherapy / thickening of subchondral bone plate, increased connective tissue proliferation, fibrocartilage formation, penetration of synovial fluid and subsequent pseudocyst formation, → ultimately filled by fibrinous scar tissue. Exostoses develop in the edge area, which are known as Heberden nodules in the interphalangeal joints.

Table 2: Morphological Stages of Osteoarthritis [21]

## 2.3 Kellgren-Lawrence classification

This classification was originally developed for degenerative changes in the knee joint, but over time it was adopted for all joints. [62, 63] Criticisms of this classification include low inter-rater reliability, the use of non-standardized X-rays and, in particular, the different ways in which the score can be interpreted. [62, 63] Independent radiological classifications have been developed for many joints, for example for the thumb saddle joint by Eaton/Littler, for the knee joint by Ahlbäck or the classification according to Tönnis for the hip joint. [62, 63]

degree of osteoarthritis	radiological findings
0: no osteoarthritis	normal findings
1: questionable osteoarthritis / normal	doubtful decrease in joint space width, discrete / questionable osteophytes (“osteophytic lipping”)
2: minimal osteoarthritis	definitive evidence of osteophytes, possible reduction in joint space width
3: moderate osteoarthritis	multiple osteophytes, reduced joint space width, mild to moderate subchondral sclerosis, possible deformity of the joint-forming bone parts
4: severe osteoarthritis	large osteophyte formations, advanced reduction in joint space width, severe subchondral sclerosis, deformity of the joint-forming bone portion

Table 3: Kellgren-Lawrence Classification [64]

The diagnosis of “osteoarthritis” is initially suspected on the basis of clinical features, but – ultimately – usually based on radiological data. Which data should be used to create valid radiological criteria was suggested by Jonas H. Kellgren and John S. Lawrence in 1957 and adopted by the WHO (= World Health Organization) in 1961. [65] In the classification named after them, JH Kellgren and JS Lawrence assess the severity of osteoarthritis based on a conventional x-ray. [64]

In the original publication from 1957, the score was evaluated on images of the hand skeleton, knee joints, cervical and lumbar spine, and hip joints. [64] Taking into account the following arthrosis signs, a classification into 5 stages is possible: detection of osteophytes, decrease in joint space width, increased subchondral sclerosis, deformity of the joint-forming bone parts. [64] In the original publication, no precise definitions of the anatomical changes (e.g. joint space narrowing or osteophytes) were given, so the findings are subject to relevant subjective interpretation. [66]

In a comparative study of 2020, they found the following:

*“Progression of knee OA is associated with changes in the morphology of the knee, [...] poor component fit and alignment and negatively impact clinical and functional outcomes after TKA. [...] changes are specific to the femoral condyles; thus, careful consideration of the fit and alignment of the femoral component is necessary, particularly for patients with advanced K-L stages of knee OA. Guidelines for femoral cut-lines and component sizing may need to consider OA grade.”*[67]

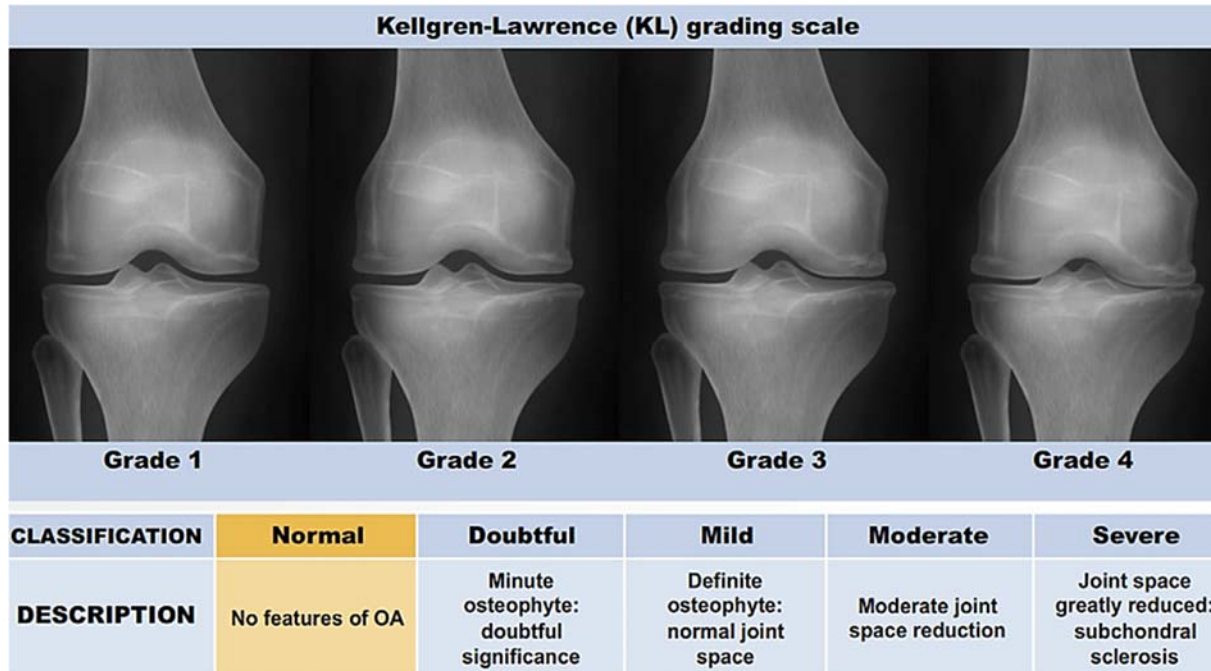


Figure 6: radiological Images of the Kellgren-Lawrence (KL) grading Scale [68]

## 2.4 Articulatio Genus – the Knee Joint

The articulatio genus is formed by 3 bones - femur, patella and tibia - and represents a **composite joint**, which can be viewed simply as a "trochoginglymus" (rotary hinge joint). [69] The two condyli femoris slide on the tibia (facies articularis superior) and together they form the articulatio femorotibialis, which can also be viewed simply as a rotating hinge joint (trocho-ginglymus). [69]

The striking incongruence of the two joint partners (tibia and femur) is balanced out by the two menisci (lateral and medial meniscus). [69] The second component of the articulatio genus is the articulatio femoropatellaris, in which the femur (facies patellaris) is in joint contact with the patella (facies articularis). [69]

If the knee joint is not in line with the hip and ankle joints, the weight is distributed unequally between the two condyles and signs of wear and tear can occur relatively early (osteoarthritis). [70-72] If the knee is too far medial (knock knees or genu valgum), the lateral condyle and the lateral meniscus are particularly stressed. [70-72] If it is too far lateral (bow legs or genu varum), the medial condyle and medial meniscus are more likely to be affected. [70-72]

Therapeutically, a so-called adjustment osteotomy can correct the joint axes but it must be noted that a misalignment of the hip can also lead to a compensatory misalignment of the knee.[70-72]

### 2.4.1 Joint Capsule of the Knee

The **joint capsule** (*stratum fibrosum*) is attached to the tibia one centimeter below the cartilage edges, runs around the condyles on the femur laterally, reaches the linea intercondylaris at the back of the joint and is fused ventrally to both the quadriceps tendon and the patella, which is why it cannot be clearly demarcated at the front. [69]

Interestingly, the joint capsule (*stratum synoviale*) is attached ventrally, medially and laterally to the knee joint to the bone-cartilage border of the tibial plateau, but surrounds the anterior intercondylar area, which means that the two cruciate ligaments are extra-articular (outside the joint) but intracapsular (enclosed by the

capsule) and nerves and vessels can reach the dorsal parts of the cruciate ligaments on both the femur and tibia. [69] Ventrally and proximally, the inner layer of the joint capsule (stratum synoviale) merges into the suprapatellar bursa. [69] Below the kneecap covers the Hoffa fat body (corpus adiposum infrapatellare) but the epicondylus femoris lie outside the capsule. [69]

## 2.4.2 Ligaments of the Knee Joint

The important **ligaments** of the knee joint are the patellar ligament (patellar ligament, arising from the quadriceps tendon), the collateral ligaments (medial / tibial and lateral / fibular collateral ligament), the popliteum obliquum ligament

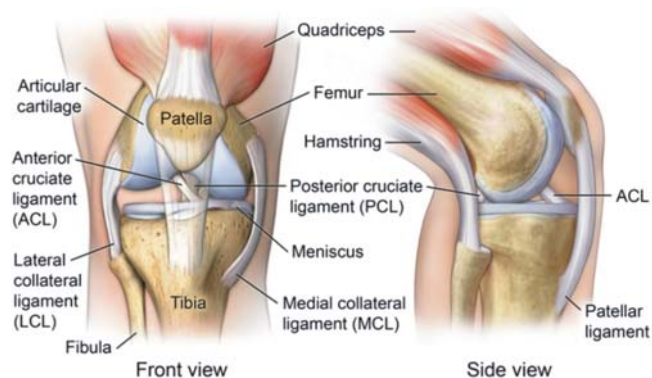


Figure 7: Ligaments of the knee joint [1]

(dorsal capsular reinforcer), the popliteum arcuatum ligament (lateral, arcuate posterior capsular reinforcer) the longitudinal (=reserve extensor apparatus) and transverse (capsule reinforcing cables) retinaculum patellae as well as the two ligamenta cruciata (anterior and posterior cruciate ligament) which, as previously mentioned, lie between the stratum synoviale and stratum fibrosum of the capsule, which means that they are extra-articular but intracapsular. [69]

*Unhappy Triad* - Skiing accidents often result in knee ligament injuries. [70-72] The so-called “Unhappy Triad”, in which the anterior cruciate ligament, the medial collateral ligament and the medial meniscus are damaged, is particularly unfavorable. [70-72] This happens when the knee is forced to bend and externally rotate, in which the knee is also in the knock-knee position (so-called valgus stress).[70-72]

### 2.4.3 Menisci

The **menisci** consist of connective tissue containing plenty of collagen fibers and cartilage-like cells. [73] These cartilage-like cells are usually located near the surface of the meniscus. The *medial meniscus* is fused to the tibial collateral ligament in a crescent shape and is very strongly connected to the surrounding structures, which is why it is significantly less mobile than the medial meniscus. [73]

In addition, the dorsal horn is much wider than the thinner anterior horn. [73] The *lateral meniscus* is almost circular and its attachment points are close together, it is the same width everywhere and is significantly more mobile than the medial meniscus because it is not fused to the fibular/lateral collateral ligament.[73]

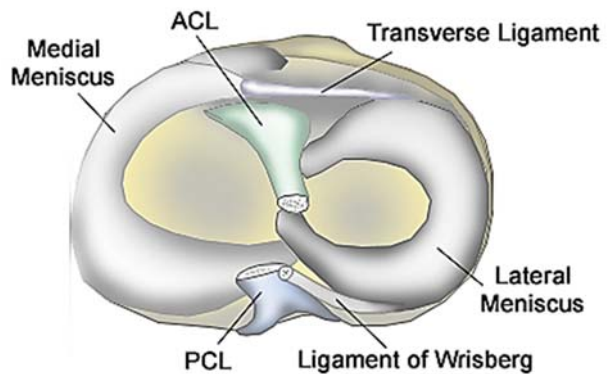


Figure 8: Image of the menisci of the knee joint [2]

Taking into account the previously mentioned, it seems logical that injuries to the less mobile and ingrown medial meniscus (especially the thinner anterior horn = Crus anterior) occur about 20 times as often as to the lateral meniscus. [73] The less mobile medial meniscus is most at risk, especially when rotational movements in the knee joint are not supported by muscles.[69]

### 2.4.4 Bursae of the Knee Joint

In the knee joint there are numerous **bursae**, some of which *communicate* with the joint cavity. [73] The largest of these communicating bursa is known to be the suprapatellar bursa, which is located ventrally and the joint space proximally. [73] Behind are the subpopliteal recess and the much smaller bursa musculus semimembranosi. [73] At the origin of the two gastrocnemoid heads there are two further bursae (bursa subtendinea musculus gastrocnemii lateralis and bursa subtendinea musculus gastrocnemii medialis). [73]

Of the *non-communicating* bursae, the subcutaneous prepatellar burs and the infrapatellar deep bursa should also be mentioned, although the latter can be connected to the joint cavity in individual cases.[73] There are also other smaller sliding bags that are not regularly available.[73]

### 2.4.5 Mechanics and Motion of the Knee Joint

The knee joint is stabilized primarily by muscles and ligaments. There is no bony guidance in the *femoropatellar joint*. [69] Only the intercondylar eminence can limit lateral displacement. [69] In articulation genu you can bend (flexion) and stretch (extension) around approximately transverse axes. [73] In addition, rotation around the lower leg axis is possible in a bent position. [73] In the most extended position, the thigh and lower leg are in a stable position. [69] In adults, active extension of the knee joint can occur up to an angle of 180° or passive extension by a further 5-10°. [69] When the knee is extended, both collateral ligaments and anterior parts of the anterior cruciate ligament are tensioned. [73] During extension, the femoral condyles slide into an extreme position, causing the medial collateral ligament to fully unfold. [73] During the last 10° of extension, before reaching the extreme position, the *final rotation* of the tibia occurs, which is approximately 5°. [73]

It is achieved by the tension of the anterior cruciate ligament and the shape of the joint bodies in the sense of an external rotation of the tibia on the freely swinging leg (= free leg). [69] If the knee joint is extended on the supporting leg, the final rotation is carried out as an internal rotation of the femur against the fixed tibia. [69]

When the knee is flexed, the lateral/fibular collateral ligament is completely relaxed, the medial/tibial collateral ligament is largely relaxed and the two cruciate ligaments are tensioned, ie: in the flexed position, rotation can be carried out by guiding the ligamenta cruciata. [73] The amount of internal rotation is less than that of external rotation but due to the inclined position of the cruciate ligaments, one cruciate ligament or parts of the cruciate ligaments are always tensioned in every position, which means that they could take over the leadership in the joint if the collateral ligaments become insufficient. [73]

During rotation, the femur and both menisci move on the tibia, while during flexion and extension, the femur moves with rolling and sliding movements on the menisci (= transportable joint). [73]

## 2.5 Total Knee Arthroplasty

### 2.5.1 Indications, Preparation and Aftercare for Knee Surgery

The absolute **indications** for a knee joint replacement include knee pain for at least 3-6 months, radiological evidence of structural damage (arthrosis, osteonecrosis), failure of conservative treatment measures ( $\geq 6$  months) and such great subjective suffering that it already limits the quality of life. [74-77]

