**DIPLOMA THESIS**

# Peroneal nerve palsy related to tumor surgery in the knee area


submitted by

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For the Academic Degree of

**Doktor der gesamten Heilkunde**
**(Dr. med. univ.)**


at the

**Medical University of Graz**

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*Graz, June 19th 2017*

*Statutory Declaration*

*I hereby formally declare that I have written the submitted thesis independently and without any outside support except for the quoted literature and other sources mentioned in the paper. I clearly marked and separately listed all of the literature and all of the other sources which I employed when producing this academic work, either literally or in content.*

*Graz, June 19th 2017* *Lorenz Trausnitz eh.*

## Acknowledgments

First and foremost, I would like to thank my three supervisors, Univ. Prof. Dr. Andreas Leithner, Ass. Dr. Magdalena Gilg and Ass. Dr. Florian Amerstorfer for their helpful and content support, encouragement and patience during the whole time of working on this diploma thesis and I am also grateful for the opportunity to create my thesis at the Department of Orthopaedic Surgery, Medical University of Graz.

I also would like to thank all my fellow students and friends, who supported me during the completion of this diploma thesis.

Furthermore, I would like to thank my family and the rest of my friends for the support during the whole time of my medical studies, especially my parents, for all the financial support and faith in me.

# Zusammenfassung


### Einleitung:

Peroneuslähmungen sind mögliche Komplikationen, die bei Tumorresektionen im Kniebereich auftreten können. In manchen Fällen muss aufgrund der Tumorausbreitung in der Operation auch der Peroneusnerv entfernt werden. Auch ohne direkte Schädigung des Nervs während der Operation kann es zum Auftreten von Peroneuslähmungen kommen. Ziel dieser Diplomarbeit war es (1) die Inzidenz dieser Nervenlähmungen zu untersuchen (2) mögliche Risikofaktoren festzustellen und (3) die Inzidenz von temporären Peroneuslähmungen zu untersuchen.

### Methoden:

Es wurde eine retrospektive Datenbankabfrage im Zeitraum zwischen 2006 bis 2016 an der Universitätsklinik für Orthopädie und Traumatologie mithilfe von relevanten Schlagwörtern durchgeführt. Ausgeschlossen wurden Patienten mit einer perioperativen Verletzung des Peroneusnervs. Weiters wurde noch eine strukturierte Literaturrecherche auf MEDLINE (via Pubmed) mit dem Algorithmus “sarcoma AND ((tibia AND proximal) OR (femur AND distal))” durchgeführt und die Daten miteinander verglichen.

### Ergebnisse:

Neun Patienten mit Peroneuslähmungen vor oder nach einer Tumorresektion im Kniebereich wurden gefunden. Bei fünf dieser Patienten handelte es sich um eine temporäre Nervenlähmung und bei weiteren vier Patienten um eine permanente Nervenlähmung. In die Literaturrecherche wurde 25 Studien eingeschlossen mit einer Gesamtzahl von 1300 Patienten, bei denen insgesamt von 82 Fällen (6.69%) mit Peroneuslähmungen berichtet wurde.

### Diskussion:

Die Inzidenz von Peroneuslähmungen im Zusammenhang mit Tumoroperationen im Kniebereich war in der Literatur höher als im eigenen Patientenkollektiv und bei anderen (nicht-tumor) Operationen im Kniebereich. Aufgrund der hohen Inzidenz,

die in der Literaturrecherche gezeigt wurde, wird ein noch sorgsamer Umgang mit dem Peroneusnerv empfohlen. Die Erhebung von Risikofaktoren für das Auftreten einer Peroneuslähmung war nur eingeschränkt möglich aufgrund von mangelnder Dokumentation sowohl bei den klinischen Studien als auch in der Literatur, weshalb in der Zukunft eine standardisierte Dokumentation von neurologischen Komplikationen bei tumororthopädischen Operationen durchgeführt werden sollte.

# Abstract

**Introduction:**

Peroneal nerve palsy (PNP) is a possible complication of tumor surgery in the knee area. In some cases, the peroneal nerve has to be sacrificed as part of the tumor resection, but also without damaging the peroneal nerve, PNP occurs in some cases. The aim of this study was to (1) investigate the overall incidence of PNP, (2) to identify possible risk factors and (3) to investigate the incidence of transient PNP following tumor resection in the knee area.

**Methods:**

All medical reports of the Department of Orthopaedic Surgery, Medical University of Graz between 2006 to 2016 were searched for relevant keywords. Patients with PNP before or after the initial tumor resection in the knee area without any damage to the peroneal nerve during surgery were included. In addition, a structured literature review on MEDLINE (via PubMed) by a search algorithm “sarcoma AND ((tibia AND proximal) OR (femur AND distal))” was performed and data was compared to the literature.

**Results:**

Nine patients with PNP before or after tumor resection in the knee area were found. Five of these cases were transient PNP and four cases were permanent PNP. In the literature review were twenty-five studies included with a total of 1300 patients with eight-seven reported cases of PNP (6.69%).

**Discussion:**

The incidence of PNP related to tumor surgery in the knee area in the literature was higher than in our own patient collective and higher than reported rates in other surgeries in knee area. Based on the high incidence of PNP shown in the structured literature review a more cautious handling of the peroneal nerve is advised. Due to the low number of patients included and the lack of documentation of specific risk

factors, these results should be interpreted with caution. Thus, more standardized documentation of neurological complication, is desirable for the future.

# Table of contents

## Abbreviations

| | |
|---|---|
| AJCC: | American Joint Committee on Cancer |
| EMG: | electromyography |
| EMBASE: | Excerpta Medica database |
| M.: | metastasis |
| mm: | millimeter |
| MBT: | malignant bone tumors |
| MEDOCS: | electronic data processing system of the styrian state hospital |
| MRI: | magnetic resonance imaging |
| N.: | nodulus |
| n. d.: | not documented |
| n. e.: | not explained |
| PNP: | peroneal nerve palsy |
| pr.: | proximal |
| T.: | tumor |

# List of figures

# List of tables

# 1 Introduction

## *1.1 Definition*

Tumor is derived from the Latin term “tumor”, meaning proliferation or swelling. In medicine the term “tumor” is used in different medicals sectors, for example to describe an expanding lesion caused for example by an inflammatory process. Also, it is used to describe the new formation of cells created by a dysregulation of growth factors. This new formation of cells can be split into two categories/types: a cell formation/tumor growing expendably without spreading into other organs and is classified as benign. A tumor on the other hand that spreads into organs or infiltrates surrounding tissue is called malignant or cancerous (1).

## *1.2 Epidemiology of primary bone tumors*

Primary malignant bone tumors are a rare tumor type and only make up for approximately 0,2% of all malignant tumors (2). In average, the peak incidence of osteosarcoma and Ewing´s sarcoma is in the second decade of the lifetime and with another peak incidence of osteosarcoma and chondrosarcoma over the age of 60 years (3). Osteosarcoma, Ewing´s-sarcoma and chondrosarcoma are the most common malignant bone tumors (MBT) as shown in figure 1 (4, 5).

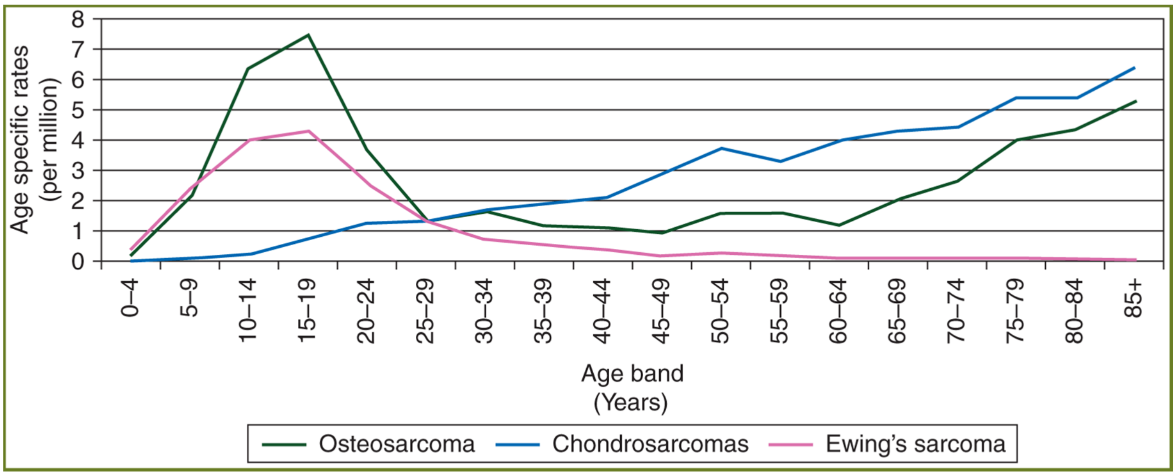


**Figure 1: Incidence of MBT(6)**

Each of these common MBT has preferred anatomical localizations. The most common localizations for osteosarcoma are in the tibia, the femur and the humerus, with 60% of them occurring in the knee area. Chondrosarcoma typically occurs in the femur, the humerus and the pelvis. Ewing´s sarcoma is often located in the femur, the pelvis and the shoulder girdle (1).

