

Diploma Thesis

Outcome of clavicle resection due to sarcoma
A retrospective and prospective study

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Graz, 19.11.2021

Statutory declaration

I declare that I have authored this thesis independently, that I have not used other than the declared sources / resources, and that I have explicitly marked all material which has been quoted either literally or by content from the used sources.

Graz, am 19.11.2021

Christian Schrader eh.

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Glossary and Abbreviations

AC.....	<i>Acromioclavicular</i>
AJCC.....	<i>American Joint Committee on Cancer</i>
CNS.....	<i>Central nervous system</i>
CT.....	<i>Computed Tomography (scan)</i>
CTX.....	<i>Chemotherapy</i>
CXR.....	<i>Chest-X-ray</i>
DASH.....	<i>Disability of arm, shoulder and hand</i>
DNA.....	<i>Deoxyribonucleic acid</i>
EURAMOS.....	<i>European and American osteosarcoma study group</i>
EURO E.W.I.N.G.	<i>European Ewing Tumor Working Initiative of National Groups</i>
FDG-PET.....	<i>fluorodeoxyglucose positron emission tomography</i>
FNA.....	<i>Fine needle aspiration</i>
FS.....	<i>Fat suppressed</i>
G-CSF.....	<i>Granulocyte-Colony Stimulating Factor</i>
GH.....	<i>Glenohumeral</i>
Gy.....	<i>Gray</i>
IFN.....	<i>Interferon</i>
LFS.....	<i>Li-Fraumeni syndrome</i>
MA.....	<i>Methotrexate and cisplatin</i>
MAP.....	<i>Methotrexate, doxorubicin and cisplatin</i>
MCC.....	<i>Merkel-cell carcinoma</i>
MDP.....	<i>Methylene diphosphonate</i>
MDT.....	<i>Multidisciplinary team</i>
MRI.....	<i>Magnetic resonance imaging</i>
MSTS.....	<i>Musculoskeletal Tumor Society</i>
ROM.....	<i>Range of motion</i>
RTX.....	<i>Radiotherapy</i>
SC.....	<i>Sternoclavicular</i>
SE.....	<i>Spin echo</i>
ST.....	<i>Scapulothoracic</i>
STIR.....	<i>Short tau inversion recovery</i>
STS.....	<i>Soft tissue sarcoma</i>
TNM.....	<i>Tumor, Lymph node, Metastasis</i>
TSE.....	<i>Turbo spin echo</i>
VAC.....	<i>vincristine, actinomycin D, and cyclophosphamide</i>
VAI.....	<i>vincristine, actinomycin D, and ifosfamide</i>
VIDE.....	<i>vincristine, ifosfamide, doxorubicin, and etoposide</i>
WHO.....	<i>World Health Organization</i>

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Kurzfassung

Einführung: Tumoren der Klavikula sind extrem selten. Die Therapie beinhaltet eine weite Resektion der Läsion bzw. der gesamten Klavikula. Das Schultergelenk gilt als das komplexeste Gelenk des menschlichen Körpers, da alle Komponenten des Gelenks in enger Interaktion stehen. Ziel dieser Diplomarbeit ist es, den Einfluss einer Resektion von Tumoren der Klavikula und somit einer Störung der Biomechanik des Schultergelenks auf das klinische, onkologische und funktionelle Outcome der PatientInnen zu eruieren.

Materialien und Methoden: Zwischen 2000 und 2018 wurden insgesamt sieben PatientInnen (n=7) wegen eines Tumors, welcher die Klavikula betrafen an *Univ. Klinik für Orthopädie und Traumatologie der Medizinischen Universität Graz, Österreich* behandelt. In die retrospektive Analyse wurden sechs dieser PatientInnen inkludiert, da eine weite Resektion des Tumors durchgeführt wurde. (n=6) Untersucht wurden patientInnen-, tumor- und behandlungsassoziierte Faktoren, sowie das Überleben der PatientInnen. Im prospektiven Teil konnten zwei der PatientInnen erneut untersucht werden. Das funktionelle Outcome im prospektiven Teil wurde mittels klinischer Untersuchung, den gängigen Tests zur Beurteilung der Schulterfunktion und mittels der beiden Fragebögen Quick-DASH- und MSTS-Score untersucht und beschrieben.