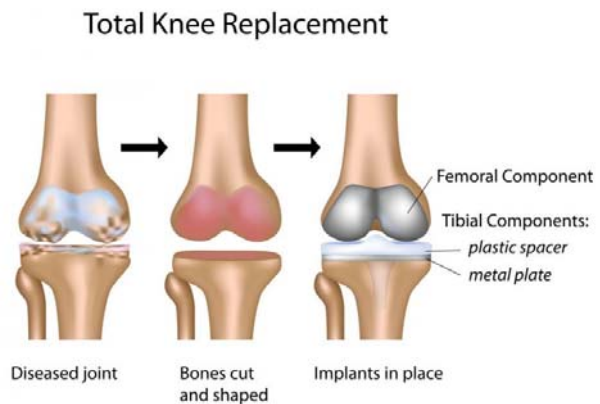


Figure 9: Image of an example for TKA [3]

**Preparation** for the joint replacement operation includes a natural X-ray (full-leg position), the collection of cruciate blood and the provision of erythrocyte concentrates as well as possibly the insertion of a pain catheter (for early postoperative, pain-free mobilization). [74-77]

The **aftercare** phase includes an X-ray check of the prosthesis fit, ossification prophylaxis (NSAIDs for 14 days) and medicinal thrombosis prophylaxis for 11–14 days postoperatively. [74-77]

### 2.5.2 Classification of Total Knee Arthroplasty

Various knee joint prostheses are available as possible surgical procedures: the unicompartmental endoprosthesis (=slide prosthesis), the patellofemoral endoprosthesis, the total endoprosthesis [74-77]

The knee replacement consists of three main components: The tibial component is a metal plate that covers the upper end of the lower leg bone (tibia). [78] This is anchored in the bone by a short, specially shaped stalk. [78] The femoral component is a metal implant that is modelled on the surface of a healthy femur. [78] After appropriate preparation of the thigh bone (femur), the implant is placed on the surface of the end of the bone. [78] A movable or locked plastic bearing that covers

the entire surface is placed on the tibial component. [78] This keeps the friction between the thigh and lower leg prosthesis parts as low as possible and enables smooth, pain-free movement. [78] If necessary, the back of the kneecap (patella) can be replaced with a plastic disc, which then slides on the metal shield of the femoral component of the knee joint. [78] When implanting a TKR, the goal is always to preserve as much intact bone as possible and only replace the damaged areas of the knee joint with the implant. [78] Depending on the degree of knee joint wear, a decision is made as to whether a total surface joint replacement (replacement of both sides of a knee joint) or only a partial replacement (unicondylar prosthesis, replacement of one half of the knee joint) is necessary. [78] Depending on the size of your knee joint, different sizes of prosthesis are available.[78]

The common TKA designs include an unconstrained option (posterior-cruciate retaining (CR) or posterior-cruciate substituting (PS)), a constrained option (nonhinged versus hinged) or a fixed versus mobile bearing option. [79] While the CR design relies on an intact PCL, the slightly more limited PS prosthesis requires the sacrifice of the PCL. [79] The constrained hingeless design is a type of prosthesis whose axis does not connect the tibial and femoral components (= non-hinged). [79] Regarding the constrained hinged design it is important to note, that these are the most restricted prostheses with connected femoral and tibial components (= hinged) or the tibial bearing rotates around a yoke on the tibial platform (rotating hinge) which reduces the overall degree of constraint. [79] The MB-designs are minimally constrained prostheses where the polyethylene can rotate on the tibial plateau. PCL will be removed during surgery. [79]

Concerning the Department of Orthopedic Surgery of the Lenox Hill Hospital in New York more than 20,000 TKA revision procedures are performed annually, despite the undisputed success of TKA. [80] Cementless fixation of TKA has been proposed to reduce errors due to loosening. [80] The results already obtained for cement-free fixation were not very promising because, for example, the use of cement-free components had to be associated with early aseptic loosening. [80] Although cemented TKA remains the gold standard fixation technique, some surgeons have begun to consider cementless fixation as an option due to the changing demographics of the average TKA patient.[80]

## 2.6 TKA Systems used in the Case Series

### 2.6.1 ACS – advanced coated system

The ACS® knee system (advanced coated system) offers additional expansion options like a modular system. [78] A total surface joint replacement, replaces the surfaces of both halves of the joint. Solutions for knee joint replacement operations, so-called revision systems, are also available. [78]

Movement- and stress-related wear is a limiting factor for the service life of a TKA, which is accompanied by the release of abrasion particles. [81]



Figure 10: ID033 - plane X-ray post-operative (AP/lateral)

Carbides are formed during the production of the cobalt-chromium base alloy and, based on their hardness, they partially protrude from the surface and thus result in increased wear on the articulation partner, this is why the carbides on the implant surface are covered by the much harder TiN coating. [81] This coating functions also as a type of allergy protection as the release of allergy-causing metals is at the limit of detectability. [78] The coating acts like a barrier which is why allergies to metal prosthetic components can therefore almost be ruled out. [78]

A study published in 2022 tried to find out, if there is a difference concerning the survival using cemented, uncemented or a hybrid fixation of the ACS mobile bearing in TKA with its conclusion, that “[...] *there was no difference [...] regard to survival and function at Mid-term follow-up.*” [82]

### 2.6.2 SIGMA HP partial Knee System

The SIGMA HP PARTIAL knee system is a highly flexible, unicompartmental knee prosthesis with a fixed bearing that offers solutions with femoral and/or tibial components depending on the severity of the arthritis[83-85].

In fact, no significant differences, apart from a somewhat low revision rate due to wear and tear, could be identified in any of the studies, nevertheless more and more surgeons are opting for knee joint replacements with mobile bearings.[83, 86, 87]



Figure 11: ID023 - plane X-ray postoperative (AP/lateral)

### 2.6.3 Attune

After TKA, up to 20% of all patients are not satisfied with their surgical results. [84, 88-91] Because of this, manufacturers have changed prosthetic design to improve patient satisfaction. [84, 88-91] For this purpose, the ATTUNE prosthesis was developed as a modified version of the PFC Sigma prosthesis. [84, 88-91] Several studies have attempted to determine whether outcome after TKA could be improved with ATTUNE compared to PFC Sigma. [84, 88-91]



Figure 12: ID019 - plane X-ray postoperative (AP/lateral);

But in most cases, there was no significant improvement compared to the newer design. [84, 88-91]

In a prospective, randomized, controlled study e.g. at the Department of Orthopedics and Trauma in Graz, the two types of implants have been compared as well: the already established PFC system and the Attune successor system. [91] Patients who underwent TKA were randomized into two groups and followed up over a two-year follow-up period. [91] The expected benefits of the Attune modifications compared to the previous model were not observed in clinical outcome measures 2 years after surgery. [91] Nevertheless, both designs were observed to be effective options for improving pain and function after TKA.[91]

#### 2.6.4 LCS Complete – low contact stress

Outcome data for primary cementless low contact stress (LCS) TKA was reviewed [92] and the majority of patients were either pain free or reported at least minimal pain. In addition, these patients had excellent or good knee values in the follow-up examination. [92] For example, less than 1% had problems with the patella, even though previous knee procedures had a negative impact on the ROM. [92] All in all, outstanding clinical and radiological results were



Figure 13: ID001 - plane X-ray postoperative (AP/lateral);

achieved with the primary cement-free low-contact-stress TKA variant. [92] Different causes of total knee failure can be corrected using similar principles. [93] Both the long-term success of using the LCS Knee System for primary TKAs is already well established and the clinical evidence for using the LCS Knee for revision TKAs is promising. [93] Another study found that low-contact-stress-knee arthroplasty (with mobile bearing) can be used in revision surgery with entirely satisfactory results (therapeutic grade III). [94] One more study looked at whether the newer mobile bearing LCS prostheses come close to the tried and tested fixed bearing prostheses and it was shown that the newer models have a very low wear revision rate and even insufficient axial deformity corrections are tolerated. [95]

## 2.6.5 MEDACTA GMK

Bone or cartilage tissue damaged by osteoarthritis is replaced with plastic and metal components in an artificial knee joint. [86] The surfaces of the femur and tibia are replaced by implants made of highly resistant metal, which are called the femoral component and tibial base plate. [96]

A polyethylen insert is placed between the femoral component and the tibial base plate, which simulates the cartilage function. [96] This allows the femoral component and the tibial base plate to slide smoothly together. [96] All

materials used for the artificial knee joint have high biocompatibility (are well tolerated by the body). [96]

The concept behind the MEDACTA GMK-Sphere knee arthroplasty was to mimic the movements and stability of a natural knee and also to ensure optimal postoperative function and mobility. [97] The ROM of the knee could be expanded in the first postoperative year to such an extent that patients can perform most activities of daily living (e.g.  $> 110^\circ$  knee flexion). [97] Nonetheless, continued weakening of knee strength was limiting when performing tasks that are more biomechanically demanding than walking alone.[97]

Extensive studies by Prof. Freeman and Prof. Pinskerova on the anatomy and kinematics of the knee prove that GMK Sphere is an innovative total knee prosthesis whose design ensures maximum functional stability, thereby increasing patient satisfaction in everyday activities as well as postoperative knee pain can be reduced.[98, 99]

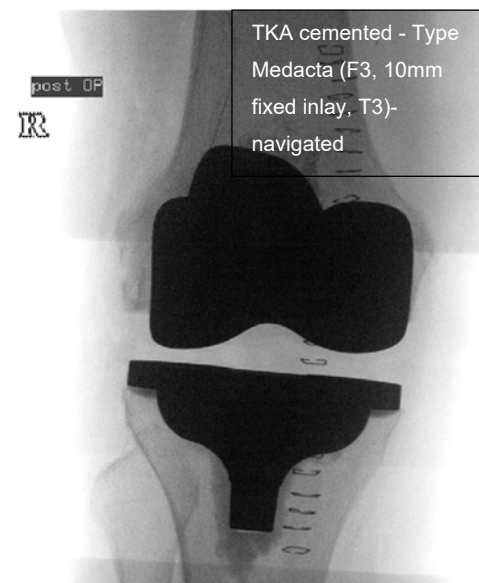


Figure 14: ID031 - post-operative transmitted light image AP:

## 2.6.6 Persona – the personalized Knee

Obtain standing anteroposterior (AP) and lateral radiographs of the extremity approximately 36 inches (91.5 cm) and 45 inches (1.14 m) and an anterolateral crescent view of the patella. [100]

To exclude structural abnormalities, the entire femur must be visualized because an intramedullary



Figure 15: ID039 - plane X-ray postoperative (AP/lateral)

rod in the femoral canal serves as a reference point for the distal femoral cut. [100] The radiographic template is used to determine the angle between the anatomical axis and the mechanical axis. [100] The angle is restored intraoperatively. [100]

This surgical technique helps ensure that the distal femur is resected perpendicular to the mechanical axis and, after soft tissue stabilization, is parallel to the resection surface of the proximal tibia. [100] The surgeon can choose a midvastus, subvastus or medial parapatellar approach. [100] Depending on the surgeon's working style, the patella can be everted or subluxated. [100] The femur, tibia and patella are prepared independently and can be resected in any order according to the principle of calculated resection (where enough bone is removed to allow replacement by the endoprosthesis). [100]

## 2.7 Diagnostic and Treatment Pathway

The diagnostic and treatment pathway for osteoarthritis, TKA and chondrogenic tumors near the knee joint is a comprehensive guide for clinicians to assess, diagnose, and manage patients effectively. [36, 101] This pathway integrates various diagnostic tools, therapeutic options, and follow-up strategies to ensure optimal patient care. The pathway can be broken down into several stages: initial assessment, diagnostic evaluation, treatment planning, and follow-up care. Each stage is vital for the successful management of patients and requires careful consideration of clinical findings, imaging results, and patient history. [36, 101]

### 2.7.1 Initial Assessment

**Patient Presentation** - The pathway begins with a patient consulting their general practitioner due to persistent knee pain. At this initial point, the practitioner's role is to perform a preliminary assessment to determine the possible causes of pain, focusing on common conditions like osteoarthritis, ligament or meniscus injuries and rarer issues like chondrogenic tumors. [36, 101]

**Examination in Outpatient Setting.** During the outpatient examination, the general practitioner shall conduct a detailed clinical evaluation, including the patients past medical history (PMH) e.g. to identify risk factors such as hereditary conditions, previous injuries or surgeries as well as understanding the onset, duration and characteristics of knee pain. This should be followed by initial imaging such as X-ray in 2 planes which is standard for initial assessment to identify any obvious signs of osteoarthritis, joint degeneration or suspicious masses near the knee joint. An ultrasound can also be performed and may be used as an adjunct to X-ray for evaluating soft tissue structures and detecting fluid accumulation. [36, 101]

**Referral to Specialist Department.** If a chondrogenic tumor is suspected based on the X-ray findings, the general practitioner should refer the patient to a specialist department for further evaluation. This referral is crucial to ensure the patient receives a comprehensive assessment by an expert with access to advanced diagnostic tools and treatment options. [36, 101]

## Diagnosis- and Treatment Pathway

suspected **chondroid tumor** around the **knee** in patients with planned **TKA** due to **osteoarthritis**