## *1.3 Tumor staging*

For the staging of the tumor spread, as well as for the prognostic factor the TNM-Classification is used. The "T" describes the size of the tumor, the "N" describes the spread into nearby lymphatic nodes and the "M" describes if there is any metastatic spread. In order to prevent misclassification, diagnostic delay and errors in staging or treatment, all suspected cases of MBT should be reviewed in multidisciplinary team meetings (7).

| | |
|---|---|
| **T- Stage** (Size of the primary tumor) | |
| TX | not assessable |
| T0 | no presence of a primary tumor |
| T1 | primary tumor is under 8cm (biggest diameter) |
| T2 | primary tumor is over 8cm (biggest diameter) |
| T3 | discontinuous tumor on primary bone side |
| **N- Stage** (lymphatic nodes) | |
| NX | not assessable |
| N0 | no mestastasis in the nearby lympathic nodes |

| | |
|---|---|
| N1 | mestastasis in the nearby lympathic nodes |
| **M- Stage** (presence of metastasis) | |
| MX | not assessable |
| M1 | no presence of metastasis |
| M2/a | metastasis only in the lung |
| M2/b | metastasis in other organs |

**Table 1: AJCC Cancer staging Manual 7th ed. 2010 (8)**

## *1.4 Therapy*

The treatment for primary MBT is depending on the tumor type. Osteosarcomas and Ewing´s sarcomas are treated within study protocols, for example. EURAMOS Protocol and EWING 2008, consisting of neoadjuvant polychemotherapy, wide resection and postoperative polychemotherapy (7). Chemotherapy is commonly given for six to ten months in osteosarcoma and ten to twelve months in Ewing´s sarcoma. If the resection of primary Ewing´s sarcoma is not possible radiotherapy is an alternative option. For chondrosarcoma, the treatment consists primary of the surgical resection of the tumor (7). The main goal of surgery of patients with an MBT is to remove the tumor with wide resection margins from the surrounding tissue to reduce the risk of a local recurrence, but also to preserve as much function as possible (9). The resection margins should be established by the criteria set under Enneking et al (1980) (10). It has been shown that limb salvage over a period of 25 years is possible in 93% of patients who have received an endoprosthetic knee replacement after a tumor resection in the distal femur (11).

## 1.5 Peripheral nerve structures

The peripheral nerve system forms the connection between the central nervous system and the end organs. The peripheral nerve is made up of different structures as illustrated in figure 2. The various structures are divided into endoneurium, perineurium and epineurium.

The endoneurium is build up of several nerve fibers, of which each is surrounded by a myelin sheath. These nerve fibers are bundled into groups, which are called fascicles. The endoneurium is surrounded by perineurium, a connective tissue containing blood vessels. The endoneurium is covered by dense connective tissue called the epineurium (12).

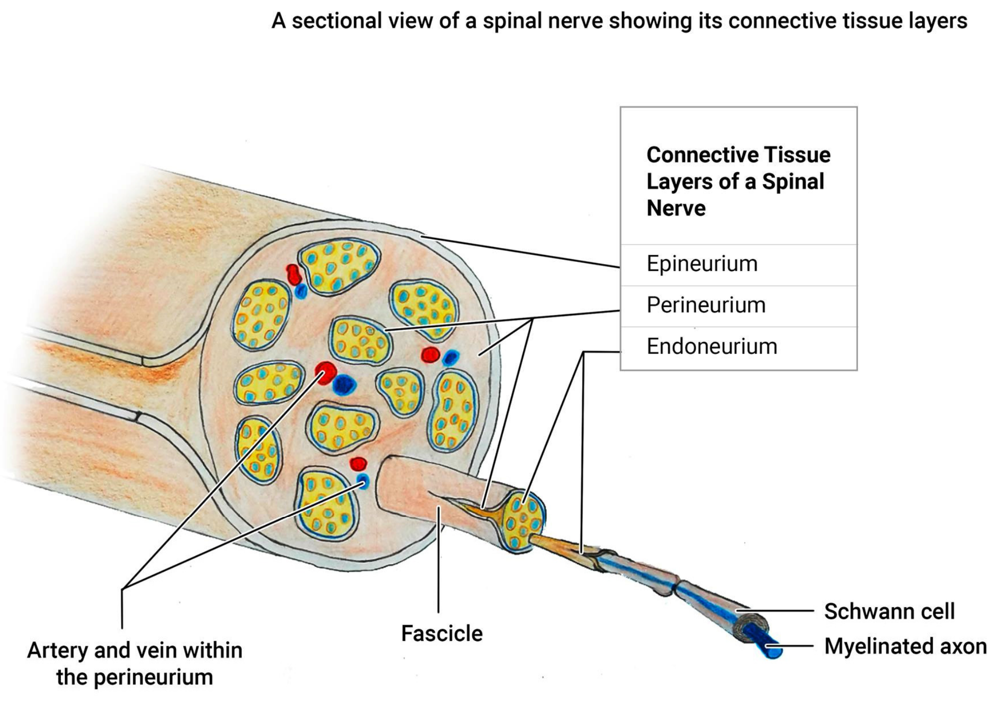


**Figure 2: Peripherial nerve structure**

## 1.6 Peripheral nerve damage

There are many different classifications for peripheral nerve injuries. The two most common ones are the Seddon-classification and the Sunderland- classification (13).

### 1.6.1 Seddon- classification

The Seddon- classification describes the function and the injury of the axon and the surrounding connecting tissue and classifies it into the three following types: neuropraxia, axonotmesis and neurotmesis as illustrated in Figure 3 (13).

#### 1.6.1.1 Neuropraxia

Neuroparxia is the lowest degree of peripheral nerve injury with functional disorders only; the endoneurium, perineurium and epineurium are still intact. This form of nerve injury is mostly caused by pressure on the nerve and can lead to painless sensorimotor deficits. Related to prolonged motor failures, muscle atrophy may occur. The prognosis for a full recovery is very good and normally requires days to weeks (13).

#### 1.6.1.2 Axonotmesis

The second degree of peripheral nerve injury "axonotmesis" is caused by an interruption of the axonal continuity. Possible localization for the interruption is the endoneurium or additionally the perineurium, while the epineurium remains still intact. Clinically, sensory and motor deficits appear distal to the lesion. The prognosis of axonotmesis is better than in neurotmesis with the potential to regain full function without the need of surgical treatment. Since the epineurium is still intact, the axon can grow back into the original target area. As the axon can grow up to 1 mm per day, the distance between the lesion and the target region is an important prognostic factor (13).

#### 1.6.1.3 Neurotmesis

Neurotmesis, the third degree, is the most severe injury of a peripheral nerve and is caused by a complete nerve dissection. Just as the axonotmesis, the neurotmesis shows sensorimotor nerve disorders distal to the lesion. Without surgical intervention the prognosis is very poor (13).

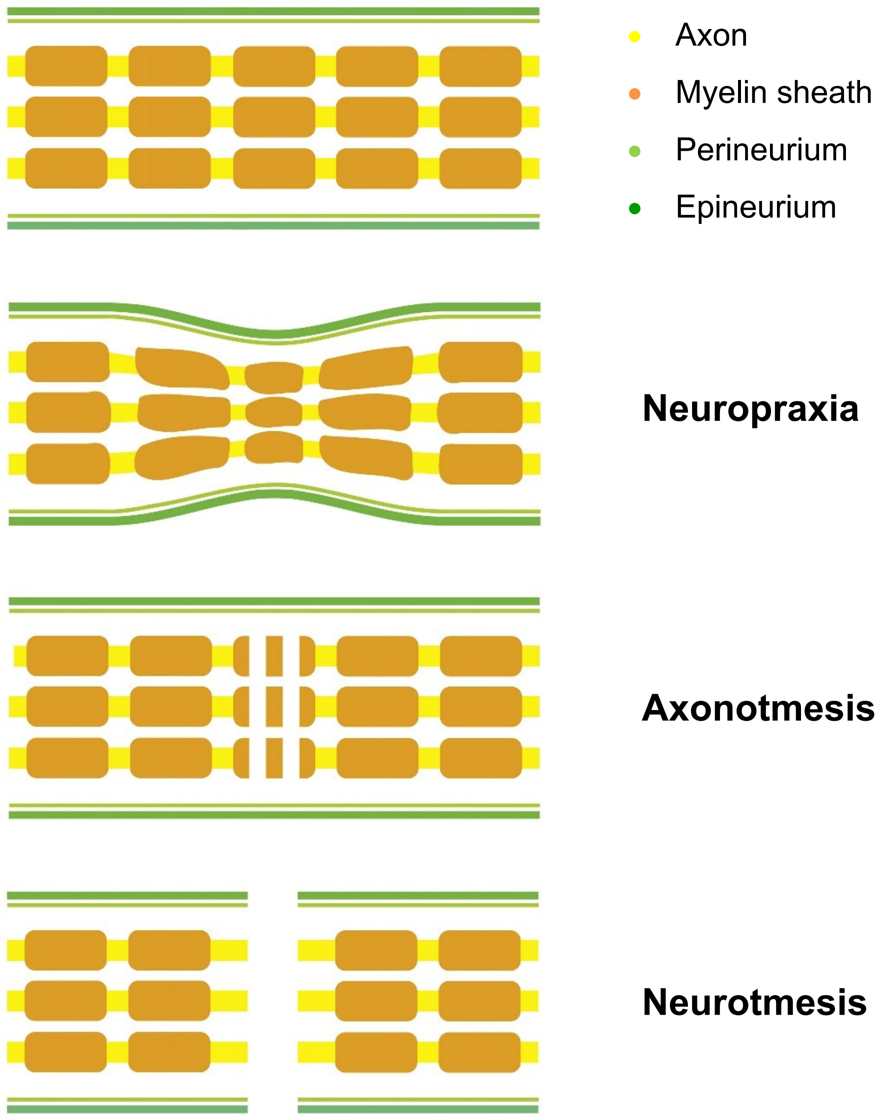


**Figure 3: SEDDON- Classification (13)**

### 1.6.2 Sunderland classification

The Sunderland classification resembles the Seddon classification, but is divided into five degrees of nerve injury. The first degree of this classification is equivalent to neuropraxia, as described above. Second degree of this classification is equivalent to axonotmesis, as described above. Third degree injury is corresponding to second degree with additionally interruption of the endoneurium, but no

interruption of the perineurium. Fourth degree corresponding to third degree but with an interruption of the perineurium. The Epineurium is still intact.
The fifth degree of the Sunderland classification is equivalent to neurotmesis of the Seddon classification, as described above (12).