Resultate: Einem der PatientInnen wurde wegen eines Spindelzellsarkoms der laterale Teil der Klavikula entfernt. Die anderen fünf PatientInnen erhielten eine Resektion der gesamten Klavikula, zwei PatientInnen aufgrund eines Ewing Sarkoms, zwei aufgrund eines Osteosarkoms und eine Patientin aufgrund einer Merkelzellkarzinom Metastase. Bei einer durchschnittlichen follow-up Zeit von 5.3 Jahren waren vier PatientInnen am Leben und weitestgehend beschwerdefrei mit guter Mobilität der oberen Extremität. Eine Patientin klagte über Schmerzen im Operationsgebiet und Problemen beim Heben schwerer Objekte. Die beiden Patienten des prospektiven Teils waren frei von Beschwerden mit guter Schulterfunktionalität und Quick-DASH-Scores von 2,27 bzw. 34,09 und MSTS-Scores von 100 bzw. 86.67.

Schlussfolgerung: Obwohl die Klavikula ein Bestandteil des komplexen Zusammenspiels der Gelenke und Bewegungen der oberen Extremität ist, kann

eine Resektion der Klavikula ohne anschließende Rekonstruktion mit zufriedenstellenden Ergebnissen und ohne gravierenden Funktionsverlust einhergehen.

Abstract

Introduction: Tumors of the clavicle are extremely rare. Therapy involves wide resection of the lesion or even the entire clavicle. The shoulder joint is considered to be the most complex joint in the human body, as all its components are in close interaction. The aim of this diploma thesis was to analyze the influence of a tumor resection of the clavicle and thus a disturbance of the biomechanics of the shoulder joint on the clinical, oncological and functional outcome of the patients.

Materials and Methods: Between 2000 and 2018, a total of seven patients (n=7) were treated at the *Department of Orthopaedics and Trauma* at the *Medical University of Graz, Austria*, because of a tumor affecting the clavicle. Six of these patients were included in the retrospective analysis because a wide resection of the tumor was performed. (n=6) Patient-, tumor- and treatment-associated factors, as well as patient survival were investigated. In the prospective part two of the patients could be reexamined. The functional outcome in the prospective part was assessed and described by clinical examination, the common tests for the assessment of shoulder function and by the two questionnaires Quick-DASH- and MSTS-Score.

Results: One of the patients had the lateral part of the clavicle removed because of spindle cell sarcoma. The other five patients underwent resection of the entire clavicle, two patients due to Ewing sarcoma, two due to osteosarcoma, and one due to Merkel cell carcinoma metastasis. At a mean follow-up time of 5.3 years, four patients were alive and mostly symptom-free with good upper limb mobility. One patient complained of pain in the surgical area and of problems lifting heavy objects. The two patients in the prospective part were free of complaints with good shoulder functionality, and Quick-DASH- Scores of 2.27 and 34.09, and MSTS-Scores of 100 and 86.67, respectively.

Conclusion: Although the clavicle is a component of the complex interaction of upper extremity joints and movements, resection of the clavicle can be accomplished with satisfactory results and without serious loss of function.

Introduction

Studying the anatomy of the human body, one quickly realizes that the shoulder is probably one of the most complex joints. Not only has it given us many evolutionary advantages, but also culturally the upper extremity has become an important part of human being.

Many different bones, joints and muscles are involved in the movements of the upper extremity. Perfect interaction between the individual components is what makes the upper extremity so special. Loss of function of an involved joint is usually followed by changes and deterioration of the remaining joints. (3)

In large bones such as the humerus bone, it is possible to regain much of the function after resection by means of a prosthetic replacement. In smaller bones such as the clavicle, reconstruction is not performed in most cases.

Therefore, this thesis will attempt an answer the question, which role the clavicle plays in the movement of the upper extremity and how good the functional outcome is after clavicle resection without subsequent reconstruction.

Besides a variety of diseases and injuries affecting the shoulder, tumors of the bone are fortunately a generally uncommon disease. That these tumors also affect the clavicle is extremely rare. For this reason, the approach to each case is unique. In such scenarios case reports of patients with similar disease courses can often be helpful. In large tumor centers and university hospitals, such as the *Department of Orthopaedics and Trauma at the Medical University of Graz, Austria*, data are prospectively collected. Thus, the largest possible number of patients with such rare diseases can be analyzed. Within the scope of this diploma thesis, six patients with such a disease will be described and partially examined in more detail.