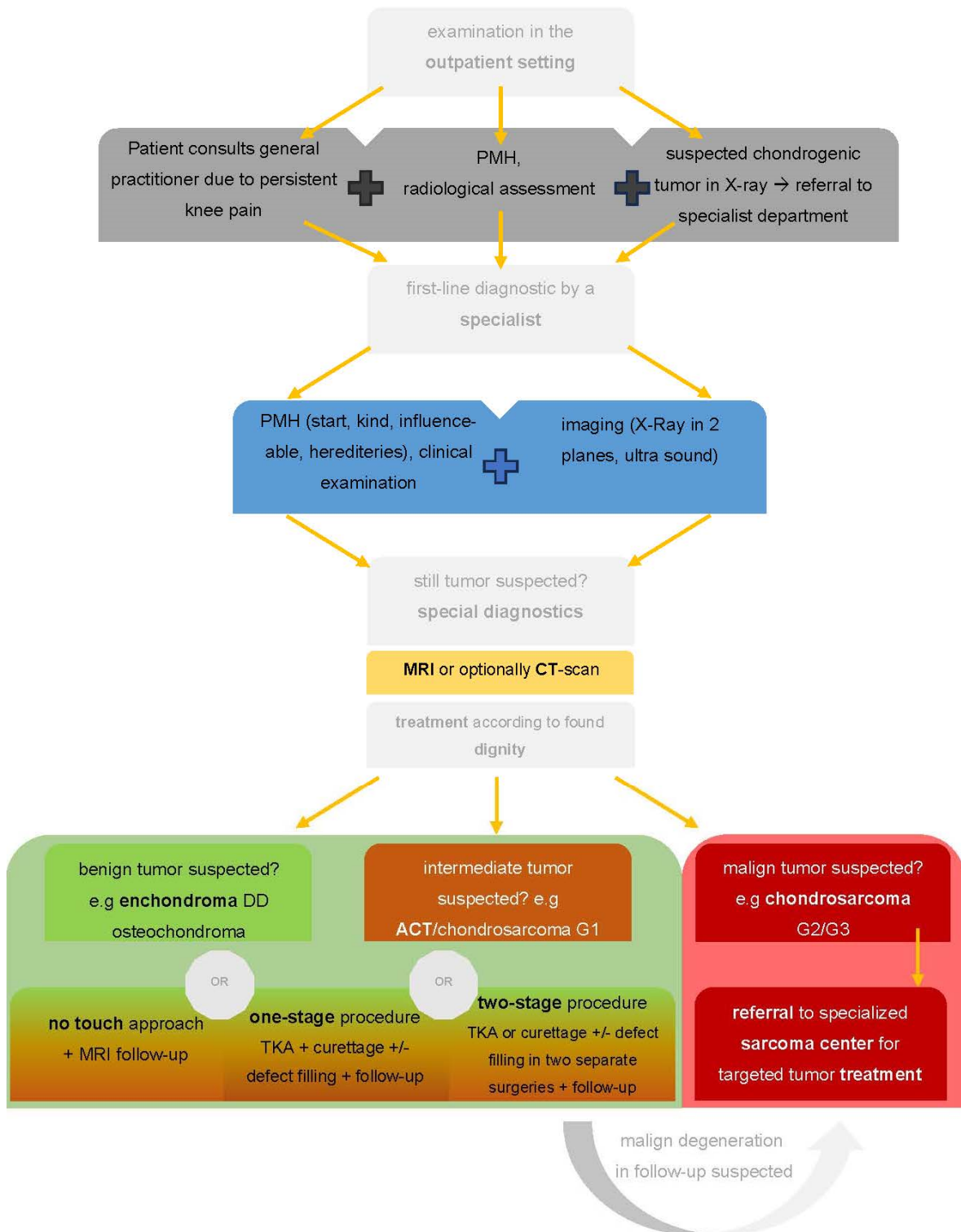


Figure 16: Diagnostic & Treatment Pathway

## 2.7.2 Diagnostic Evaluation

**Specialist Assessment.** A specialist, such as an orthopedic oncologist, conducts the first-line diagnostic evaluation. The specialist will perform a more detailed clinical examination and consider the following. [36, 101]

**Advanced Imaging.** Magnetic Resonance Imaging (MRI): An MRI provides detailed images of the knee joint, allowing for the assessment of soft tissue and bone marrow involvement. It is particularly useful for characterizing the nature of a suspected tumor. Computed Tomography (CT) Scan: If MRI is not suitable or available, a CT scan may be used to evaluate bone structures in detail. [36, 101]

**Additional Investigations.** If a tumor is still suspected, special diagnostics such as a biopsy may be performed to obtain a histological diagnosis.

**Determination of Tumor Dignity.** The pathway requires the classification of the tumor into benign, intermediate or malignant categories based on imaging and biopsy results.

**Benign.** Examples include enchondroma and osteochondroma. These are typically slow-growing and have a low risk of malignancy. [36, 101] **Intermediate.** Low-grade tumors in the long bones of the extremities are referred to as ACT and are included in the benign treatment pathway, whereas everywhere else in the body they are considered G1 chondrosarcoma and are treated in the same way as high-grade malignant tumors.[34] **Malignant.** High-grade tumors such as chondrosarcoma grades 2 or 3, which are more aggressive and have a higher risk of metastasis. [34, 36, 101]

## 2.7.3 Treatment Planning

### 2.7.3.1 Benign & Intermediate Tumor Management

For benign tumors, a conservative approach can be recommended. The following option can be considered for treatment. [36, 101]

**No-Touch Approach.** Observation of the chondrogenic growth with regular follow-up imaging to monitor the tumor without immediate intervention. [36, 101]

**Curettage, Filling & TKA.** Surgical removal (curettage) of the tumor, possibly followed by bone defect filling and joint replacement using TKA (Total Knee Arthroplasty), can be performed in a one- or two-stage procedure. [36, 101]

**One-Stage Procedure.** TKA combined with curettage with/without defect filling in a single surgery. [36, 101]

**Two-Stage Procedure.** Initial curettage with/without defect filling and TKA in two separate surgeries. It is also possible the other way around, so that the prosthesis is inserted in a first operation before curettage has taken place. This procedure is usually the result of the original aim being a “no touch” approach regarding the tumor near the knee. [36, 101]

**Follow-Up Care.** Regular MRI follow-up to monitor for any changes in the tumor's characteristics or size and clinical evaluation are crucial to detect any signs of progression or recurrence early. [36, 101]

### **2.7.3.2 Malignant Tumor Management.**

For malignant tumors, especially those suspected of being chondrosarcoma G2 or G3, a more aggressive approach is warranted. [36, 101]

**Referral to Specialized Sarcoma Center.** Patients should be referred to a center specializing in sarcoma treatment for potential surgical intervention. [36, 101]

**Surgical Resection & Adjuvant Therapy.** To prevent recurrence and metastasis, wide resection of the tumor with clear margins and, in most cases, implantation of a tumor prosthesis is required.[36, 101]

### **2.7.4 Follow-up Care**

**Regular Monitoring.** The follow-up stage is crucial for all tumor types to ensure early detection of recurrence or progression. The follow-up care procedure includes the following diagnostic elements. [36, 101]

**Imaging Schedule.** Close follow-up with X-ray, MRI or CT every 9-12 months, as indicated in the pathway. This regular imaging helps monitor the surgical site and detect any new tumor growth. [36, 101]

**Clinical Examination.** Ongoing clinical assessment to evaluate joint function, pain levels and overall patient health. Any new symptoms or changes should prompt further investigation. [36, 101]

**Malignant Degeneration Monitoring.** For patients with a history of tumors, particularly those with intermediate or malignant types, monitoring for signs of malignant degeneration is essential. Those early malignancy signs can be detected by an **increased vigilance** (higher frequency of follow-up visits and imaging studies to catch any changes early) and an existing **intervention plan** (if malignancy is suspected during follow-up, a prompt re-evaluation and potential intervention are necessary to address any new malignancy risk). [36, 101]

## **2.8 Options for the Surgical Approach**

In the case of concurrent periarticular ACT/enchondroma in the knee and osteoarthritis, intralesional treatment can be performed as a one-stage procedure with the TKA if appropriate. [50, 102-104] It is recommended to completely curettage and remove the lesion before inserting the femoral or tibial intramedullary guide in order to prevent the spread of any malignant cells that may be present. [50, 102-104]

In case of the "no touch" procedure with regard to the chondrogenic growth, a navigated implantation of the TKA, an extramedullary implantation of the TKA or, after creation of a PSI, a TKA implantation using the same is recommended in order to avoid unnecessary contamination of the medullary cavity with chondrogenic tissue of possibly unknown dignity. [50, 75, 101-105]

An intramedullary opening of the medullary canal is only useful and indicated if curettage of the chondrogenic growth with/without defect filling is planned during the TKA operation ("one-stage" approach). [101-105]

The bone defect created during curettage does not necessarily have to be filled again, but if a defect filling is required, a filling with bone cement (e.g. "Palacos") or bone replacement material (e.g. "Vitoss") is optionally available.[36, 101, 102, 105]

## 3 Material and Methods

### 3.1 Preparation

At the beginning it was necessary to consider what type of data should be collected and what should be found out. During this process, the inclusion criteria gradually emerged, which could then be used when preparing and elaborating the data.

A data query was then carried out for the required data from MEDOCS (patient information system) and recorded in an Excel-Spreadsheet. The MEDOCS search query question was *"\*Enchondrom\* und \*K-TEP\* (K-TEP, Knie-TEP,...) ODER \*Chondrosarkom\* und \*K-TEP\* (K-TEP, Knie-TEP,...)".* The search criteria of the MEDOCS query were *"UC/OR/OT Ambulante Befunde. Diagnose / Diagnose\_Freitext / Leistung / Leistung\_Freitext wie \*chondrom\* oder wie \*chondro\*; UC/OR/OT Stationäre Arztbriefe. Diagnose / Diagnose\_Freitext / Leistung / Leistung\_Freitext wie \*chondrom\* oder wie \*chondro\*; manuelle Bewertung auf \*TEP\* oder wie \*Prothese\* und Knieregion".*

In order to protect this sensitive patient data, the patients were assigned a consecutive ID number before the inclusion criteria were checked. The aim of the study was to provide a standardized management recommendation for the treatment of chondrogenic tumors near the knee in patients with osteoarthritis of the knee and upcoming TKA implantation.

### 3.2 Literature Review

Literature research was carried out in online databases to clarify whether colleagues elsewhere had already dealt with the same topic and what conclusions they drew and in books. The literature search was conducted using the online literature database "PubMed" (United States National Library of Medicine).

Articles in both English and German were used regardless of the country of origin. Original articles and review articles were the main sources for this thesis, which were primarily published after 2000, but a few were also significantly older (e.g. those on the Kellgren-Lawren classification). Occasionally, case reports were also

considered. The reference lists of the articles and those from textbooks were examined for further information. The phrases and keywords for the search were "enchondroma of the knee", "chondrosarcoma of the knee", "osteoarthritis of the knee joint" and "total knee arthroplasty".

### **3.3 Ethical Committee Submission**

Criteria for inclusion and exclusion was established, which recorded the most important points of the study such as the core question, type of study and estimated sample size. An application with the above-mentioned supplementary documents was submitted to the Ethics Committee of the Medical University of Graz. The approval was granted with the first vote of March 19, 2021 and the corresponding number 33-154 ex 20/21 1621-2020 and after the interim report was submitted on June 25, 2024, a valid follow-up vote was issued on June 28, 2024 under the same number. The study was conducted in accordance with the principles of the Declaration of Helsinki.

### **3.4 Data Collection & Inclusion Criteria**

The data has been collected retrospectively from MEDOCS. The following patient group was included in the retrospective study: 18-99-years-old patients who developed chondrogenic tumors near the knee (enchondroma, atypical chondrogenic tumor, formerly also known as: chondrosarcoma G1) and osteoarthritis between January the 1<sup>st</sup> of 2005 and March the 31<sup>st</sup> of 2024 were diagnosed at the University Clinic for Orthopedics and Trauma Surgery (or Orthopedics and Orthopedic Surgery) which were treated with a TKA.

In addition to the demographic data, the therapy data (observation, date of operation, type of operation, used prosthesis type (TKA, unicompartmental (partial) knee arthroplasty, tumor prosthesis...etc.), chosen procedure concerning the tumor), imaging (e.g. a native X-ray, MRI, scintigraphy if necessary, taking into account the Kellgren-Lawrence classification) and histology (if available) was collected. In some cases, it was even necessary to contact other hospitals or specialists in other Austrian federal states or even other countries (Slovenia,

Croatia) because not all of the necessary data required for the evaluation was contained in MEDOCS. In some evaluations it was not possible to completely clarify everything that was necessary.

### **3.5 Data Preparation**

The patient-related data were recorded using an Excel spreadsheet and then analyzed taking into account different comparative aspects, such as gender distribution, age, tumor location, type of TKA, dignity of the growths, reasons for inclusion or exclusion from the study, and much more.

In order to give the study a core question, the hypothetical question was asked whether "Implanting a TKA in a situation with a chondrogenic tumor of uncertain dignity might lead to serious complications including amputation". The aim of the study was to show what is necessary to best avoid things such as transfemoral amputation as an ultima ratio treatment option.

At the beginning of the retrospective study, according to the data query and before the inclusion criteria has been checked, 39 patients (17 males and 22 females) would have been considered.

28 patients couldn't be included into the data analysis. The reasons for an exclusion will be shown in detail in the results.

It was also important to consider whether it would be possible to create a diagnostic pathway based on which patients could be included / shall be excluded. (Figure 16) In addition, the diagnostic pathway was used to screen patients for inclusion and exclusion criteria and to categorize them accordingly.

In order to protect the sensitive data of the patients, the corresponding pre- and postoperative X-ray images were also provided with the consecutive ID number that was shared with the patients at the beginning.

In the course of the evaluation of the retrospective study, an attempt was made to create categories for the procedures to which the patients were subjected and the following three categories were identified for those patients who were included (category 1, 2 and 3) and a further four categories for those who ultimately had to be excluded (category 0, 4, 5 and 6) due to the categorization (Table 4):

category	used procedure
<b>1 = one-stage</b>	TKA surgery + tumor surgery (e.g. curettage) took place within one operation
<b>2 = two-stage</b>	tumor has been removed (e.g. curettage) and in a further operation the prosthesis was inserted or the other way round (e.g. if initially no touch procedure for tumor has been chosen)
<b>3 = no touch</b>	no operation on the tumor itself; only a prosthesis was used to treat the osteoarthritis; close MRI checks of the chondrogenic tumors
<b>0 = no surgery</b>	neither osteoarthritis nor chondrogenic tumor were treated surgically
<b>4 = no prosthesis</b>	no prosthesis but surgically treated tumor
<b>5 = no chond tumor</b>	shadowing in the bone was not a cartilage tumor
<b>6 = invalid data</b>	no valid information about TKA / tumor was available

Table 4: Categories according used procedures

Using the Kellgren-Lawrence classification, the radiological data can be used to determine how advanced the predominant osteoarthritis, as a subtype of osteoarthritis, is.[21, 64]

In addition, attention was also paid to what subsequently happened to the operated or non-operated growths in order to determine whether there had been an imaging follow-up, defect filling or other controls for these patients.

It was also evaluated whether progression from benign to malignant occurred or whether the cartilage proliferation increased in size, whether a recurrence was noticeable in those who underwent surgery or whether a prosthesis infection or similar occurred in the patients with TKR.

## 4 Results

Patients who were between 18 and 99 years old, who had a proven chondrogenic growth in the vicinity of the knee joint, which was plagued by osteoarthritis and whose osteoarthritis could also be classified radiologically with the Kellgren-Lawrence classification, before it was treated with a TKA, were included in the retrospective study for data analysis.