| ***Seddon*** | ***Sunderland*** | ***Structural damages and lost functions*** |
|---|---|---|
| Neuropraxia | 1 | **Damage of the myelin sheath**<br>block or failure of nerve conduction |
| Axonotmesis | 2 | **Interruption of axonal continuity**<br>Endoneurium intact. No nerve conduction distal of the lesion |
| | 3 | **Additionally, interruption of the endoneurium**<br>Perineurium intact. No nerve conduction distal of the lesion |
| | 4 | **Additionally, interruption of the perioneurium**<br>Epineurium intact. No nerve conduction distal of the lesion |
| Neurotmesis | 5 | **Complete nerve dissection**<br>No nerve conduction distal of the lesion |

**Table 2: SEDDON- & SUNDERLAND- Classification (13)**

### 1.6.3 Etiology of peripheral nerve injuries

Nerve injuries may be a result of physical trauma, neuropathy or ischemia. Physical traumas can be caused by compression, traction or friction. The influencing factors for physical traumas are: the dimension of force which is acting on the nerve, the duration of impact and the direction in which the force affect the nerve (12). These nerve injuries caused by compression are more common in the upper limb based on nerve exposition. The most frequent affected nerves by compression are the ulnar and radial nerve. The compressing force can also affect the vascular circulation and lead to ischemia. Also, radiation and nerve toxic drugs can lead to nerve injuries. The duration of the injury is taken into account and is divided into acute or chronic injuries (12). The symptoms of nerve injuries may occur years after the initial radiation therapy (14). In some very rare cases the radiation therapy can also lead to the development of neurofibromas(15).

### 1.6.4 Peroneal nerve palsy

The common peroneal nerve arises of the sciatic nerve and descends on the medial margin of the musculus biceps femoris to the head of the fibula. The nerve winds around the neck of the fibula and is than divided into the superficial peroneal nerve and the deep peroneal nerve. The superficial peroneal nerve innervates the musculus peroneus longus and brevis where the deep peroneal nerve innervates the musculus tibialis anterior, the musculus extensor digitorum longus and the musculus hallucis longus (16).

Peroneal nerve palsy (PNP) leads to a significant limitation of a person´s mobility in daily life. Typical consequences of such a lesion are drop foot, the need for orthosis or increased risk of falls, gait changes and sensory disorders.
In some cases, PNP following endoprosthetic reconstruction of the knee has been reported(17).

According to studies by Park et al. (2013) and Cruz-Martinez et al. (2000) mechanical stretching, radiation- induced injury, rapid weight loss or inflammation have been identified as possible risk factors for PNP (18, 19). Regarding orthopedic oncology, PNP has been reported as a rare complication following tumor endoprosthetic reconstruction around the knee (17). The underlying causes of peroneal nerve palsy often remain unclear.

### 1.6.5 Therapy

The two main options for the treatment of a peripheral nerve injury are surgical intervention or conservative treatment. Depending on the severity of the nerve damage and the cause, different procedures are indicated.
The prognosis of a peripheral nerve injury can be estimated after four weeks when the EMG shows a spontaneous activity, which is an indicator of axonal damages. All lesions of first degree with a good prognostic factor ought to be treated conservatively. Lesions of second degree or lesions with uncertain localization are best treated conservatively for a span of twelve weeks. When there is no sign of recovery after 12 weeks, a surgical treatment should be taken in account. Lesions of third degree should be treated by surgical treatment as soon as possible (13). Nerve suturing or nerve grafting are possible treatments of lesions of third degree with is limited results, but with good prognosis with timely surgery and nerve lesion is under six centimeters (20-23).

The aim of this study was to (1) investigate the overall incidence of PNP, (2) to identify possible risk factors and (3) to investigate the incidence of transient PNP following tumor resection in the knee area.

# 2 Methods

## *2.1 Patients*

A retrospective database review of MEDOCS was performed to identify all patients with the diagnosis of a perioperative PNP. Clinical reports and outpatient records of the Department of Orthopedic Surgery Medical University of Graz were searched for relevant patients treated between 2006 to 2016 by searching for the keywords “Peroneuslähmung”, “Peroneusparese”, “Fußheberschwäche” and “Fußheberlähmung”. The cutoff at 2006 was chosen because all clinical reports before that time were not available in digital form.
All results of this search were evaluated and investigated for cases of tumor resections in the knee area. For this review, we included patients of every age and both sexes. All clinical reports considered for this review either contained PNP before or after surgery. Cases with possible nerve injuries during surgery were systematically excluded by reviewing all surgery reports of the patients.

885 cases were found by searching the medical data of the Department of Orthopaedic Surgery, Medical University of Graz for the relevant key-words as described above. After removing all duplicates 542 cases were left. 523 of those cases were non-relevant, with most of them involving patients with intervertebral disc operations. From nineteen related to tumor resections in the knee area left, eleven had to be excluded, as the peroneal nerve was sacrificed during surgery (n=4), PNP was on the contralateral side following resection of fibula as bone graft (n=1), PNP following a car accident (n=1), clinical data was not available (n=1) and PNP following endoprosthetic replacement of the knee (n=1). Thus, eleven cases were identified to meet all inclusion criteria and were finally included in this study as shown in figure 4. Eleven patients suffering from PNP, with three patients before and eight patients after a tumor resection in the knee area, were identified.