Anatomy of the shoulder joint

With the human evolution towards an upright gait, the lower extremity developed into a stabilizing unit consisting of a massive femur, deep acetabular cup and strong ligaments, which enable an upright stance with minimal energy expenditure and protection against luxation. (4) This shift in tasks is also reflected in the functional adaptation of the upper extremity, which developed into a prehensile organ with a

significantly increased mobility. (5) The increase in mobility is made possible via two anatomical features. On the one hand, the actual upper arm-shoulder joint, the glenohumeral (GH) joint, is a typical ball-and-socket joint with three degrees of freedom, consisting of a small “socket” (i.e., glenoid fossa) in relation to the “ball”, i.e., the head of humerus. On the other hand, the glenoid socket itself can be moved relative to the trunk within the scapulothoracic (ST) joint with three additional degrees of freedom. (2, 4) The clavicle, with its two joints, i.e. the medial sternoclavicular (SC) joint and the lateral acromioclavicular (AC) joint, is the only real articulating connection of the upper extremity to the trunk. (4)

Due to the sparse bony stability of the shoulder girdle and especially the disproportion in size between the head of humerus and the glenoid fossa, the soft tissue support in the shoulder girdle is of particular importance. (6) Thus, in addition to the ligamentous apparatus of all joints involved, pronounced muscular support, particularly of the upper arms, is required. The muscular stability of the glenohumeral joint is provided by the so-called rotator cuff, consisting of four small muscles. (7)

The biomechanics of the shoulder is of particular interest, as it is composed of many individual joint movements. The mechanics of the SC joint specifically seems to be decisive for the movement of the scapula in relation to the thorax. (4)

Osseous structures

The human shoulder is composed of various bones and joints that allow extremely complex movements. The three main bones involved in the formation of the shoulder girdle are the clavicle, scapula and humerus. (5, 7)

Scapula

The scapula is a triangular, flat bone with a slightly concave curvature located near the ribs at the back of the thorax. In neutral position, the scapula extends from the 2nd to 7th ribs and is slightly laterally tilted. (2) Viewed from the back of the scapula, its almost horizontally running spine divides the shoulder blade into a smaller upper and a larger lower part, thus creating different origins for muscles of the rotator cuff.

Laterally, the bony crest ends in the so-called acromion and, together with the clavicle, forms the connection to the thoracic aperture as the AC joint. Directly below the acromion, the glenoid fossa forms the socket of the humeral joint. The joint surface is directed slightly anteriorly and outwardly, allowing for an almost coincident human field of vision and movement of the upper extremity. (2) In front of the joint, the coracoid process originates from the neck of the shoulder blade. It is broad-based and flattened and serves as a muscle attachment point for parts of the biceps muscle, the coracobrachialis muscle and the minor pectoral muscle. (5)

Clavicle

The clavicle is an S-shaped bone, between 12-15 cm long in adults and of high intra-individual variance in size and shape. It is the only structure directly connecting the upper limb to the trunk via the AC and SC joints laterally and medially, respectively. (2) On the medial side, the clavicle faces the sternal limb, where it connects with the sternal articular surface to the manubrium, in a ventral convex direction. On the lateral side toward the flattened acromial end, it is concavely curved ventrally and, together with the acromial articular surface, forms the junction with the acromion of the scapula. (2, 5) A distinctive characteristic of the clavicle compared to all other bones of the musculoskeletal system is its partial desmal ossification, i.e., its predominantly connective tissue ossification, whereas only the two joint-forming ends ossify via chondral ossification. (4, 7) However, the bony nucleus at the sternal end does not ossify with the remaining clavicle until the age of 21 to 24 years. (7)