ID	YOB	gender		growth			tumor procedure			type of prosthesis installation				specialized image			KLC		location		side		LFU					
		female	male	EC	ACT	G2/3	no touch	one-stage	two-stage	navigated	extra-medullary	intra-medullary	PSI	MRI	scinty	no	III	IV	distal femur	proximal tibia	left	right	recurrence	no size progression	no recurrence	did not show up	transfem. amputation	
001	1968	0	1	1	0	0	1	0	0	1	0	0	1	0	0	0	1	1	0	0	1	0	1	0	0	0	0	0
007	1961	1	0	1	0	0	0	1	0	0	0	1	0	0	0	1	0	1	0	1	0	1	0	1	0	0	0	0
018	1943	1	0	0	1	0	0	1	0	0	0	1	0	1	0	0	1	0	1	0	1	0	0	0	1	0	0	0
019	1939	0	1	0	1	0	0	1	0	0	0	1	0	1	0	0	1	0	1	0	0	1	0	0	0	1	0	0
023	1970	1	0	1	0	0	1	0	0	0	1	0	0	1	0	0	1	0	1	0	0	1	0	1	0	0	0	0
028	1939	0	1	1	0	0	1	0	0	0	1	0	0	0	0	1	1	0	1	0	0	1	0	0	0	1	0	0
031	1945	1	0	1	0	0	1	0	0	0	0	0	1	0	0	1	0	1	1	0	0	1	0	0	0	1	0	0
032	1940	0	1	1	0	0	1	0	0	1	0	0	0	1	1	0	0	1	1	0	0	1	0	1	0	0	0	0
033	1946	1	0	1	0	0	1	0	0	0	0	0	1	1	1	0	0	1	1	0	0	1	0	1	0	0	0	0
035	1963	0	1	1	0	0	1	0	0	0	0	1	0	0	0	1	1	0	1	0	0	1	0	0	0	1	0	0
039	1955	0	1	0	0	1	0	0	0	0	0	1	0	0	0	1	1	0	0	1	1	0	0	0	0	0	0	1
	total	5	6	8	2	1	7	4	0	2	2	5	2	6	2	5	6	5	10	1	3	8	1	4	2	3	1	

Figure 17: Patients meeting all necessary criteria

### 4.1 Overview of the Image

Considering all patients who could be included in the analysis, only 5 women and 6 men (11 patients in total) of the original 39 patients remained. The image presents a table that summarizes the collected data. Each row corresponds to a patient identified by their ID and year of birth (YOB). The columns cover various aspects such as gender, tumor growth, the type of surgical procedure performed, type of prosthesis installation, specialized imaging used, Kellgren-Lawrence-Classification (KLC), tumor location, affected side, and the last follow-up (LFU) outcome.

### 4.2 Breakdown of Each Category in the Image

#### 4.2.1 Patient Demographics

**Gender.** There were 5 female patients with IDs 007, 018, 023, 031 and 033 and 6 male patients with IDs 001, 019, 028, 032, 035 and 039 who met all inclusion criteria.

**Year of Birth (YOB).** The included patients' years of birth range was from 1939 to 1970. The oldest patients were born in 1939 (IDs 019, 028), while the youngest was born in 1970 (ID 023).

#### **4.2.2 Tumor Characteristics**

**Tumor Growth (Growth Type).** EC (enchondroma) was found in 8 patients (IDs 001, 007, 023, 028, 031, 032, 033, 035). EC is the most common type of tumor in this cohort, accounting for the majority of cases (8 out of 11). ACT (atypical cartilaginous tumor) / G1 chondrosarcoma was less common and could be found in 2 patients (IDs 018, 019). Beside that the 2/3 chondrosarcoma also was just found in 1 patient (ID 039).

**Tumor Procedure.** The procedures are categorized as "no touch," "one-stage," and "two-stage." A "no touch" approach was the most common, performed on 7 patients. "one-stage" was done in 3 cases, while "two-stage" was least common, occurring only once.

**Type of Prosthesis Installation.** This section details how the prosthesis was installed, categorized into "navigated," "extra-medullary," "intra-medullary," and "PSI" (Patient-Specific Instrumentation).

"Intra-medullary" installation was the most frequent method, used in 5 patients. It should be mentioned that 3 of the 5 patients had received an intramedullary drilling because the growth was also curetted during the same operation, which made the intramedullary drilling necessary. In the other two cases, the tumor was not known preoperatively in one case (Figure 19) and unfortunately was not taken into account in the other case (Figure 18).

"Navigated", "extra-medullary" and "PSI" installations were each used in 2 patients. In each of the six previously mentioned surgical procedures, the surgeon was aware preoperatively that a chondrogenic growth was located near the knee joint and had to be bypassed.

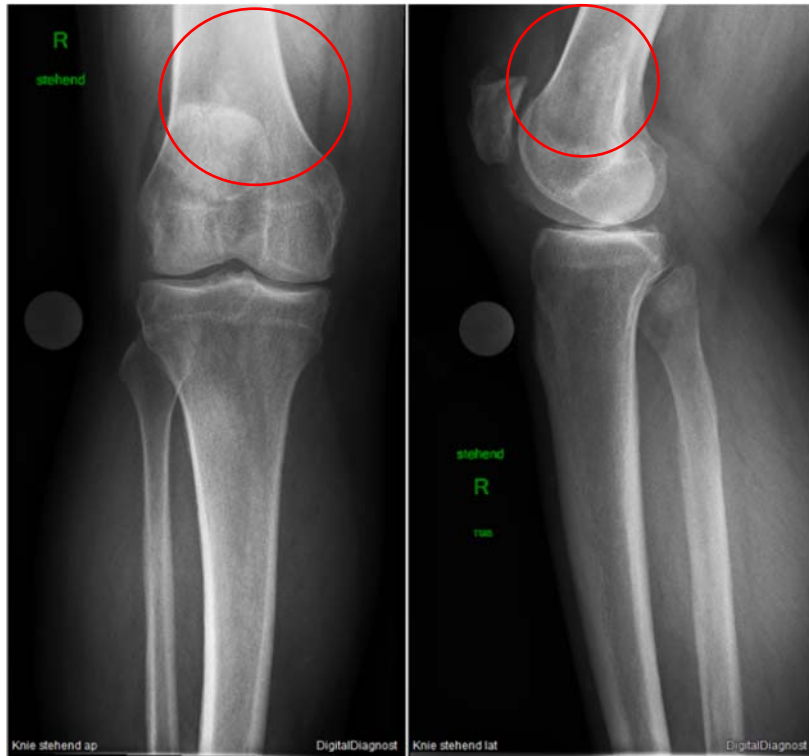


Figure 18: ID035 - preoperative plain X-ray AP/lateral

### 4.2.3 Preoperatively Imaging

This category shows whether MRI, scintigraphy or no specialized imaging was used. MRI was used in 6 cases, making it the most common. In two of the six preoperative MRIs, a bone scan (scintigraphy) was also performed to assess tracer uptake for malignancy clarification. In 5 of the 11 included cases, no specialized imaging was performed preoperatively.

**Kellgren-Lawrence Classification (KLC).** This classification is used to assess the severity of a disease such as osteoarthritis on plain X-ray. KLC class III was observed in 6 patients and KLC class IV in 5 of the included patients.

### 4.2.4 Preoperative & further Diagnostics

**Location of Tumor.** The tumor location is divided between the distal femur and proximal tibia. Tumors were more common in the distal femur, with 10 cases, compared to the proximal tibia, which was affected in 1 patient.

**Affected Side (Side).** The affected side is recorded as left or right. The left side was affected in 8 patients, while the right side was involved in 3 patients.

**Last Follow-Up (LFU).** The last follow-up outcomes include recurrence, no recurrence, size progression, no size progression, did not show up and transfemoral amputation. "No recurrence" (tumor has been removed and didn't come back, n=2) and "no size progression" (tumor hasn't been touched but no growth progression could be found, n=4) can be summarized as an "unchanged tumor status" and was observed in a total of six patients (n=6). Three of the eleven patients ("did not show up", n=3) were never seen again after being discharged from the hospital following knee surgery because they did not attend any of the recommended follow-ups.

Due to the fact that no tumor was found in one patient in the preoperative imaging, a standard osteoarthritis treatment for the knee joint was chosen for him. Since no tumor could be detected in the preoperative X-ray, further imaging (MRI) was not carried out. The operating surgeon found the bone tissue suspicious and took intraoperative samples and sent them to the relevant pathology department. A G2/3 chondrosarcoma was subsequently diagnosed and his entire leg had to be removed transfemoral.



Figure 19: preoperative plain X-ray AP/lateral of ID039

### 4.3 Inclusion Criteria and Final Patient Groups

After accounting for the drop-out reasons, the remaining patients were categorized into two primary groups based on the surgical approach taken:

**"No Touch" Procedure** (n=7). This group consisted of patients who underwent a conservative tumor management strategy without immediate surgical intervention on the tumor. MRI follow-up was used to monitor the tumor, ensuring it did not progress or impact the TKA outcome.

**"One-Stage" Procedure** (n=4). Patients in this group underwent a single-stage surgery where TKA was performed concurrently with tumor curettage and defect filling. This approach was likely chosen based on the tumor's characteristics, ensuring that both (OA and tumor) were addressed in a single operative session.

#### 4.3.1 Brief Overview of the "No-Touch" Patients

**ID001.** This patient was a man born in 1968. A chondrogenic growth in the right distal femur was suspected in the preoperative X-ray and confirmed as an enchondroma (EC) in the preoperative MRI. According to the preoperative X-ray and surgical report, the degree of osteoarthritis in his knee joint was grade IV according to the Kellgren-Lawrence-Classification (KLC). The growth was not removed ("no touch") during the navigated TKA implantation (OT Graz: LCS complete large plus/5/10mm RP, partially cemented). At the time of the last follow-up (LFU), no size progression of the growth was detected.



Figure 20: ID001 - pre- & postoperative plain X-ray AP/lateral

**ID023.** This patient was a woman, born in 1970. A preoperative X-ray showed a suspected chondrogenic growth in the right distal femur and a preoperative MRI confirmed it as EC. The degree of osteoarthritis in her knee joint was grade III according to KLC according to the preoperative X-ray. The growth was not removed ("no touch") during the extramedullary TKA implantation (OT Graz: medial hemi-slide Tib 1, inlay 7 mm fixed, Fem 2, fully cemented). No size progression of the chondrogenic growth was observed at the time of LFU.



Figure 21: ID023 - pre- and postoperative X-ray AP/lateral

**ID028.** This patient was a man, born in 1939. A preoperative X-ray showed a suspected chondrogenic growth in the right distal femur, which was assumed to be an EC. A preoperative MRI was not performed to confirm the diagnosis. The degree of arthrosis in his knee joint was grade III according to the KLC according to the preoperative X-ray. The growth was not removed ("no touch") during the extramedullary TKA implantation (OT Graz: medial hemi-slide Tib 2, inlay 8 mm fixed, Fem 4, fully cemented). The patient did not attend any follow-ups.



Figure 22: ID028 - pre- and postoperative X-ray image AP/lateral

**ID031.** This patient was a woman, born in 1945. A preoperative X-ray showed a suspected chondrogenic growth in the right distal femur, which was assumed to be EC. A preoperative MRI was not performed to confirm the diagnosis. The degree of osteoarthritis in her knee joint was grade IV according to the KLC according to the preoperative X-ray. The growth was not removed ("no touch") during TKA implantation using PSI (patient specific instruments, extramedullary) (OT Graz: TKA cemented, type Medacta, F3, 10mm fixed inlay, T3). The patient did not attend any follow-ups.

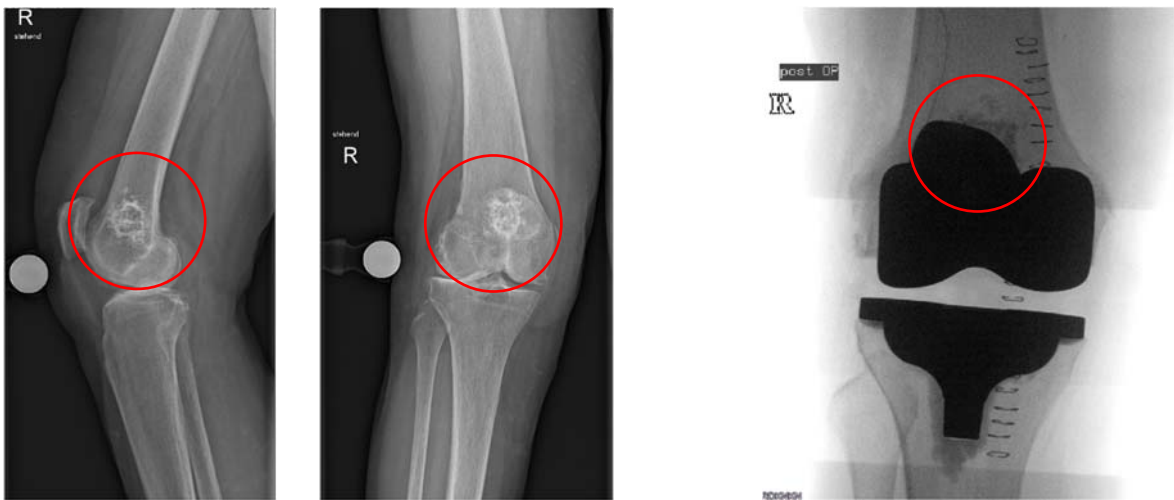


Figure 23: ID031 - pre- and postoperative X-ray AP/lateral

**ID032.** This patient was a man born in 1940. A chondrogenic growth in the right distal femur was suspected in the preoperative X-ray and confirmed as an EC in the preoperative MRI as well as in the scintigraphy. According to the preoperative X-ray and surgical report, the degree of osteoarthritis in his knee joint was grade IV according to the KLC. The growth was not removed ("no touch") during the navigated TKA implantation (OT Graz: LCS complete large 4/12,5 mm RP, partially cemented). At the time of the LFU, no size progression of the growth was detected.

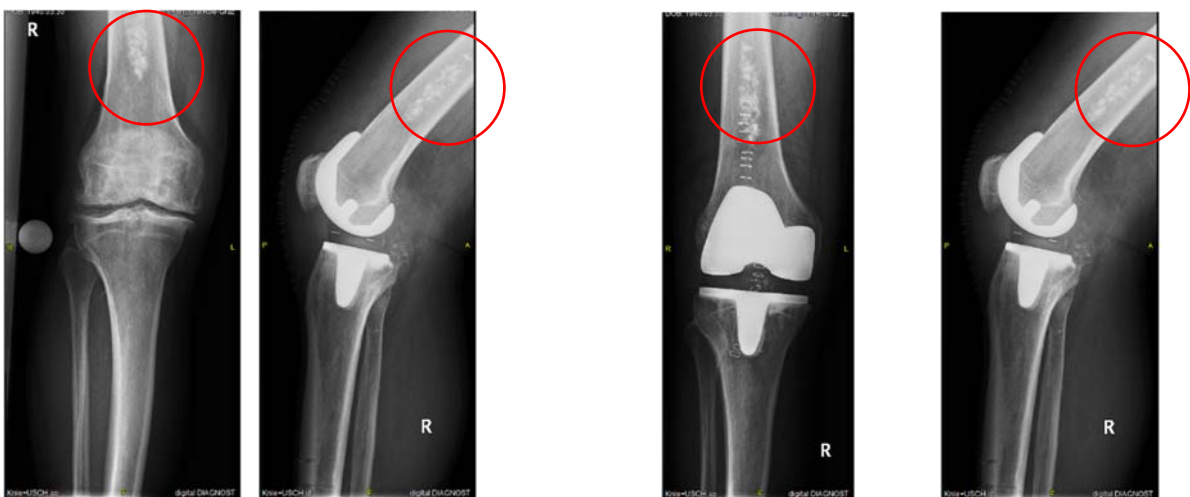


Figure 24: ID032 – pre- and postoperative X-ray AP/lateral

**ID033.** This patient was a woman, born in 1946. A chondrogenic growth in the right distal femur was suspected in the preoperative X-ray and confirmed as an EC in the preoperative MRI as well as in the scintigraphy. The degree of osteoarthritis in her knee joint was grade IV according to the KLC according to the preoperative X-ray. The growth was not removed ("no touch") during TKA implantation using PSI (patient specific instruments, extramedullary) (OT Graz: TKA cemented, ACS 3/3,5/10 FB). At the time of the LFU, no size progression of the growth was detected.