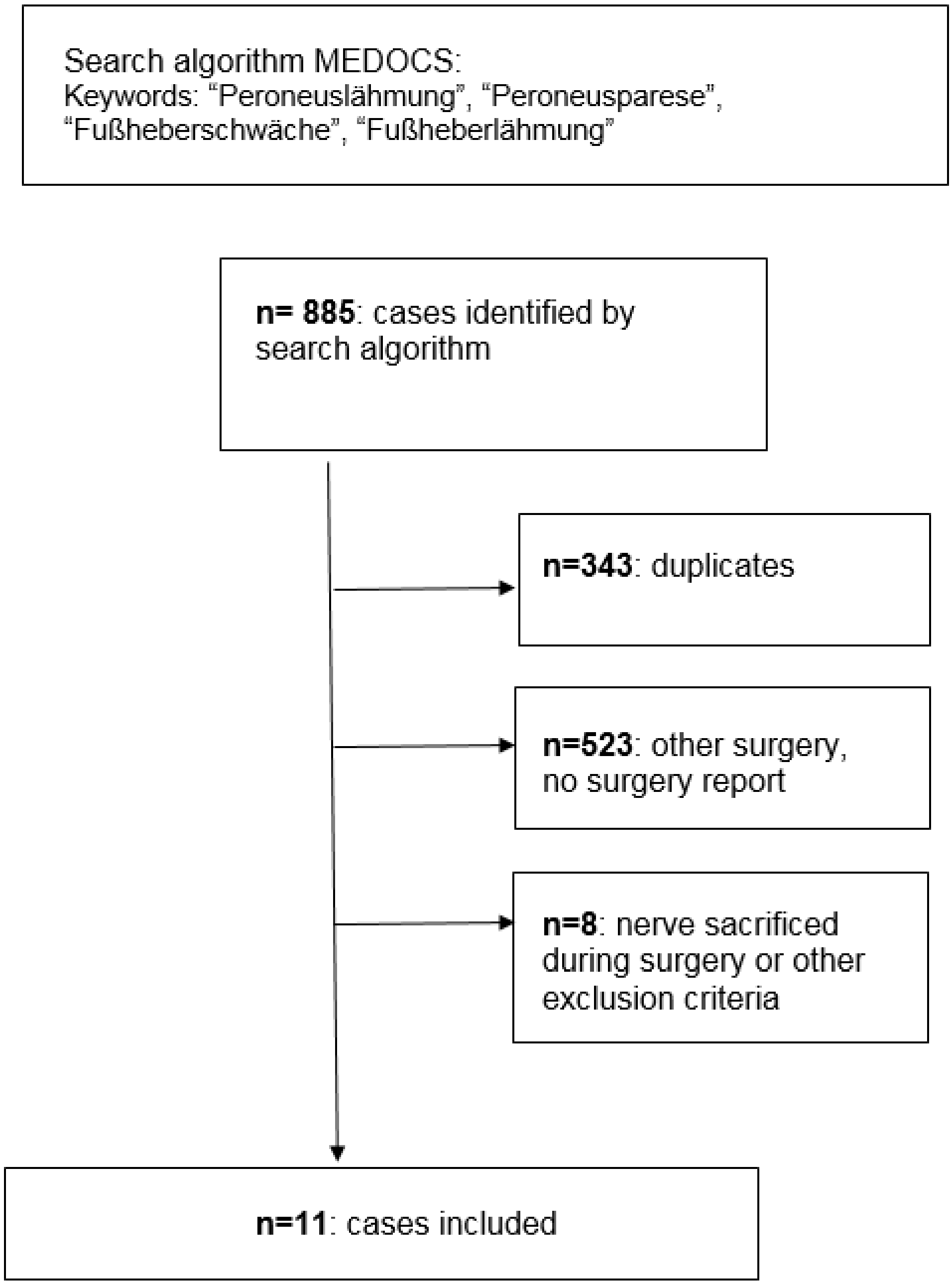


**Figure 4: Search algorithm MEDOCS**

## 2.2 Data

Patient data was extracted from MEDOCS and collected in anonymized database. Patients medical data was scanned for following data: age, age at initial surgery, sex, tumor type (osteosarcoma, chondrosarcoma, Ewing´s sarcoma, ganglion, benign bone tumor, other tumor), tumor localization(distal femur, proximal tibia, proximal fibula, proximal tibiofibular-joint, knee joint), side of the lower limb (left, right), surgical procedure, positioning of the patient during surgery, surgery time (in min), pressure of tourniquet (mmHg), complications during surgery, duration of hospitalization (in days) and treatment after surgery. The knee area was defined in this study as all locations in the knee joint, the distal femur, the proximal tibia, the proximal fibula, the tibiofibular-joint, the patella and all tissue, that directly surrounds these locations. If there was any report of recovery of the PNP, it was considered as transient PNP, with no defined cutoff time. All PNP without recovery were considered as permanent PNP.

## 2.3 Systematic literature review

Based on the final number of cases with PNP after a tumor resection in the knee area identified at Department of Orthopedic Surgery Medical University of Graz, a systematic literature review was performed. This review included relevant studies published from 1979 up to February 2017. The research was done on MEDLINE (via PubMed) with relevant key-words which lead to following algorithm:

“sarcoma AND ((tibia AND proximal) OR (femur AND distal))”

In addition, a manual search by screening bibliographies of included articles for further relevant data on PubMed to improve our search results was performed. We excluded for this literature review case- reports and papers which were in another language than English or German.

The following data was collected from all included studies: number of included patients, number of included women and men, mean age, range of age, tumor type (osteosarcoma, chondrosarcoma, Ewing´s sarcoma, other MBT, benign bone tumor, other tumor), tumor localization (distal femur, proximal tibia, proximal fibula, total femur (proximal femur or diaphyseal femur), other locations), cases of PNP (total number, cases of transient PNP, cases of permeant PNP).

773 studies were found by the algorithm used on Medline (via PubMed) and three additional studies were included by manual search via PubMed. 63 studies were immediately excluded as they were published in another language than English or German. Also, case reports (n=279) were excluded from this literature review. 431 studies underwent abstract review, of those 229 did not contain relevant data on peroneal nerve injuries and had to be excluded. Further 180 were excluded after a study review as they did not contain relevant data. Twenty-five (22 by literature review and three by manual search) studies fulfilled the inclusion criteria: 1) the study had to be published in English or German, 2) the study had to be performed in humans 3) the study had to be no case report, 4) the study had to contain relevant data on peroneal nerve palsies related to a tumor in the knee area, 5) no damage or sacrifice of peroneal nerve during surgery. Finally, twenty-five studies were included in this study. As illustrated in Figure 5.

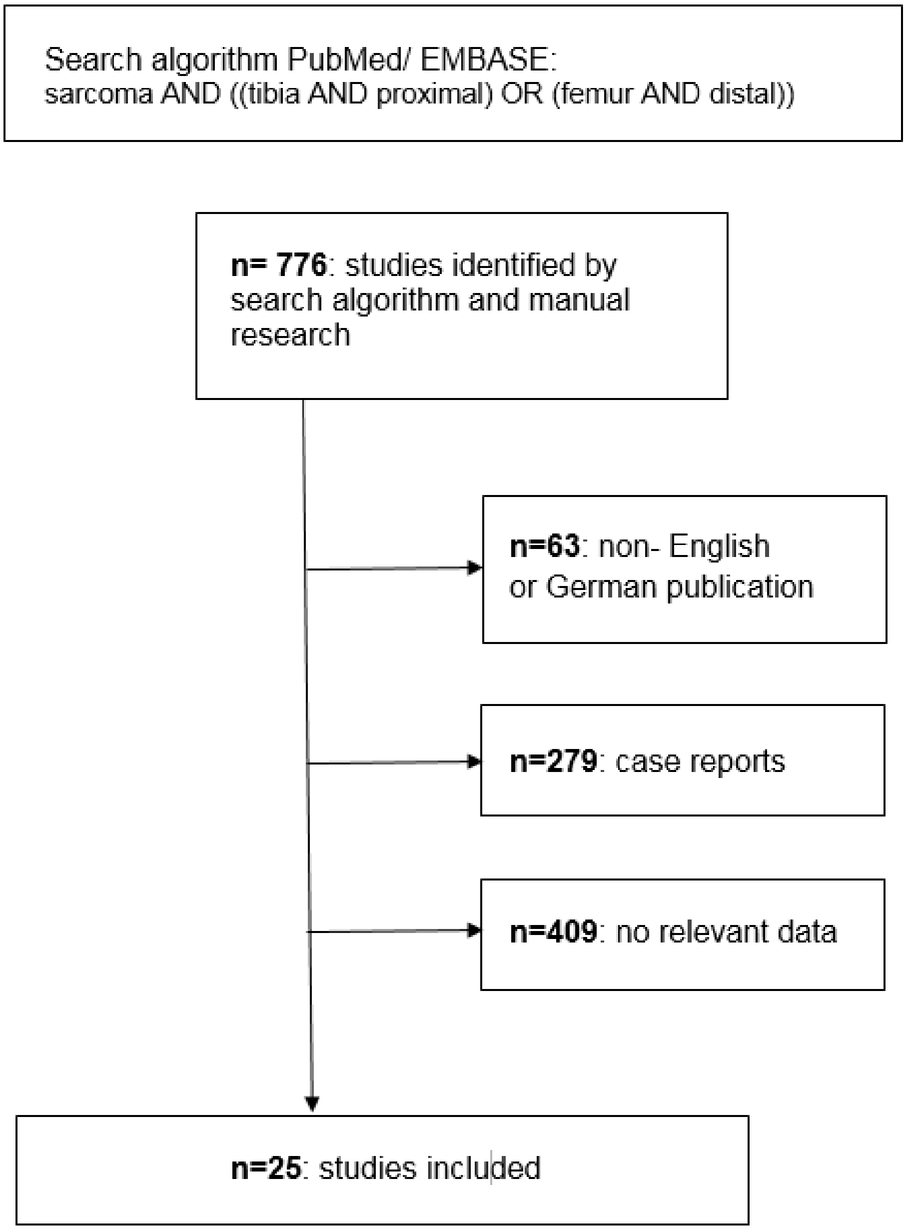


**Figure 5: Search algorithm literature review**

Descriptive statistics were calculated using means, range and percentage. All statistical calculations were performed using IBM SPSS 22 and Excel (Microsoft). Two-sided p-values <0.05 were considered statistically significant.

# 3 Results

## *3.1 Results of patient data*

### 3.1.1 Patients with preoperative PNP

There were three male patients in which PNP occurred before the initial tumor resection, with a mean age of 58.3 years. All three patients had a ganglion, two of them located in the tibiofibular joint and one located in the proximal tibia. Details shown in table 3.

.

| Patient | Sex | Age at inital surgery [years] | Tumor type | Tumor region | Side |
|---|---|---|---|---|---|
| 1 | M | 63 | ganglion | proximal tibiofibular joint | left |
| 2 | M | 46 | ganglion | proximal tibiofibular joint | right |
| 3 | M | 66 | ganglion | proximal tibia | right |

**Table 3: Patient data - preoperative PNP**

All three cases were treated by extirpations of ganglions. All three patients were in supine position during the operation und a tourniquet was used in all three cases. No complications during surgery were reported in all three patients. The mean surgery time was 84.7 minutes (range, from 50 to 125 minutes) as shown in table 4.

| Patient | Tumor type | Surgical procedure | Pneumatic tourniquet [mmHg] | Surgery time [minutes] | Interoperative Complication |
|---|---|---|---|---|---|
| 1 | ganglion | extirpation | Yes, pressure n. d. | 79 | none |
| 2 | ganglion | extirpation | Yes, pressure n. d. | 50 | none |
| 3 | ganglion | extirpation | Yes, pressure n. d. | 125 | none |

**Table 4: Surgical data - preoperative PNP**

The mean time of hospitalization after the initial tumor resection was 10.3 days (range from four to twenty days). All three cases were transient PNP with full recovery after the initial tumor resection. The time interval between first occurrence and recovery was, 16 days in case 1, four days in case 2 and 70 days in case 3. Details shown in table 5.

| Patient | Period of time (occurence of PNP –Initial surgery) [days] | Recovery of PNP | Period of recovery [days] | Hospitalization [days] |
|---|---|---|---|---|
| 1 | 16 | yes | 16 | 7 |
| 2 | 4 | yes | 4 | 4 |
| 3 | 70 | yes | 70 | 20 |