Humerus

As the largest tubular bone of the upper extremity, the humerus is the counterpart to the femur of the lower extremity from an evolutionary point of view. The proximal part is formed by an almost perfect hemisphere, the humeral head. (4) Together with the glenoid fossa of the scapula, the humerus forms a ball-and-socket joint with significantly increased freedom of movement in relation to the lower extremity. In addition to the above-mentioned mobility of the scapula relative to the trunk, this increased mobility is made possible by the large humeral head compared to the relatively small joint socket. (4) The axis of the humeral head an angle of 135° to

the axis of the humeral shaft and is rotated backwards by 14° to 20° in relation to the flexion-extension axis of the epicondyles of the elbow joint. (4) This torsion angle decreases during the growth process from approximately 60° in newborns to 14° to 20° in adults, whilst an opposite change in the orientation of the scapula is observed, as the glenoid fossa turns into a sagittal rather than ventral plane during skeletal development. (2) Two different definitions of the “neck of the humerus” exist. One is the so-called anatomical neck, which runs along a narrow constriction at the lower limit of the joint surface, and the other is the clinically more significant surgical neck, which forms a predilection site for extra-articular fractures of the proximal humerus further distal than the anatomical neck, just below the two tubercles. (2, 5) The two ventrally located tubercles, the greater tubercle, which is positioned more laterally, and the lesser tubercle, which is localized further medially, form the border of the bicipital sulcus or intertubercular groove, which serves as the sliding bearing for the long biceps’ tendon. In addition, these two tubercles and their bar-shaped extensions are important insertion points for the large pectoral muscle and the muscles of the rotator cuff. (4) The distal end of the humerus is formed by the medial trochlea and the lateral capitulum and is the proximal part of the elbow joint. (4)

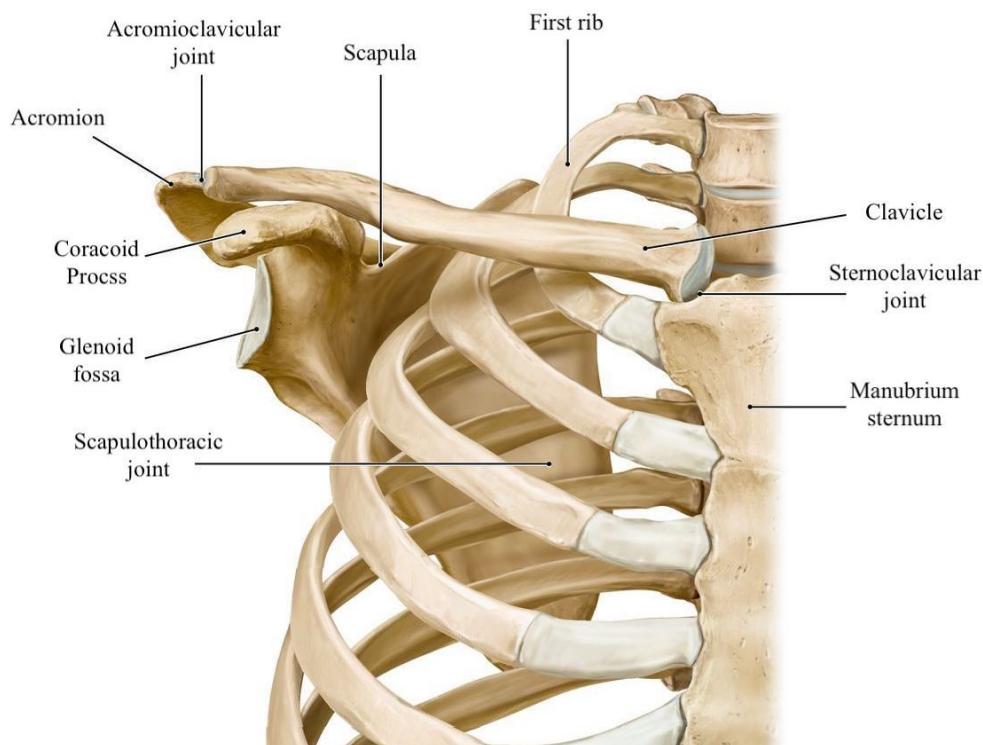


Figure 1 Bones of the right shoulder girdle in their normal position in relation to the trunk skeleton. Picture from Prometheus Lernatlas. (2)