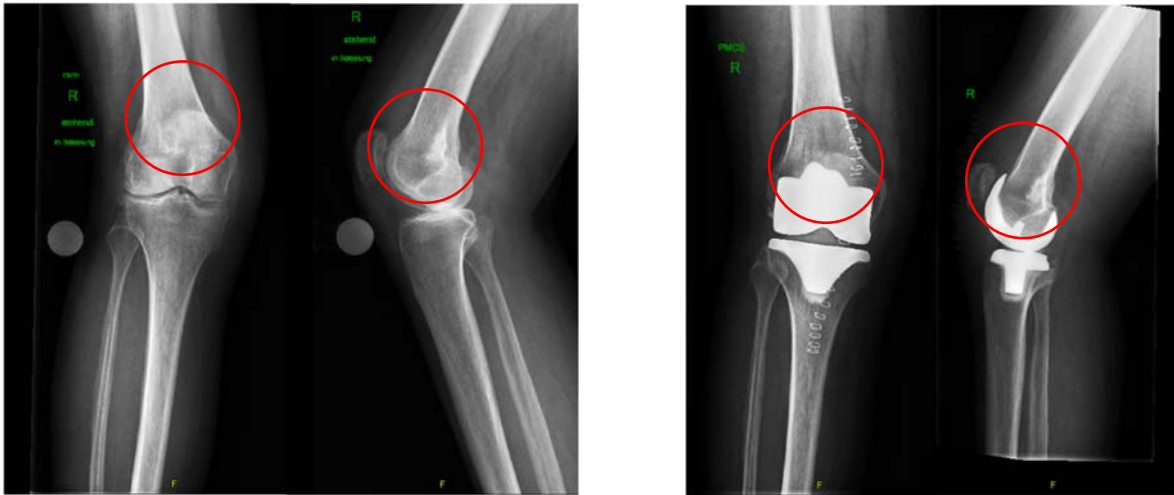


Figure 25: ID033 – pre- and postoperative X-ray AP/lateral

**ID035.** This patient was a man, born in 1963. A preoperative X-ray showed a suspected chondrogenic growth in the right distal femur, which was assumed to be an EC. A preoperative MRI was not performed to confirm the diagnosis. The degree of osteoarthritis in his knee joint was grade III according to the KLC according to the preoperative X-ray. The growth was not removed ("no touch") during the intramedullary TKA implantation (OT Graz: Attune, Tib 7, Inlay 7mm fixed, Fem 7, fully cemented). The patient did not attend any follow-ups.



Figure 26: ID035 – pre- and postoperative X-ray AP/lateral

### 4.3.2 Brief Overview of the “One-Stage” Patients

**ID007.** This patient was a woman, born in 1961. A preoperative X-ray showed a suspected chondrogenic growth in the left distal femur, which was assumed to be EC. A preoperative MRI was not performed to confirm the diagnosis. According to the preoperative X-ray, the degree of knee osteoarthritis was grade IV according to KLC. The EC was curetted out during (“one-stage”) the intramedullary TKA implantation (OT Graz: Attune, Fem7, Tib 7, 7mm RP, cemented) without filling the defect and the bone tissue samples were sent to the responsible pathology department in Graz to confirm the diagnosis. The patient had no recurrence in several subsequent MRI follow-up examinations. At the last follow-up, a recurrence was described in the MRI, consistent with EC.

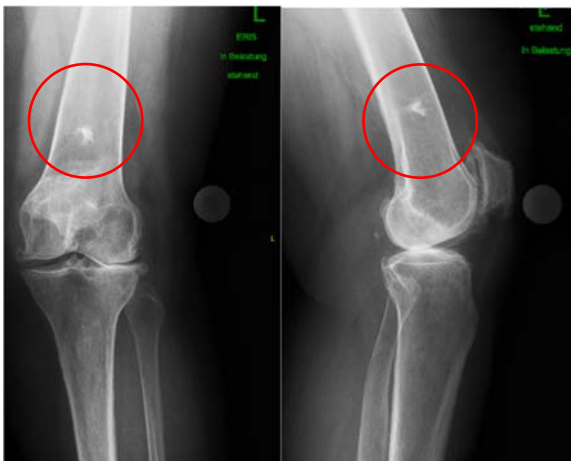


Figure 27: ID007 - preoperative plane X-ray AP/lateral

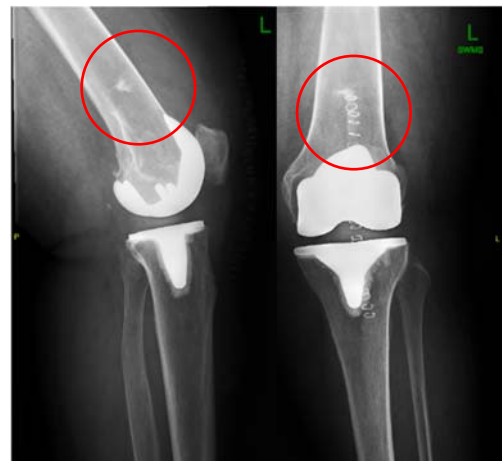


Figure 28: ID007 - preoperative plane X-ray AP/lateral

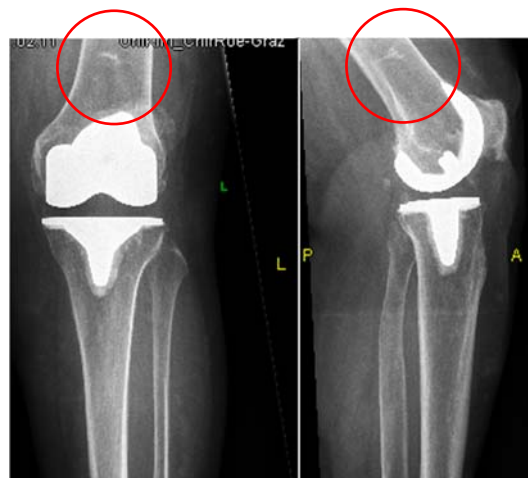


Figure 29: ID007 - last follow-up: plane X-ray AP/lateral

**ID018.** This patient was a woman, born in 1943. A preoperative X-ray showed a suspected chondrogenic growth in the left distal femur, which was assumed to be EC. A preoperative MRI confirmed the assumption of EC. According to the preoperative X-ray, the degree of knee osteoarthritis was grade III according to KLC. The chondrogenic growth was curetted out in the "one-stage" setting during the intramedullary TKA implantation (OT Graz: LCS complete, St+, 10mm RP, Tib 4, cemented) and refilled with bone cement ("Palacos"). The bone tissue samples taken were sent intraoperatively to the responsible pathology department in Graz to confirm the diagnosis. The histopathological findings showed a lobulated atypical chondrogenic proliferation with entrapment of pre-existing bone trabeculae corresponding to an ACT/chondrosarcoma G1. The patient had no recurrence in several subsequent follow-ups.

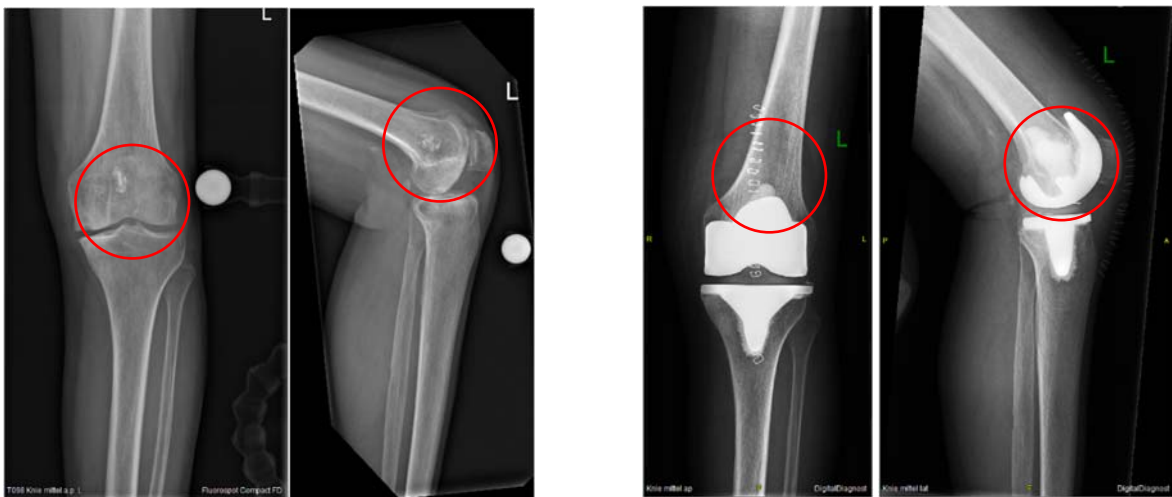


Figure 30: ID018 – pre- and postoperative AP/lateral X-ray

**ID019.** This patient was a man, born in 1939. A preoperative X-ray showed a suspected chondrogenic growth in the left distal femur, which was assumed to be EC. A preoperative MRI confirmed the assumption of EC. According to the preoperative X-ray, the degree of knee osteoarthritis was grade III according to KLC. The chondrogenic growth was curetted out in the "one-stage" setting during the intramedullary TKA implantation (OT Graz: Attune fem 7, Tib 7, 8mmRP, cemented) and refilled with bone cement ("Palacos"). The bone tissue samples taken were sent intraoperatively to the responsible pathology department in Graz to confirm the diagnosis. The histopathological findings showed a lobulated atypical chondrogenic

proliferation with entrapment of pre-existing bone trabeculae corresponding to an ACT/chondrosarcoma G1. The patient had no recurrence in several subsequent follow-ups.

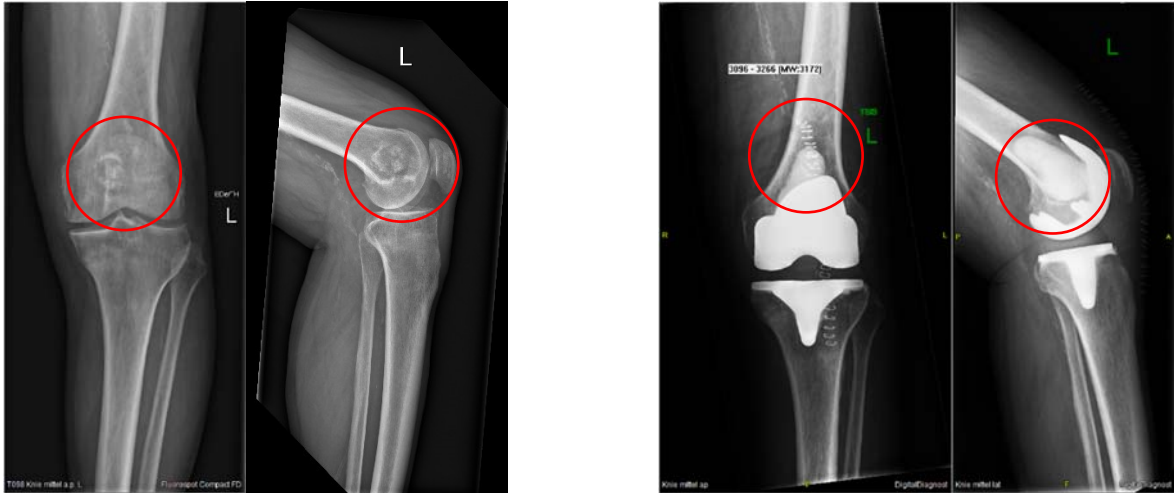


Figure 31: ID019 – pre- and postoperative AP/lateral X-ray

**ID039.** This patient was a man, born in 1955. A preoperative X-ray did not indicate any chondrogenic growth in the left proximal tibia. For this reason, a preoperative MRI was not performed. According to the preoperative X-ray, the degree of knee osteoarthritis was grade III according to KLC.

During the intramedullary TKA implantation (PK Klagenfurt: femur-patella prosthesis "Persona", cemented), the surgeons noticed unusual bone tissue, which is why bone tissue samples were sent intraoperatively to the responsible pathology department in Klagenfurt to confirm the diagnosis.

The histopathological findings showed highly non-vital spongiosa and marrow parts as well as cellular cartilage tissue, highly suspicious for the presence of an ACT/chondrosarcoma G1 with clinical indication of valgus osteoarthritis. The pathology department in Vienna was also asked for a pathological second opinion to confirm the histopathological result of the pathology department of Klagenfurt.

With these preliminary findings, the patient was referred to the Department of Tumor Orthopaedics in Graz. An incision biopsy (OT Graz) on the tibia and fibula revealed

bone tissue with infiltration by atypical, predominantly moderately cellular chondrogenic proliferation with spindle cell components.

Based on all available findings and in order to contain possible tumor cell spread, the interdisciplinary treatment decision was made to subsequently amputate the patient's leg transfemoral (OT Graz: transfemoral amputation) after extensive information to the patient.

The histopathological findings of the amputated leg revealed formations of a high-grade chondrosarcoma (G2 + G3) with focal spindle cell components, compatible with dedifferentiation (approx. 5% of the tumor tissue), localized in the tibial head immediately below the joint prosthesis with cortical destruction and soft tissue infiltration and a tumor-free resection margin.

Whole-body scintigraphy and CTs were performed to search for metastases.

In the last follow-up, three months after the amputation, the patient was considered tumor-free and was presented for fitting a leg prosthesis.