**Table 5: PNP data – preoperative**

### 3.1.2 Patients with postoperative PNP

There were seven male patients and one female patient with a mean age of 29.5 years at the time of the operation (range from eleven to fifty-seven years). Six patients had a resection of a primary MBT (two osteosarcomas, two chondrosarcomas and two Ewing´s sarcomas), one patient a resection of a osteochondroma and one patient a resection of a ganglion. Four tumors were located in the proximal tibia, two tumors were in the proximal fibula and one each in the proximal tibiofibular joint and the distal femur. Details shown in Table 6.

| Patient | Sex | Age at inital surgery [years] | Tumor type | Tumor region | Side |
|---|---|---|---|---|---|
| 4 | M | 57 | ganglion | proximal tibiofibular joint | right |
| 5 | M | 45 | chondrosarcoma | proximal fibula | left |
| 6 | F | 37 | osteochondroma | proximal fibula | right |
| 7 | M | 20 | osteosarcoma | proximal tibia | left |
| 8 | M | 28 | chondrosarcoma | distal femur | left |
| 9 | M | 11 | Ewing´s sarcoma | proximal tibia | left |
| 10 | M | 13 | osteosarcoma | proximal tibia | left |
| 11 | M | 25 | Ewing´s sarcoma | proximal tibia | left |

**Table 6: Patient data - postoperative PNP**

There were five wide tumor resections with endoprosthetic reconstruction, one extirpations of ganglions, one resection of an exostosis and one partial resection of the proximal fibula. All eight patients were in supine position during the operation und a tourniquet was used in all cases. No complications during surgery were reported in all eight patients. The mean surgery time was 157.2 minutes (range, from 66 to 274 minutes in two cases the surgery time was not available via MEDOCS) as shown in table 7.

| Patient | Tumor type | Surgical procedure | Pneumatic tourniquet [mmHg] | Surgery time [minutes] | Interoperative complication |
|---|---|---|---|---|---|
| 4 | ganglion | resection | Yes, pressure n. d. | 86 | none |
| 5 | chondrosarcoma | partial resection of px. fibula | Yes, pressure n. d. | 122 | none |
| 6 | osteochondroma | resection of the exostosis | 350 | 66 | none |
| 7 | osteosarcoma | wide resection + prosthesis | 350 | 274 | none |
| 8 | chondrosarcoma | wide resection + prosthesis | Yes, pressure n. d. | 178 | none |
| 9 | Ewing's sarcoma | wide resection + Prosthesis | Yes, pressure n. d. | n. d. | none |
| 10 | osteosarcoma | wide resection + Prosthesis | Yes, pressure n. d. | n. d. | none |
| 11 | Ewing´s sarcoma | wide resection + Prosthesis | Yes, pressure n. d. | 217 | none |

**Table 7: Surgical data - postoperative PNP**

The mean time of hospitalization after the initial tumor resection was 11.6 days (range from six to thirty days). Depending on the surgical procedure and the physical condition of the patient, an adequate therapy was chosen for further medical treatment. There were five cases of permanent PNP and three cases of transient PNP. In Patient 7 the PNP occurred one day after the initial tumor resection and was, according to the clinical report, most likely caused by too tight bandage. In two patients (Patient 9,10) transient PNP occurred very late after the initial tumor resection, 4.5 years in case 9 and 4.9 years in case 10. Both patients were treated by wide tumor resections and a minimally-invasive growing prosthesis was implanted for reconstruction, which must be adapted manually to the individual bone growth of each patient. In case 9 the prosthesis was expanded shortly before the occurrence of the PNP. Patient 9 had a lengthening of 14.4 mm of the expandable endoprosthesis one days before the first record of PNP. In Patient 10 a revision from HMRS prosthesis to GMRS tumor endoprosthesis was preformed one day before the first record of PNP. The time interval between first occurrence and recovery was, 127 days in case 6, 623 days in case 9 and 571 days in case 10. Details shown in table 8.

| Patient | Period of time (Initial surgery – occurence of PNP) [days] | Recovery of PNP | Period of recovery [days] | Hospitalization [days] |
|---|---|---|---|---|
| 4 | 24 | no | - | 6 |
| 5 | 40 | no | - | 6 |
| 6 | 40 | yes | 127 | 7 |
| 7 | 1 | no | - | n. d. |
| 8 | 44 | no | - | 9 |
| 9 | 1* | yes | 623 | n. d. |
| 10 | 1** | yes | 571 | 30 |
| 11 | 11 | no | - | n. d. |

**Table 8: PNP data - postoperative**

* PNP occurred one day following manual minimally invasive lengthening of a growing prosthesis
**PNP occurred one day following revision from HMRS prosthesis to GMRS tumor endoprosthesis

As illustrated in figure 6, the MBT´s (two osteosarcomas, two chondrosarcomas and two Ewing´s- sarcomas) were combined in one group to allow a better comparison, four were in the proximal tibia, one in the proximal fibula and one in the distal femur. One ganglion was in the proximal tibiofibular joint and one osteochondroma was in the proximal fibula located.

627 Patients with a tumor around the knee between 2006 to 2016 underwent surgery according to our local tumor registry. For the overall incidence of PNP only cases of patients with postoperative PNP were considered. The cases of preoperative PNP were excluded for the incidence PNP to allow the comparison with other studies. The eight reported cases of postoperative PNP lead to a PNP incidence of 1.3% in our own patient collective. The overall incidence of PNP is divided into a permanent PNP incidence of 0.8% and a transient PNP incidence of 0.5%.

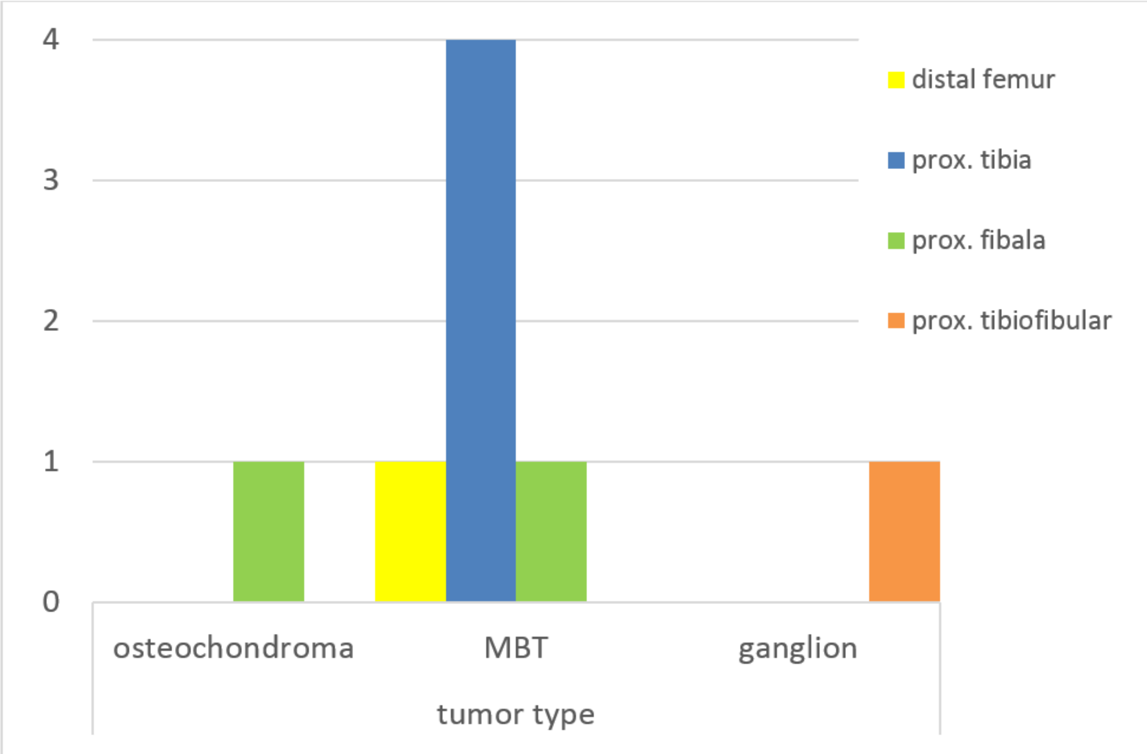


**Figure 6: Diagram tumor type and region**

## 3.2 *Results of the literature review*

The total number of patients investigated in the included 25 studies (24-48) was 1300. There were 729 male patients and 571 female patients (ratio 1,27 m/f). The mean age was 24.2 years (range from three to eighty-eight years). There were 1048 cases of MBT, 201 cases of benign bone tumors and 46 cases of other tumors. Also, five cases (0.38%) of nontumor causes were included in this study (reoperation in four patients and disappearing bone disease in one). The most common diagnosis was osteosarcoma in 793 patients (61.00%), second was chondrosarcoma in 105 patients (8.08%). Sixty-three patients (4.85%) had an Ewing´s- sarcoma and eighty-seven (6.69%) had another type of MBT.