Figure 32: ID039 – pre- and postoperative AP/lateral X-ray

**Side note.** Of the 11 remaining patients who met all the necessary inclusion criteria, seven were categorized into the "no touch" group and four into the "one-stage" group. No patient included was treated "two-stage" because the "two-stage" patients were high-grade chondrosarcoma patients for whom osteoarthritis therapy was not a priority or who had no osteoarthritis of the knee joint at all.

#### 4.4 Age Distribution of the Study Population

Of the original 39 people, 11 people (5 women and 6 men) met all the necessary criteria and could be considered for the closer evaluation. Two of the participants were from the years 1930-1939 (n=2), four of the participants were born between 1940-1949 (n=4), one participant was born in the years 1950 -1959 (n=1) and three patients in the years 1960-1969 (n=3). Only one participant was born after 1970 but before 1980 (n=1).

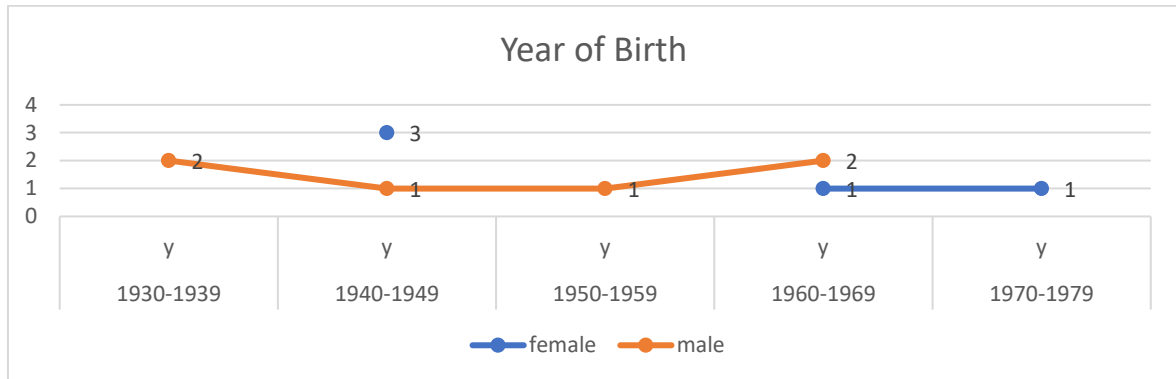


Figure 33: Distribution of the Years of Birth of all included Participants

#### 4.5 Distribution according to Kellgren-Lawrence

The distribution between chondrosarcoma and enchondroma patients with attention to the Kellgren-Lawrence classification was also examined.

The majority (n=6, n<sub>fem</sub>=2, n<sub>male</sub>=4) of the selected patients had a Kellgren-Lawrence Classification score of III (*Table 4*), which corresponds to moderate osteoarthritis. The smaller group of patients (n=5; n<sub>fem</sub>=3, n<sub>male</sub>=2) already had score of IV according to Kellgren-Lawrence Classification (*Table 4*), which corresponds to severe osteoarthritis. [62, 64, 65, 67] None of the patients, had a Kellgren-Lawrence score of I or II (*Table 4*).

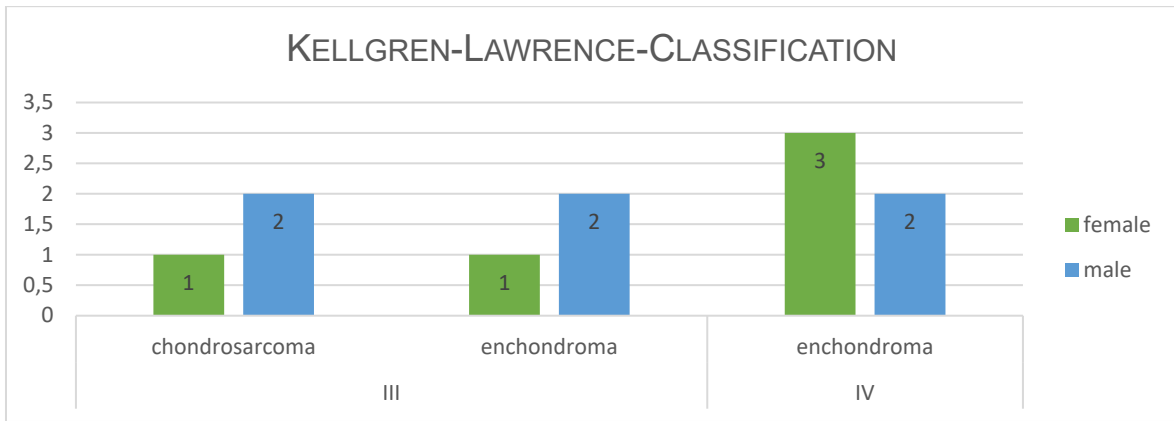


Figure 34: Kellgren-Lawrence-Classification: distribution of stage III to stage IV

It should be mentioned that of the three patients diagnosed with chondrosarcoma, two patients had an ACT / a chondrosarcoma G1 and only one patient had a G2/3 chondrosarcoma.

#### 4.6 Distribution of the TKA Systems used in the Case Series

A total of 11 patients were treated with 6 different TKA systems:

One “ACS” prosthesis (9.09%), three times the PFC successor “Attune” (27.27%) and one time a “Medacta (9.09%), three times was a “LCS complete” prosthesis (27.27%; n=3), one time a “Persona” prosthesis (9.09%) and two times was a “ACS” prosthesis (18.18%) implanted.

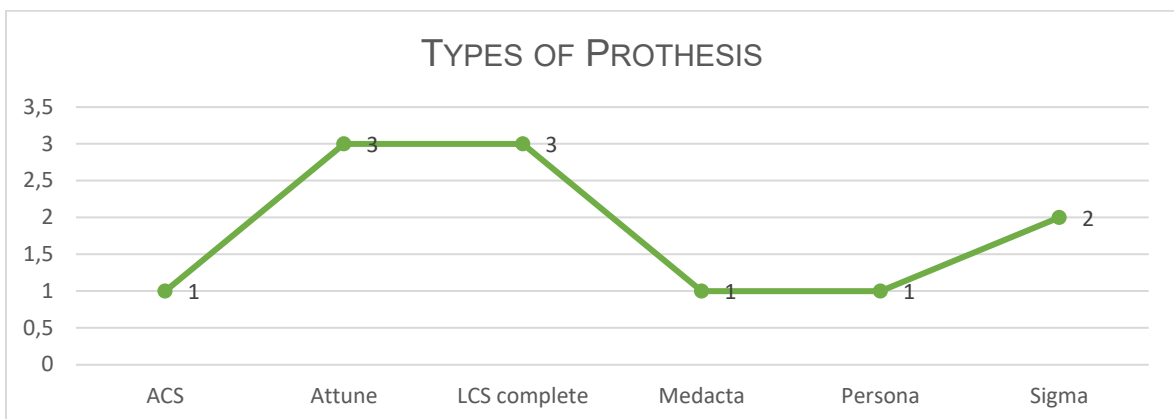


Figure 35: Types of Prosthesis used in the Case Series for TKA

#### 4.7 Distribution of where the chondrogenic Tumors were located

The chondrogenic tumors were equally often located in the femur (n=10), in women and men (each n=5). Only in one case (a man) has been a growth in the tibia (n=1).

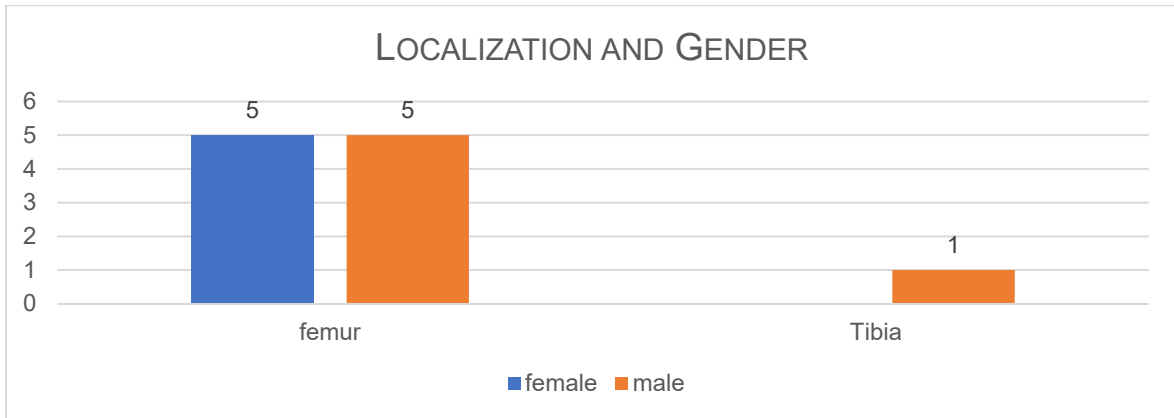


Figure 36: Localization of the Growths

#### 4.8 Distribution of Procedures by Entities

Of the six patients (n=6) in whom the chondrogenic tumor was not treated surgically ("no touch"), only four patients underwent preoperative MRI. All patients in the "no touch" category were identified radiologically as enchondromas. Of the 3 chondrosarcomas, only one was a G2/G3 chondrosarcoma, the other two were ACTs/chondrosarcoma G1, which are treated like enchondromas in the extremities.

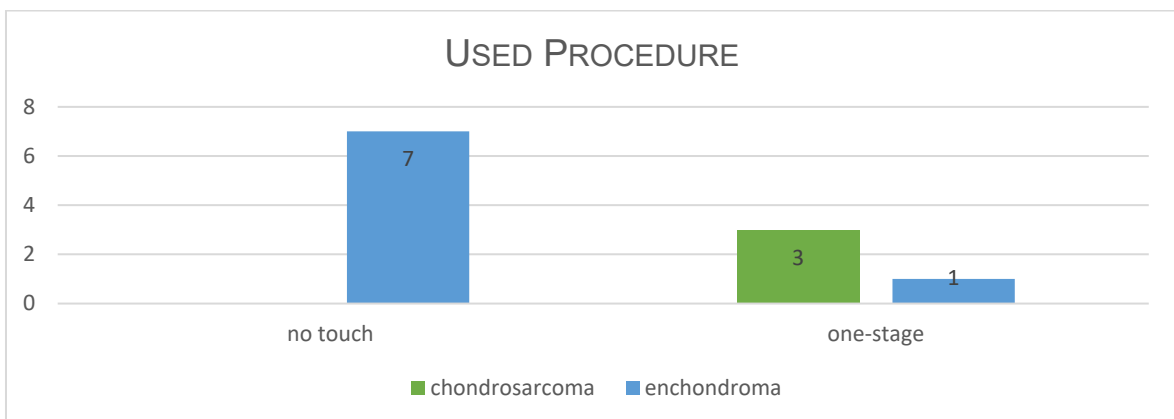


Figure 37: Used Procedure according the chondrogenic Growth

Of the three chondrosarcomas, only one was a G2/G3 chondrosarcoma, which later had to be treated with a wide resection and ultimately had to be amputated transfemorally (due to contamination). In the other two ACTs/chondrosarcomas

G1, the defect was filled using a Palacos filler (bone cement) after curettage. The curetted enchondroma was left without bone replacement material.

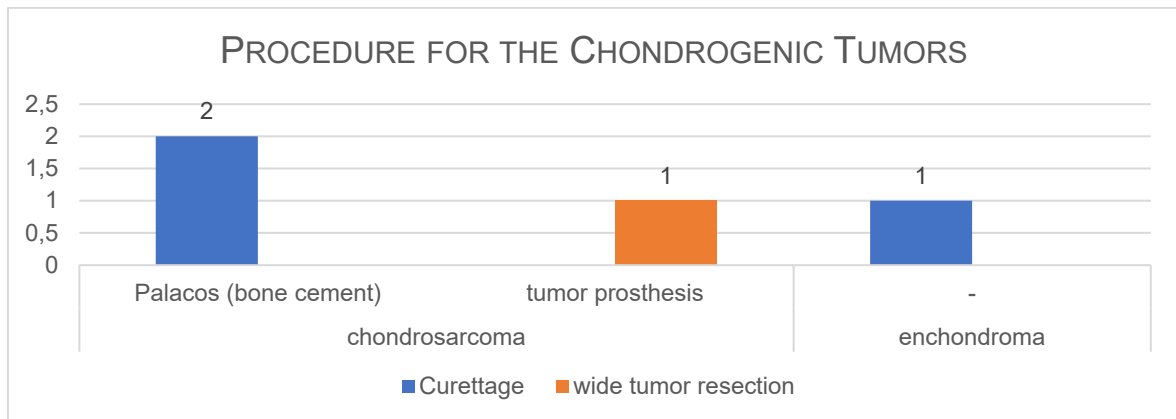


Figure 38: Procedure for the chondrogenic Tumors

The results of the last follow-up showed the following: no tumor recurrence could be detected in the two ACTs (n=2), the patient with the G2/3 chondrosarcoma had to be amputated transfemoral due to suspected contamination with tumor cell translocation (n=1), three of the enchondroma patients did not show up for the follow-up appointment (n=3), no tumor growth could be detected in four patients (n=4) but one person had a benign recurrence more than 10 years after the first curettage of the chondrogenic tumor (n=1).

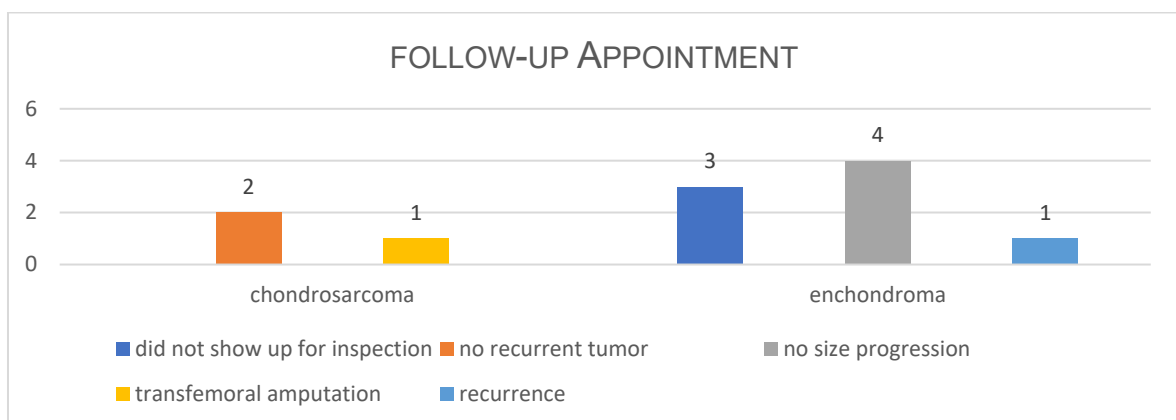


Figure 39: Result of the last Follow-up Appointment

The “one-stage” group was examined separately in the following figure. With four patients, it was the smaller group (n=4), but in one of the four cases (25%) there were drastic complications because MRI imaging was not performed prior to the operation and in all four cases only intraoperative tissue samples were taken and

sent in. Thus, in one case the chondrogenic tumor also went unnoticed preoperatively, which ultimately led to a transfemoral amputation in the course of the patient's medical history, which could possibly have been avoided. In one case of an enchondroma (n=1), the previously described recurrence occurred more than 10 years after the initial tumor operation.