Tumors were located in the distal femur (n=742 (57,08%)), the proximal tibia (n=271 (20.85%)), the proximal fibula (n=153 (11.77%), proximal or diaphyseal femur (n=55 (4.23%)), another tumor site (n=86 (6.62%)).

| Patients characteristics | | n | % |
|---|---|---|---|
| *Total number of patients* | | 1300 | |
| *Gender* | male | 729 | 56.1 |
| | female | 571 | 43.9 |
| *Histology* | osteosarcoma | 793 | 61.0 |
| | chondrosarcoma | 105 | 8.1 |
| | Ewing´s - sarcoma | 63 | 4.9 |
| | other MBT | 87 | 6.7 |
| | benign bone tumor | 201 | 15.5 |
| | other tumor | 46 | 3.5 |
| *Localization* | distal femur | 742 | 57.1 |
| | proximal tibia | 271 | 20.9 |
| | proximal fibula | 153 | 11.8 |
| | diaphyseal or proximal femur | 55 | 4.2 |
| | other location | 86 | 6.6 |
| *PNP* | total number of PNP cases | 87 | 6.7 |
| | Cases of transient PNP | 54 | 4.2 |
| | Cases of permanent PNP | 6 | 0.5 |

**Table 9: Patients characteristics – literature review**

In all papers included in this study, eighty-seven cases of PNP (6.69%) were found. Those eighty-seven cases divided into fifty-four cases of transient peroneal nerve injury (4.15%) and six cases of permanent PNP (0.46%). In twenty-seven cases (2.08%), distinction between transient or permanent PNP was not possible with the available data. As shown in table 10. Due to the lack of differentiation between transient and permanent PNP, the number of transient and permanent PNPs is missing in four studies (24, 25, 33, 35).

Only one of the 25 included studies presumed a possible cause for the incidence of PNP. Decilveo et al. (2016) assumed that the mobilization of the peroneal nerve during surgery can lead to transient PNP (46). All other included studies did not report any risk factors or possible causes for the nerve injury.

| Author | Number of patients | PNP total | | PNP permanent | | PNP transient | |
|---|---|---|---|---|---|---|---|
| | | Cases | [%] | Cases | [%] | Cases | [%] |
| Yu XC (2014) | 10 | 1 | 10,00 | n.e. | | n.e. | |
| D Donati (2002) | 92 | 10 | 10,87 | n.e. | | n.e. | |
| D Donati (2007 | 62 | 7 | 11,29 | 0 | 0,00 | 7 | 11,29 |
| Sharma S (2006) | 77 | 3 | 3,90 | 0 | 0,00 | 3 | 3,90 |
| Matsumine A (2011) | 69 | 4 | 5,80 | 0 | 0,00 | 4 | 5,80 |
| Grimer RJ (2000) | 20 | 4 | 20,00 | 0 | 0,00 | 4 | 20,00 |
| Bickels J (2006) | 24 | 3 | 12,50 | 0 | 0,00 | 3 | 12,50 |
| Ham SJ (1998) | 32 | 1 | 3,13 | 1 | 3,13 | 0 | 0,00 |
| Futani H (2006) | 33 | 1 | 3,03 | 0 | 0,00 | 1 | 3,03 |
| Capanna R (1994) | 95 | 3 | 3,16 | n.e. | | n.e. | |
| Bi W (2013) | 104 | 3 | 2,88 | 0 | 0,00 | 3 | 2,88 |
| Niimi R (2012) | 63 | 13 | 20,63 | n.e. | | n.e. | |
| Titus V (2008) | 10 | 2 | 20,00 | 1 | 10,00 | 1 | 10,00 |
| Campanacci L (2015) | 18 | 2 | 11,11 | 0 | 0,00 | 2 | 11,11 |
| Biau D (2006) | 91 | 5 | 5,49 | 1 | 1,10 | 4 | 4,40 |
| Campanacci M (1979) | 26 | 2 | 7,69 | 0 | 0,00 | 2 | 7,69 |
| Safran MR (1994) | 151 | 7 | 4,64 | 0 | 0,00 | 7 | 4,64 |
| Muschler GF (1995) | 37 | 1 | 2,70 | 0 | 0,00 | 1 | 2,70 |
| Rao BN (1983) | 32 | 3 | 9,38 | 0 | 0,00 | 3 | 9,38 |
| Malawer MM (1989) | 7 | 4 | 57,14 | 0 | 0,00 | 4 | 57,14 |
| Florez B (2008) | 113 | 1 | 0,88 | 1 | 0,88 | 0 | 0,00 |
| Betz M (2011) | 6 | 1 | 16,67 | 0 | 0,00 | 1 | 16,67 |
| Decilveo AP (2016) | 7 | 2 | 28,57 | 0 | 0,00 | 2 | 28,57 |
| Abdel MP (2012) | 112 | 2 | 1,79 | 0 | 0,00 | 2 | 1,79 |
| Erler K (2004) | 9 | 2 | 22,22 | 2 | 22,22 | 0 | 0,00 |
| Total: | 1300 | 87 | | 6 | | 54 | |
| Percentage: | | 6,69 % | | 0,46 % | | 4,15 % | |

**Table 10: PNP incidence - literature review**

# 4 Discussion

Peroneal nerve palsy is a possible complication after a tumor resection in the knee area. In some cases, it is necessary to sacrifice the peroneal nerve to ensure a complete tumor resection leading to a PNP. But PNP may also occur without direct damaging of the peroneal nerve during surgery. Known causes of PNP are pressure or infections but PNP can also be of idiopathic causes.

Thus, the aim of this study was to (1) investigate the overall incidence of PNP, (2) to identify possible risk factors and (3) to investigate the incidence of transient PNP following tumor resection in the knee area.

The incidence of postoperative PNP was 1.3% in our own patient collective and 6.62% in the systematic literature review. To our knowledge, no study has investigated the overall incidence of PNP after tumor resection in the knee area before. Other studies showed a lower incidence of PNP related to surgery in the knee area. A retrospective study by Nercessian et al. (2005), which compared several studies with a large number of patients (>1000), found an incidence of 0.3 to 1.3% of PNP after total knee arthroplasty (49). Similarly, Amotz et al. (2014) reported, in a structured literature review of 15 studies, an incidence of 2,6 % of permanent PNP after resection of the proximal fibula as bone graft (50).

Decilvio et al. (2016) assumed the mobilization of the peroneal nerve during the operation as possible cause for transient PNP (46). In all the other included studies, were no risk factor or possible causes for PNP reported. Other studies have investigated the risk factors for PNP related to knee surgery in general. A study of Idusuyi et al. (1996) investigated the occurrence of PNP after total knee arthroplasty and found a high rate of delayed PNP. They assumed that the PNP occurred in some cases of the postoperative positioning of the leg under the influence of anesthesia, leading to a vulnerability of the peroneal nerve (51). Also, the double crush phenomenon was seen as a possible cause in further studies (51-53). Beller et al. (2008) investigated the combination of several nerve damaging impacts during total knee arthroplasty, which can lead to PNP (52). They found a decrease of the risk of PNP by reducing the pressure of the pneumatic tourniquet to (<320 mmHg) (52).

The incidence of transient PNP was 0.5% in our own patient collective and 4.15% in the systematic literature review. The transient PNP was the most frequent type of PNP with fifty-four out of eight-seven cases (62.07%) and permanent PNP was only reported in six out of the eight-seven cases (6.90%). In a very large number of cases (31.03%) there was no distinction between transient or permanent PNP.

In the literature review of the present study, a total of eight-seven cases of PNP were identified, leading to an overall incidence of 6.69% of all 1300 patients of twenty-five studies. The highest rate of PNP was reported in a study of Malawer et. al. (1989) with an incidence of transient PNP of 57.14% (43). In this study, seven patients received a resection of high grade MBT in the proximal tibia including a minimum follow up of two years, with four of them developing a transient PNP. All the four reported cases of PNP were transient, which recovered in all patients. There were no possible causes for the PNP reported. However, the total number of patients under investigation was only seven included in this study. In the other studies, the incidence of PNP ranged from 0.88% to 28.57%. In general, only a small number of papers reported the incidence of PNP as complications after or before a tumor resection in the knee area. Most of the studies did not report any neurological complications (54-56). Because there was no standardized data collection, a detailed statistical evaluation was not possible. To improve the awareness and research of this possible complication, it is highly recommended for the documentation of PNP to become more standardized in the future.

Out of 885 patients, found from MEDOCS by an algorithm only eleven cases could be included in this study. Out of these eleven cases, six patients showed transient PNP and five patients showed permanent PNP. Three of these transient PNP occurred before the initial tumor resection and recovered full after the operation. All four cases of ganglion resections included in this study were men. Similarly, Rein et. al. (2005) reported that 73% of cases of ganglion located the proximal tibiofibular joint occur in men (57). There are different opinions on potential pathomechanisms for PNP caused by a ganglion cyst. Some studies suggest that the stretching of the peroneal nerve is the main cause (58). Another possible cause suggested by some authors is the compression of the peroneal nerve between the head of the fibula and the peroneus longus fascia and muscle (59, 60). An ultrasound scan allows a quick recognition of ganglion cysts, but to exclude possible differential diagnoses an MRI- examination should be taken in consideration (61, 62).

Regarding pediatric patients with osteo- or Ewing´s sarcoma there are several surgical options to overcome leg-length discrepancies following tumor resection around the knee. One possibility is the implantation of an expandable prosthesis (63, 64). If the expected growth of the patient is more than 30 mm an expandable prosthesis is recommended (63). Lengthening of the prosthesis can be carried out open minimally invasively or non-invasively. Depending on the type of expandable prosthesis and number of lengthening procedures different complications rates occur (65). In two patients (Patient 9,10) PNP occurred very late after the initial tumor resection. Both patients were treated by wide tumor resections and a minimally-invasive growing prosthesis was implanted for reconstruction, which must be lengthened manually under general anesthesia to the individual bone growth of each patient. In both cases the prosthesis was expanded shortly before the occurrence of the PNP. In case 9 the prosthesis was expanded shortly before the occurrence of the PNP. Patient 9 had a lengthening of 14.4 mm of the expandable endoprosthesis one days before the first record of PNP. In Patient 10 a revision from HMRS prosthesis to GMRS tumor endoprosthesis was preformed one day before the first record of PNP. Most likely, total amount of lengthening was too much and damaging the nerve. In addition, Abed et al. (2010) the lengthening of expandable prosthesis should be under 10 mm each time to avoid the risk of nerve injury (63). After all, expandable prosthesis with non-invasive lengthening mechanisms, which allow for gradual expansion of the prosthesis over may days, are mainly implanted nowadays (63).

This study has shown that the incidence of PNP related to tumor surgery in the knee area is higher in the literature than detected in our own patient collective. Most of the reviewed studies did not mention any neurological complications, in particular the occurrence of PNP and focused instead on prosthesis failure, infections and other complications. We estimate therefore that the real incidence of PNP related to tumor surgery in the knee area is in reality higher than the incidence calculated from the included studies due to a lack of documentation. In addition, it is difficult to investigate the incidence and possible causes of PNP due to the lack of reported data of neurological complications in a retrospective study. Instead, a prospective study design with the implementation of the Henderson – classification would be more suitable for research on this topic, due to the fact that the Henderson – classification includes a record of neurological complications (66).

In addition, there should be an increased awareness of the surgeon for the positioning of the patient during operation and postoperative, the pressure of the pneumatic tourniquet and mobilization of the peroneal nerve during surgery to prevent PNP, as studies discussed above have shown (46, 51-53).

Considering the high incidence of PNP, patients should be informed in more detail of possible neurological complications like peroneal nerve injuries prior undergoing tumor surgery around the knee.

## *4.1 Limitations*

The limitations of this study are divided into individual limitations of the retrospective review and the structured literature review.
The small number of patients included in the retrospective review and the lack of control groups, lead to major limitations of the statistical analyses and comparisons. Since all reports before 2006 were not available in digital format, only the clinical reports of the Department of Orthopaedic Surgery, Medical University of Graz between 2006 and 2016 could be investigated. Furthermore, it is possible that in some cases involving PNP, the clinical report did not include PNP or patients treated at the Department of Orthopaedic Surgery underwent follow-up investigations at external institutions or the primary referring institutions. Thus, an unknown number of patients suffering from PNP might not have been detected. Furthermore, it is planned to review all the cases of distal femur and proximal tibia replacements treated at the Department of Orthopaedic Surgery, Medical University of Graz to identify additional patients with PNP. To overcome this limitation an additional systematic literature review was conducted and compared to our own data.

In the performed structured literature review, only studies that clearly reported the incidence of PNP, were included. But the incidence of PNP was rarely reported in most of the studies, also the subdivision into transient or permanent PNP was sometimes not reported. Only three studies (42, 46, 48) of the 25 included reported the individual cases of patients with PNP with data containing information about gender, age, tumor type, localization and complications. All other studies reported only the incidence of PNP, but with no data of the individual cases, which would be necessary for further investigation and identification of risk factors. Also, the inclusion of only studies in English or German can lead to a “tower of babel bias” by not including relevant data of studies, which were published in another language (67).

## 4.2 Conclusion

The incidence of PNP related to tumor surgery in the knee area in this study was higher than expected, compare to the incidence of PNP in other surgeries in knee area. Based on the results of this study, permanent PNP is a rare complication after tumor resections in the knee area without any nerve damage during operation. It also showed that transient PNP is a more common complication. Due to the low number of patients and studies included in the structured literature review these results should be assessed with caution. Statistical analyses of the structured literature review were not possible due to the missing data of the individual cases of PNP. It is necessary that more comparable data, including control groups, should be collected and further research should be done. To obtain a representative result of the incidence of PNP after tumor resection in the knee area, clinical reports ought to be more standardized so that PNP related data can be found more easily. A possible way to improve the number of cases would be a multicenter prospective study with standardized documentation of neurological complications related to tumor surgery in the knee area.

# 5 Appendix

| Patients | Case 1 | Case 2 | Case 3 |
|---|---|---|---|
| **Sex** | M | M | M |
| **Age at surgery [years]** | 63 | 46 | 66 |
| **Tumor typ** | ganglion | ganglion | ganglion |
| **Tumor region** | prox. tibiofibular joint | prox. tibiofibular joint | prox. tibia |
| **Side** | left | right | right |
| **Time interval (PNP occurence - initial surgery) [days]** | 16 | 4 | 70 |
| **Surgical technique** | excision | excision | excision |
| **Position during surgery** | n.d. | n.d. | Supine |
| **Tourniquet [mmHg]** | yes, pessure n.d. | yes, pessure n.d. | yes, pessure n.d. |
| **Surgery time [min]** | 79 | 50 | 125 |
| **Complication during surgery** | none | none | none |
| **Hospitalization time after initial tumor resection [days]** | 7 | 4 | 20 |

| Patients | Case 4 | Case 5 | Case 6 | Case 7 | Case 8 |
|---|---|---|---|---|---|
| **Sex** | M | M | F | M | M |
| **Age at surgery [years]** | 57 | 45 | 37 | 20 | 28 |
| **Tumor typ** | ganglion | chondrosarcoma G1 | osteochondroma | osteosarcoma | chondrosarcoma G2 |
| **Tumor region** | prox. tibiofibular joint | prox. fibula | prox. fibula | prox. tibia | distal femur |
| **Side** | right | left | right | left | left |
| **Time interval (initial surgery - PNP occurence) [days]** | 24 | 40 | 40 | 1 | 44 |
| **Surgical technique** | excision | partial resection of px. fibula | resection of the exostosis | wide resection + prosthesis | wide resection + prosthesis |
| **Position during surgery** | supine | supine | supine | supine | supine |
| **Tourniquet [mmHg]** | yes, pessure n.d. | yes, pessure n.d. | 350 | 350 | yes, pessure n.d. |
| **Surgery time [min]** | 86 | 122 | 66 | 274 | 178 |
| **Complication during surgery** | none | none | none | none | none |
| **Hospitalization time after initial tumor resection [days]** | 6 | 6 | 7 | n.d. | 9 |

| Patients | Case 9 | Case 10 | Case 11 |
|---|---|---|---|
| **Sex** | M | M | M |
| **Age at surgery [years]** | 11 | 13 | 25 |
| **Tumor typ** | Ewing´s - sarcoma | osteosarcoma | Ewing´s - sarcoma |
| **Tumor region** | prox. tibia | prox. tibia | prox. tibia |
| **Side** | left | left | left |
| **Time interval (initial surgery - PNP occurence) [days]** | 1* | 1** | 11 |
| **Surgical technique** | wide resection + prosthesis | wide resection + prosthesis | wide resection + prosthesis |
| **Position during surgery** | supine | supine | supine |
| **Tourniquet [mmHg]** | yes, pessure n.d. | yes, pessure n.d. | yes, pessure n.d. |
| **Surgery time [min]** | n.d. | n.d. | n.d. |
| **Complication during surgery** | none | none | none |
| **Hospitalization time after initial tumor resection [days]** | n.d. | 30 | n.d. |

* PNP occurred one day following manual minimally invasive lengthening of a growing prosthesis
**PNP occurred one day following revision from HMRS prosthesis to GMRS tumor endoprosthesis

| **Author** | Yu XC (24) | D Donati (25) | D Donati (26) | Sharma S (27) | Matsumine A (28) |
|---|---|---|---|---|---|
| **Year of publication** | 2014 | 2002 | 2007 | 2006 | 2011 |
| **Number of patients** | 10 | 92 | 62 | 77 | 69 |
| **Gender male** | 7 | 51 | 42 | 38 | 41 |
| **Gender female** | 3 | 41 | 20 | 39 | 28 |
| **Mean age of patients (years)** | 20,1 | 23 | 24 | 42 | 48 |
| **Age of patient (range)** | 15-24 | 7-39 | 11-77 | 12-87 | 10-79 |
| **HISTOLOGY:** | | | | | |
| **Osteosarcoma** | 10 | 59 | 39 | 40 | 40 |
| **Ewing´s - sarcoma** | 0 | n.e | 7 | 3 | 1 |
| **Chondrosarcoma** | 0 | 5 | 3 | 11 | 8 |
| **Other MBT** | 0 | 7 | 7 | 13 | 9 |
| **Benige bone tumor** | 0 | 10 | 2 | 2 | 4 |
| **Other tumor** | 0 | 0 | 0 | 8 | 7 |
| **ANATOMICAL LOCALIZATION:** | | | | | |
| **Distal femur** | 10 | 72 | 0 | 77 | 69 |
| **Proximal tibia** | 0 | 20 | 62 | 0 | 0 |
| **Proximal Fibula** | 0 | 0 | 0 | 0 | 0 |
| **Total femur (proximal or diaphyse)** | 0 | 0 | 0 | 0 | 0 |
| **Other location** | 0 | 0 | 0 | 0 | 0 |
| **PNP:** | | | | | |
| **Cases of PNP** | 1 | 10 | 7 | 3 | 4 |
| **Incidence of PNP total [%]** | 10,00 | 10,87 | 11,29 | 3,90 | 5,80 |
| **Cases of transient PNP** | n.e. | n.e. | 7 | 3 | 4 |
| **Incidence of PNP transient [%]** | | | 11,29 | 3,90 | 5,80 |
| **Cases of permanent PNP** | n.e. | n.e. | 0 | 0 | 0 |