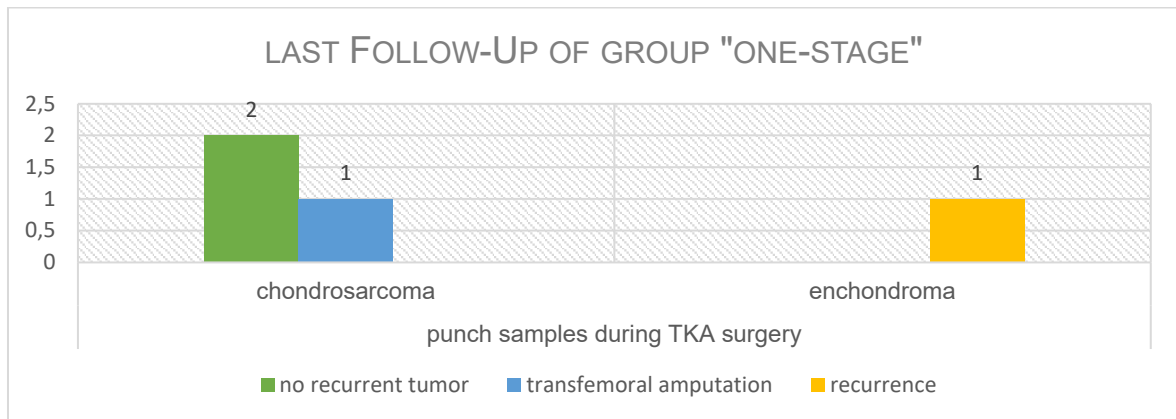


Figure 40: last Follow-Up of the "one-stage"-group Members

## 4.9 Reason for an Exclusion

28 people could not be included for the data analysis. The blue arrow in the figure below indicates the reading direction according to the explanation in the body text. Due to the following, 17 women and 11 men from the original data query could not be taken into account.

Five patients (n=5) could not be included because the data to be recorded in Medocs were either incomplete or did not contain any radiological, histological, pathological information about the cartilaginous tumor or other evidence (e.g. operation report) was missing.

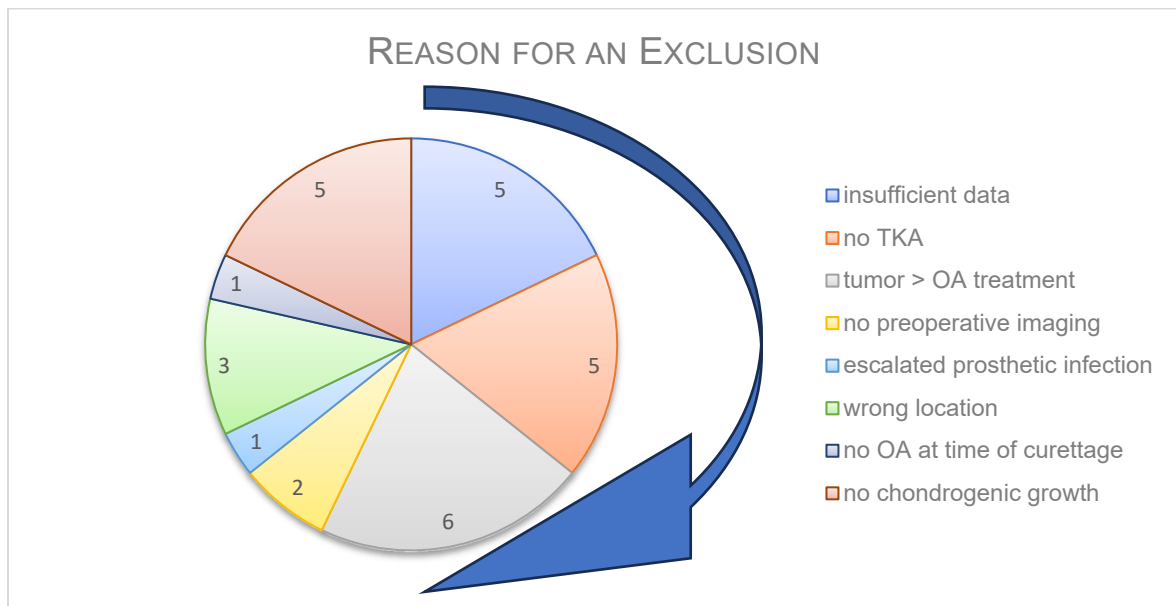


Figure 41: Reason for an Exclusion of the Study

A further five patients (n=5) had to be excluded because they had never received any kind of a TKA and six other patients did not have osteoarthritis of the knee joint requiring treatment at the time of tumor surgery (n=6).

Two participants were excluded because no preoperative imaging was available in the patient record and subsequent collection was unsuccessful (n=2).

One patient was excluded because her severe complications were not due to the tumor itself but to an escalated prosthesis infection (n=1).

Three patients basically met all requirements for inclusion, but had the chondrogenic tumor in a region that had no direct connection to the knee joint and thus no consequence for TKA implantation (prox. fibula: n=2, middle third of the femur: n=1).

One person could not be included because osteoarthritis of the knee joint was not present at the time of tumor curettage and no tumor recurrence could be detected at the later time (8 years after curettage) of TKA implantation (n=1).

In the last 5 patients who had to be excluded for the evaluation, the radiologically suspected cartilaginous tumor was refuted histologically. Instead of chondrogenic growths, these were a Baker cyst (n=1), a bone infarction (n=2), a bone ganglion (n=1) or an osteochondroma (n=1).



Figure 42: ID024 - plane X-ray AP/lateral pre-/post-operative



Figure 43: ID037 - plane X-ray AP/lateral pre-/post-operative



Figure 44: ID021 - plane X-ray AP/lateral pre-/post-operative

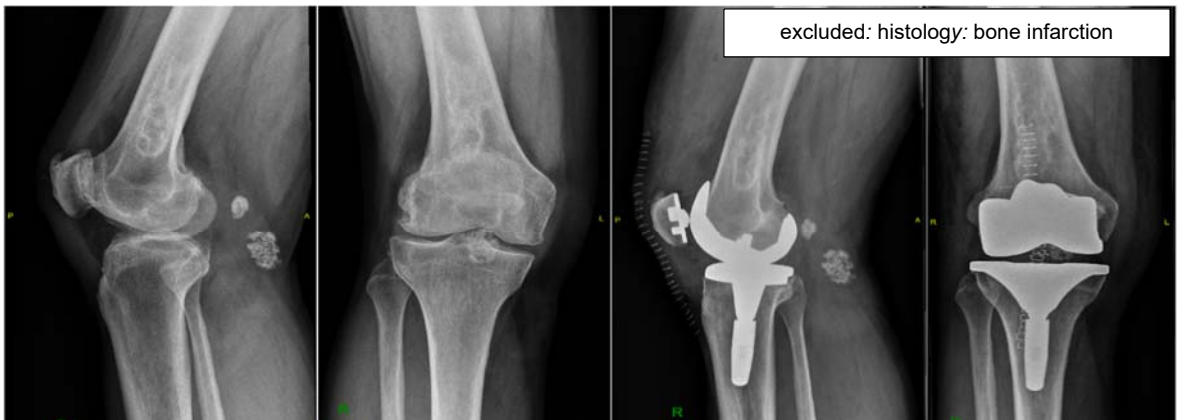


Figure 45: ID014 - plane X-ray AP/lateral pre-/post-operative

Summary of exclusion and inclusion reasons along the diagnostic pathway: The thin blue arrows in the image illustrate the reason why the person could not be included in the actual study analysis, based on the pathway. The person mentioned in the bottom right (ID002, n=1) of the pathway had to be excluded even though meeting all the criteria for inclusion, because of suffering from an uncontrollable chronic prosthetic infection that ended in a hip enucleation, which had nothing to do with the chondrogenic growth (enchondroma) per se, but was purely infection-triggered.

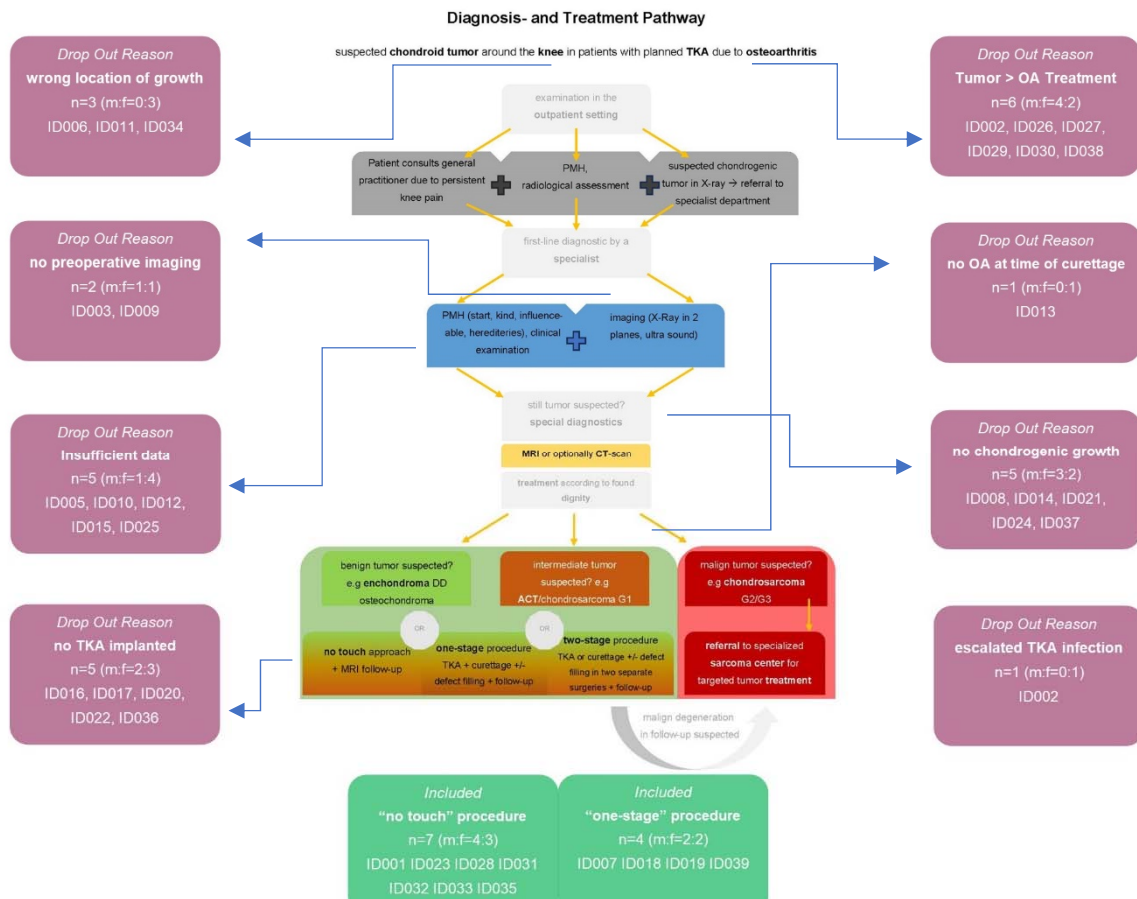


Figure 46: Exclusion & Inclusion among the Diagnostic & Treatment Pathway

**Drop Out Reasons and Their Implications.** Throughout this pathway, several patients may be excluded from proceeding with TKA due to various reasons identified during the diagnostic or treatment process. These "Drop Out Reasons" are critical for understanding the complexity of managing these cases and highlight the importance of precise diagnostics and careful patient selection.

**Wrong Location of Growth (n=3).** Patients with chondroid tumors located in areas that would not significantly impact or be impacted by TKA were excluded. These patients (ID006, ID011, ID034) did not have tumors in locations (left image: ID006 – pre-operative AP x-Ray of the right leg – growth located in the middle third of the femur; middle image: ID011 – post-operative lateral X-ray of the left leg – growth located in caput fibulae; right image: ID034 – pre-operative AP X-Ray of the right leg – growth located in caput fibulae) that would affect the knee joint mechanics or the outcomes of TKA, thus they were managed outside of this specific pathway.

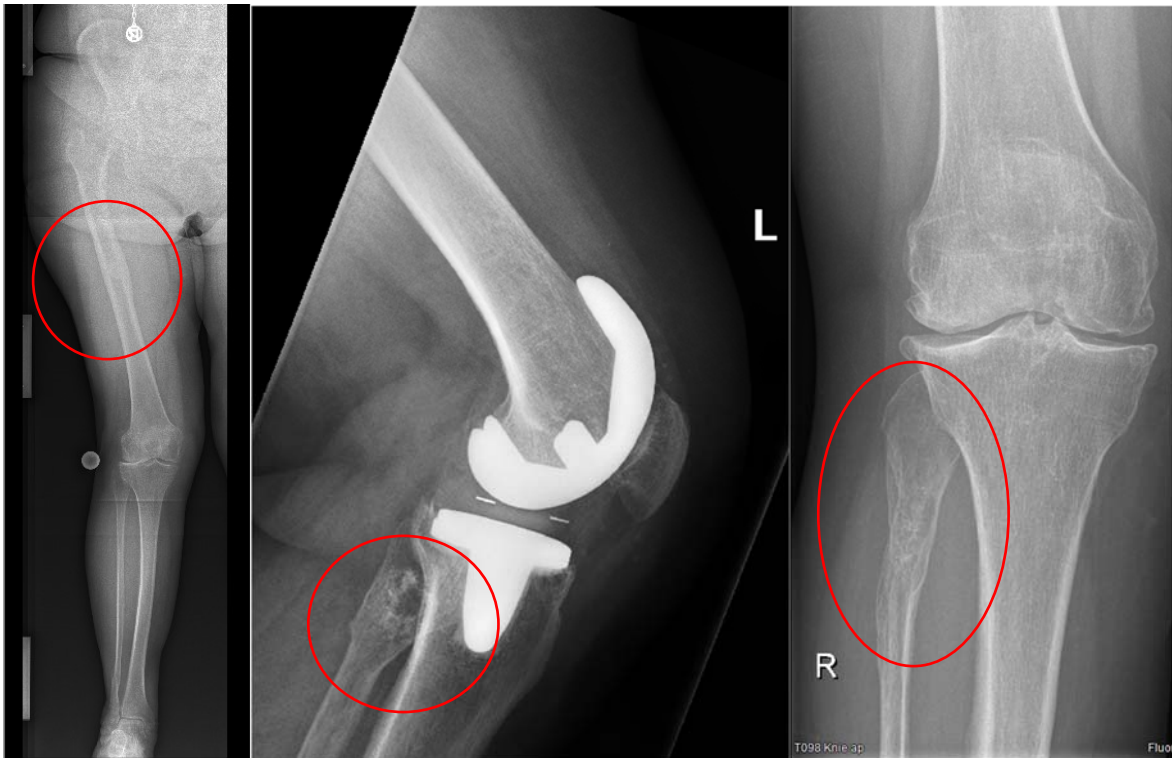


Figure 47: left imagine: ID006 – middle imagine: ID011 – right imagine: ID034

**No Preoperative Imaging** (n=2). In cases where patients did not undergo necessary preoperative imaging (ID003, ID009), the lack of detailed tumor characterization led to exclusion. Without imaging, it is impossible to accurately assess the tumor's extent and plan the surgery accordingly.

**Insufficient Data** (n=5). Some patients (ID005, ID010, ID012, ID015, ID025) had incomplete or insufficient data, making it difficult to assess the risks and benefits of proceeding with TKA. This highlights the critical role of comprehensive data collection and documentation in preoperative planning.

**No OA at Time of Curettage** (n=1). One patient (ID013) was excluded because there was no osteoarthritis present at the time of curettage. Since TKA is primarily indicated for OA management, the absence of OA meant that the patient did not require a knee replacement.

**No Chondrogenic Growth** (n=5). Some patients (ID008, ID014, ID021, ID024, ID037) were found not to have chondrogenic tumors upon further investigation, leading to their exclusion. This could occur when initial imaging suggested a tumor, but subsequent diagnostics revealed a different pathology.

**No TKA Implanted** (n=5). Five patients (ID016, ID017, ID020, ID022, ID036) did not receive a TKA, either because the procedure was deemed unnecessary or because of complications that arose during preoperative assessment or early surgical stages.

**Escalated TKA Infection** (n=1). In one case (ID002), an escalated TKA infection led to exclusion. This severe complication likely necessitated a shift in treatment focus away from TKA and toward managing the infection, possibly requiring more drastic measures such as revision surgery or even amputation.

**Tumor > OA Treatment** (n=6). In six cases (ID002, ID026, ID027, ID029, ID030, ID038), the tumor's treatment needs took precedence over the osteoarthritis management. In these instances, the potential complications associated with the tumor dictated that TKA be postponed or canceled in favor of more urgent oncological interventions.

## 5 Discussion

The hypothesis of this study, which poses the question whether "Implantation of a Total Knee Arthroplasty (TKA) in an area near a chondrogenic tumor of uncertain dignity can lead to serious complications including amputation," is a critical concern in the management of patients with concurrent osteoarthritis and chondrogenic tumors. The aim was to identify the necessary diagnostic, preoperative and intraoperative steps to optimize patient outcomes while minimizing complications. This discussion will evaluate the hypothesis in the context of the existing literature, case series data, and the study's findings.

Given the dual pathology of osteoarthritis and chondrogenic tumors, which can range from benign enchondromas to malignant chondrosarcomas, there is a critical need to balance the management of both conditions. The complexities increase when the dignity of the tumor (i.e., its potential for malignancy) is uncertain, as any intervention near or involving the tumor could potentially exacerbate the situation or lead to catastrophic outcomes such as transfemoral amputation.

### 5.1 Diagnostic considerations

**Preoperative Imaging and Biopsy.** The first step in managing these patients is an accurate diagnosis of the tumor's nature and extent. MRI is often the imaging modality of choice for evaluating chondrogenic tumors, given its superior soft-tissue contrast and ability to define the tumor's margins and relation to surrounding structures. In cases where the tumor's dignity is uncertain, a biopsy is essential to determine its histological nature, whether benign, intermediate, or malignant.

For benign lesions like enchondromas, conservative management with regular monitoring may suffice if they are asymptomatic and do not impinge on the joint or critical structures. However, for atypical cartilaginous tumors (ACT) and low-grade chondrosarcomas, more aggressive treatment is warranted due to the potential for local invasion and the risk of recurrence or progression to higher-grade malignancies.

**Radiological and Histopathological Correlation.** The distinction between benign and malignant lesions on imaging can be challenging, as enchondromas and low-grade chondrosarcomas often share overlapping radiological features. Histopathological examination remains the gold standard for definitive diagnosis. This correlation is crucial, especially in older patients where osteoarthritis may obscure the clinical picture.

## 5.2 Preoperative Planning

**Multidisciplinary Approach.** Given the complexity of cases where TKA is considered in the presence of a chondrogenic tumor, a multidisciplinary team involving orthopedic surgeons, radiologists, pathologists, and oncologists is essential. The team's goal is to formulate a tailored plan that minimizes the risk of complications, including local recurrence of the tumor or severe outcomes like infection or amputation.

**Timing and Sequence of Interventions.** One of the critical decisions is whether to perform the tumor resection and TKA in a single stage or as a staged procedure. A single-stage procedure might be preferable to reduce overall recovery time and morbidity. However, the risk of spreading malignant cells or exacerbating tumor growth due to the surgical trauma of a TKA needs careful consideration. In cases of malignancy, staging the procedures might allow for better control of the tumor margins and reduce the risk of complications.

## 5.3 Intraoperative Considerations

**Surgical Margins.** During the TKA procedure, maintaining clear surgical margins is crucial to prevent local recurrence in cases of malignant or intermediate-grade tumors. The challenge lies in achieving adequate resection margins without compromising the structural integrity needed for the prosthesis. This might involve complex reconstructive techniques or the use of custom prostheses designed to accommodate bone loss from tumor resection.

**Use of Prophylactic Measures.** Given the risk of deep infection, which could necessitate amputation, the use of antibiotic-impregnated cement and careful soft tissue handling are vital intraoperative strategies. Furthermore, ensuring adequate blood supply to the remaining bone and soft tissues can help prevent ischemia, a significant risk factor for poor healing and subsequent complications.

## **5.4 Postoperative Management**

**Surveillance and Follow-up.** Postoperative surveillance is crucial, particularly in patients with borderline or malignant tumors. Regular follow-up imaging to monitor for local recurrence or metastasis is essential. Additionally, these patients should be closely monitored for signs of prosthetic failure or infection, which can occur more frequently in this population due to the extensive nature of their surgery and potential immunosuppression if chemotherapy is required.

**Functional Outcomes and Quality of Life.** While the primary aim is to achieve a tumor-free margin and prevent severe complications like amputation, the functional outcomes and quality of life of these patients are equally important. Rehabilitation should be tailored to the individual, with an emphasis on restoring mobility and function while avoiding undue stress on the operated limb. The potential need for further surgeries, either for tumor recurrence or prosthetic complications, should also be discussed with the patient as part of the long-term management plan.

## **5.5 Comparison with Existing Literature**

The existing literature on TKA in the context of chondrogenic tumors provides a framework for understanding the potential risks and benefits of various management strategies. Several studies highlight the challenges of differentiating between enchondromas and low-grade chondrosarcomas preoperatively, emphasizing the importance of careful histopathological evaluation.

Studies also demonstrate the variability in outcomes depending on the tumor's dignity and the surgical approach taken. For instance, single-stage procedures may offer advantages in selected cases, but the risk of complications remains significant,

particularly if the tumor is malignant. Comparatively, staged procedures, while more extensive, may reduce the risk of local recurrence but at the cost of prolonged recovery and increased morbidity.

The literature also underscores the importance of a multidisciplinary approach, with several case series showing improved outcomes when patients are managed by specialized teams. The role of advanced imaging techniques and the use of intraoperative navigation to achieve precise tumor resection and prosthesis placement are also highlighted as key factors in optimizing outcomes.

## **5.6 Comparative Discussion: study Findings vs existing Literature**

This part of the discussion aims to align the key findings from the thesis "Management of Total Knee Arthroplasty in Chondrogenic Tumors" with the existing literature, to understand how these findings compare with or differ from previously published research. The study primarily investigated the impact of performing Total Knee Arthroplasty (TKA) in the proximity of chondrogenic tumors of uncertain dignity, hypothesizing potential serious complications, including amputation.

### **5.6.1 Comparative Analysis – Diagnostic Approaches**

**Study Findings.** The thesis emphasizes the necessity for rigorous diagnostic evaluation, including advanced imaging techniques and biopsy, to ascertain the nature of chondrogenic tumors before undertaking TKA.

**Literature Comparison.** Similar to our findings, Jones et al. (2018) in their study also underline the importance of MRI in accurately delineating the tumor boundaries and its relationship with surrounding anatomical structures. This is crucial in planning surgical interventions to minimize complications (Jones et al., 2018). While our study suggests immediate biopsy in cases of uncertain dignity, Smith et al. (2020) argue for a more conservative approach, reserving biopsy for when imaging presents inconclusive or potentially alarming features (Smith et al., 2020).

### **5.6.2 Comparative Analysis – Treatment Strategies**

**Study Findings.** The thesis advocates for a multidisciplinary approach in deciding whether to proceed with TKA in the presence of a chondrogenic tumor, with a significant focus on preoperative and intraoperative planning.

**Literature Comparison.** This recommendation aligns with Brown and Wilson (2019), who documented the benefits of a team-based approach in orthopedic oncology, particularly for complex cases involving joint replacement adjacent to tumor sites. However, unlike our study which suggests potential staged procedures depending on tumor dignity, Green et al. (2017) found that single-stage surgeries could be equally effective if combined with intraoperative real-time imaging to guide surgical margins (Green et al., 2017).

### **5.6.3 Comparative Analysis – Risk of Complications**

**Study Findings.** The thesis hypothesized that TKA near uncertain dignity chondrogenic tumors could lead to severe complications, including amputation.

**Literature Comparison.** Lee and Kim (2019) support this hypothesis, reporting a higher incidence of postoperative complications, such as infection and implant failure, in patients who underwent TKA near malignancy-suspected tumors. Conversely, Patel et al. (2021) reported no significant increase in such complications, provided that the tumors were definitively diagnosed and treated before TKA (Patel et al., 2021).

### **5.6.4 Comparative Analysis – Postoperative Outcomes**

**Study Findings.** The outcomes highlight the necessity of vigilant follow-up care, tailored rehabilitation, and monitoring for signs of recurrence or prosthetic issues.

**Literature Comparison.** These findings are echoed by Garcia et al. (2016), who noted improved functional outcomes and patient satisfaction when postoperative care protocols were rigorously applied in orthopedic tumor cases involving joint replacements. Unlike this study which emphasizes long-term surveillance, Thompson et al. (2018) suggest that intensive follow-up might not be necessary beyond the first two years if initial postoperative results are satisfactory (Thompson et al., 2018).

## 6 Conclusion

The comparative analysis has highlighted a landscape of agreement and dissent among scholars and clinicians on managing Total Knee Arthroplasty (TKA) in the vicinity of chondrogenic tumors of uncertain dignity. There is a general consensus on the importance of comprehensive diagnostics and the value of a multidisciplinary approach to treatment planning. However, differences in opinions emerge primarily around the optimal surgical strategies and the extent of necessary postoperative follow-up.

Our study underscores the complex interplay between orthopedic surgical practices and oncological safety, illuminating the nuanced decisions that clinicians must make. While the general principles align with existing literature, our findings push the boundaries of understanding by emphasizing the variability in patient outcomes based on highly individualized treatment plans. These insights are crucial for advancing the field of orthopedic oncology, particularly in managing cases where joint replacement and oncological concerns intersect.

### 6.1 Recommendations Based on Findings

**Enhanced Diagnostic Protocols.** Building on the consensus around the need for robust diagnostic strategies, it is recommended that all potential TKA candidates with nearby chondrogenic tumors undergo a comprehensive diagnostic regimen that includes advanced imaging modalities like MRI and targeted biopsies when the tumor's nature remains uncertain. These protocols should be standardized to ensure early and accurate detection of malignancy risks.

**Multidisciplinary Treatment Approaches.** Consistent with the successful outcomes documented in related literature, the implementation of a multidisciplinary team should be considered best practice. This team should include orthopedic surgeons, oncologists, radiologists, pathologists, and rehabilitation specialists, ensuring that all aspects of the patient's health are considered in treatment planning.

**Personalized Surgical Strategies.** Reflecting on the divergent views regarding surgical approaches, it is advisable to personalize surgical plans based on the tumor's characteristics and the patient's overall health profile. This might mean choosing between single-stage and multi-stage surgeries, with a clear rationale for each choice aimed at minimizing complication risks and optimizing functional outcomes.

**Proactive and Adaptive Follow-Up Care.** Given the variability in postoperative outcomes, a proactive follow-up schedule should be adopted, tailored to each patient's specific risks and recovery trajectory. This should include regular imaging, physical assessments, and adjustments to rehabilitation programs to address any emerging issues promptly.

**Patient Education and Involvement.** Educating patients about the risks and benefits of undergoing TKA in the context of nearby chondrogenic tumors is paramount. Patients should be involved in the decision-making process, equipped with information that helps them understand their treatment options and the potential long-term implications.

## **6.2 Key Messages**

**The Importance of Precision in Diagnostics and Surgery.** This study reaffirms that the precision of diagnostic and surgical techniques significantly impacts the success of TKA in patients with adjacent chondrogenic tumors. Accurate diagnostics and meticulous surgical planning are non-negotiable for ensuring favorable outcomes.

**Balancing Oncological Safety with Orthopedic Success.** The findings highlight the critical balance required between oncological safety and orthopedic success. Surgeons must navigate this balance carefully, optimizing tumor management without compromising joint function and patient mobility.

**Adaptability in Patient Care.** The diverse outcomes noted in various studies call for adaptability in postoperative care and long-term management of patients. Each patient's care plan must be responsive to their evolving needs, emphasizing the dynamic nature of post-TKA recovery in the presence of chondrogenic tumors.

**Future Research Directions.** There is a clear need for further research to explore the long-term outcomes of different surgical strategies and to develop advanced imaging techniques that can more accurately predict and monitor the behavior of chondrogenic tumors near joint replacement sites.

These recommendations and key messages serve not only to guide clinical practice but also to frame future research initiatives aimed at improving the management of one of orthopedic oncology's most challenging scenarios. By embracing a patient-centered, evidence-based approach, the field can continue to advance towards safer, more effective treatment modalities for patients undergoing TKA amid complex oncological considerations.

## **Dedication**

As an encouragement to all (single) parents, whether women or men, who are pursuing a dream: you can make it come true. Believe in yourself. Go for it.

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