| Author | Grimer RJ (29) | Bickels J (30) | Ham SJ (31) | Futani H (32) | Capanna R (33) |
|---|---|---|---|---|---|
| **Year of publication** | 2000 | 2006 | 1998 | 2006 | 1994 |
| **Number of patients** | 20 | 24 | 32 | 33 | 95 |
| **Gender male** | 13 | 8 | 19 | 13 | 55 |
| **Gender female** | 7 | 16 | 13 | 20 | 40 |
| **Mean age of patients (years)** | 9,9 | 29 | 20,5 | 10 | 23 |
| **Age of patient (range)** | 5-14 | 17-56 | 10-67 | 6-11 | 11-69 |
| **HISTOLOGY:** | | | | | |
| **Osteosarcoma** | 14 | 6 | 24 | 39 | 63 |
| **Ewing´s - sarcoma** | 7 | 3 | 0 | 1 | 2 |
| **Chondrosarcoma** | 0 | 4 | 6 | 0 | 6 |
| **Other MBT** | 2 | 1 | 2 | 0 | 7 |
| **Benige bone tumor** | 0 | 10 | 0 | 0 | 10 |
| **Other tumor** | 0 | 0 | 0 | 0 | 7 |
| **ANATOMICAL LOCALIZATION:** | | | | | |
| **Distal femur** | 0 | 0 | 20 | 40 | 95 |
| **Proximal tibia** | 20 | 0 | 2 | 0 | 0 |
| **Proximal Fibula** | 0 | 24 | 0 | 0 | 0 |
| **Total femur (proximal or diaphyse)** | 0 | 0 | 10 | 0 | 0 |
| **Other location** | 0 | 0 | 0 | 0 | 0 |
| **PNP:** | | | | | |
| **Cases of PNP** | 4 | 3 | 1 | 1 | 3 |
| **Incidence of PNP total [%]** | 20,00 | 12,50 | 3,13 | 3,03 | 3,16 |
| **Cases of transient PNP** | 4 | 3 | 0 | 1 | n.e. |
| **Incidence of PNP transient [%]** | 20,00 | 12,50 | 0,00 | 3,03 | |
| **Cases of permanent PNP** | 0 | 0 | 1 | 0 | n.e. |

| Author | Bi W (34) | Niimi R (35) | Titus V (36) | Campanacci L (37) | Biau D (38) |
|---|---|---|---|---|---|
| **Year of publication** | 2013 | 2012 | 2008 | 2015 | 2006 |
| **Number of patients** | 104 | 63 | 10 | 18 | 91 |
| **Gender male** | 70 | 34 | 6 | 8 | 53 |
| **Gender female** | 34 | 29 | 4 | 10 | 38 |
| **Mean age of patients (years)** | 20 | 29 | 48 | 11 | 27 |
| **Age of patient (range)** | 8-61 | 11-79 | 15-80 | 6-15 | 12-78 |
| **HISTOLOGY:** | | | | | |
| **Osteosarcoma** | 104 | 45 | 3 | 14 | 54 |
| **Ewing´s - sarcoma** | 0 | 0 | 0 | 4 | 2 |
| **Chondrosarcoma** | 0 | 3 | 1 | 0 | 9 |
| **Other MBT** | 0 | 3 | 0 | 0 | 13 |
| **Benige bone tumor** | 0 | 5 | 3 | 0 | 11 |
| **Other tumor** | 0 | 7 | 3 | 0 | 2 |
| **ANATOMICAL LOCALIZATION:** | | | | | |
| **Distal femur** | 65 | 45 | 0 | 0 | 56 |
| **Proximal tibia** | 39 | 14 | 10 | 18 | 35 |
| **Proximal Fibula** | 0 | 0 | 0 | 0 | 0 |
| **Total femur (proximal or diaphyse)** | 0 | 0 | 0 | 0 | 0 |
| **Other location** | 0 | 4 | 0 | 0 | 0 |
| **PNP:** | | | | | |
| **Cases of PNP** | 3 | 13 | 2 | 2 | 5 |
| **Incidence of PNP total [%]** | 2,88 | 20,63 | 20,00 | 11,11 | 5,49 |
| **Cases of transient PNP** | 3 | n.e. | 1 | 2 | 4 |
| **Incidence of PNP transient [%]** | 2,88 | | 10,00 | 11,11 | 4,40 |
| **Cases of permanent PNP** | 0 | n.e. | 1 | 0 | 1 |

| Author | Campanacci M (39) | Safran MR (40) | Muschler GF (41) | Rao BN (42) | Malawer MM (43) |
|---|---|---|---|---|---|
| **Year of publication** | 1979 | 1994 | 1995 | 1983 | 1989 |
| **Number of patients** | 26 | 151 | 37 | 32 | 7 |
| **Gender male** | 10 | 85 | 18 | 17 | 5 |
| **Gender female** | 16 | 66 | 19 | 15 | 2 |
| **Mean age of patients (years)** | 28,3 | n.e. | 25 | n.e. | 28,7 |
| **Age of patient (range)** | 10-59 | 4-88 | 13-62 | 3-21 | 13-45 |
| **HISTOLOGY:** | | | | | |
| **Osteosarcoma** | 4 | 105 | 32 | 32 | 4 |
| **Ewing´s - sarcoma** | 0 | 9 | 1 | 0 | 0 |
| **Chondrosarcoma** | 1 | 19 | 2 | 0 | 1 |
| **Other MBT** | 1 | 10 | 2 | 0 | 2 |
| **Benige bone tumor** | 19 | 5 | 0 | 0 | 0 |
| **Other tumor** | 1 | 3 | 0 | 0 | 0 |
| **ANATOMICAL LOCALIZATION:** | | | | | |
| **Distal femur** | 17 | 81 | 37 | 16 | 0 |
| **Proximal tibia** | 9 | 11 | 0 | 6 | 7 |
| **Proximal Fibula** | 0 | 0 | 0 | 2 | 0 |
| **Total femur (proximal or diaphyse)** | 0 | 27 | 0 | 1 | 0 |
| **Other location** | 0 | 32 | 0 | 7 | 0 |
| **PNP:** | | | | | |
| **Cases of PNP** | 2 | 7 | 1 | 3 | 4 |
| **Incidence of PNP total [%]** | 7,69 | 4,64 | 2,70 | 9,38 | 57,14 |
| **Cases of transient PNP** | 2 | 7 | 1 | 3 | 4 |
| **Incidence of PNP transient [%]** | 7,69 | 4,64 | 2,70 | 9,38 | 57,14 |
| **Cases of permanent PNP** | 0 | 0 | 0 | 0 | 0 |

| Author | Florez B (44) | Betz M (45) | Decilveo AP (46) | Abdel MP (47) | Erler K (48) |
|---|---|---|---|---|---|
| **Year of publication** | 2008 | 2011 | 2016 | 2012 | 2004 |
| **Number of patients** | 113 | 6 | 7 | 112 | 9 |
| **Gender male** | 67 | 4 | 2 | 54 | 9 |
| **Gender female** | 46 | 2 | 5 | 58 | 0 |
| **Mean age of patients (years)** | 18,8 | 11 | 10 | 27,6 | 23,6 |
| **Age of patient (range)** | 6-58 | 6-16 | 8-12 | 5-86 | 20-48 |
| **HISTOLOGY:** | | | | | |
| **Osteosarcoma** | 0 | 5 | 6 | 49 | 2 |
| **Ewing´s - sarcoma** | 0 | 1 | 1 | 21 | 0 |
| **Chondrosarcoma** | 0 | 0 | 0 | 26 | 0 |
| **Other MBT** | 0 | 0 | 0 | 8 | 0 |
| **Benige bone tumor** | 113 | 0 | 0 | 0 | 7 |
| **Other tumor** | 0 | 0 | 0 | 8 | 0 |
| **ANATOMICAL LOCALIZATION:** | | | | | |
| **Distal femur** | 34 | 4 | 4 | 0 | 0 |
| **Proximal tibia** | 14 | 1 | 3 | 0 | 0 |
| **Proximal Fibula** | 6 | 0 | 0 | 112 | 9 |
| **Total femur (proximal or diaphyse)** | 17 | 0 | 0 | 0 | 0 |
| **Other location** | 42 | 1 | 0 | 0 | 0 |
| **PNP:** | | | | | |
| **Cases of PNP** | 1 | 1 | 2 | 2 | 2 |
| **Incidence of PNP total [%]** | 0,88 | 16,67 | 28,57 | 1,79 | 22,22 |
| **Cases of transient PNP** | 0 | 1 | 2 | 2 | 0 |
| **Incidence of PNP transient [%]** | 0,00 | 16,67 | 28,57 | 1,79 | 0,00 |
| **Cases of permanent PNP** | 1 | 0 | 0 | 0 | 2 |

# 6 Literature

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