Joints

The three real joints involved in the movements of the upper extremity are composed of the SC joint, the AC joint and the GH joint. Additionally, the ST joint plays a role in upper extremity motion. However, it is more of a physiological, rather than an anatomical joint, as no joint surfaces articulate directly with each other. (2, 4)

The non-real ST joint also plays an important role in shoulder motion and will be considered in the following subchapter “Biomechanical Considerations of Shoulder Motion”. In order to gain freedom of movement, a significant amount of stability of the shoulder joint had to be given up. Since stability is provided only to a small extent by bony skeletal components and ligamentous apparatus, muscular securing of the shoulder plays a major role. (2)

Sternoclavicular joint

The SC joint is the only articulated connection between the entire upper extremity and the trunk. It connects the medial part of the clavicle to the manubrium sternum. In addition to these two bones, it also includes a discus which compensates for the incongruities of the two saddle-shaped articular surfaces. (2) Especially anteriorly and posteriorly, the joint capsule is strengthened by the two anterior and posterior SC ligaments. The costoclavicular ligament is particularly strong and connects the first rib to the clavicle. It is significantly involved in limiting all directions of motion of this joint. The two clavicles are connected by the interclavicular ligament and inhibit the lowering of the clavicle. (5) Because of this tight joint capsule, SC joint injuries are very rare compared to other shoulder injuries. (8) The function of this tight ball-and-socket joint allows three degrees of freedom. These include elevation of the clavicle by 50° , depression by 5° , protraction and retraction by 30° respectively, and rotation by 30° . (5, 7)

Acromioclavicular joint

Like the SC joint, the AC joint is functionally a ball-and-socket joint with three degrees of freedom, which interact with the movement of the SC joint. The articular

surfaces of the two articulating bones, the acromion, and the lateral end of the clavicle, are both approximately flat. (4, 5) Therefore, a discus, a meniscoid discus, or remnants of a discus can be found intraarticularly in most cases. (9) These compensate for the incongruities of the planar articular surfaces. (8, 10) The cohesion of the clavicle and scapula is secured by a tight ligamentous apparatus. Cranially, the joint capsule is strengthened by the AC ligament, which connects the acromion of the scapula to the outer clavicle and protects against anteroposterior dislocation. (4, 8) The bipartite coracoclavicular ligament connects the coracoid process to the clavicle. The conoid ligament forms the medial part and the trapezoid ligament the lateral part of the coracoclavicular ligament. These two ligaments limit the movement of the clavicle towards the acromion of the scapula. (4) Unlike the SC joint, the AC joint is a joint relatively frequently affected by trauma, accounting for up to 9% of all shoulder injuries. Trauma mechanisms almost always affect the ligamentous apparatus, whereas extensive force is usually required to lead to additional bony injuries (8, 11)

Glenohumeral joint

The glenohumeral joint consists of the approximately spherical humeral head and the oval glenoid cavity of the scapula. They form the most mobile ball-and-socket joint in the human body. (5, 7) The articular surface of the scapula is directed laterally and ventrally in normal posture and amounts to only about 25% of the surface of the humeral head. (12) Although the joint surface is increased to about 50% compared to the humeral head by a glenoid labrum (i.e. a fibrocartilaginous joint rim attached to the edge) it provides little stability to the joint whilst providing the greatest possible mobility. (2, 13) In addition to the poor bony connection, the ligamentous apparatus of the shoulder joint is also only weakly developed. In the upper part, it is formed by the strong coracohumeral ligament, which connects the two tubercles of the humerus to the coracoid process. The insertion points of this ligament on the two tubercles form a guidance for the long biceps tendon of the humerus. The coracohumeral ligament particularly inhibits external rotation when the arm is adducted. (2, 4) The three weaker parts of the anterior joint capsule are divided into superior, medial and inferior parts. The superior GH ligament extends from the superior glenoid rim to the lesser tubercle of the humerus and tightens with

inferior translation. The middle GH ligament originates just below the superior GH ligament and extends from the superior glenoid rim to the anatomic neck of the humerus. It is particularly protective against anterior and posterior translation. (2, 12) The inferior GH ligament consists of a total of three parts, an anterior and posterior fiber traction and an axillary recess, which serves as an approximately 1 cm long reserve pocket for the extensive range of motion. (5) The inferior GH ligament plays a special role in anterior and inferior shoulder stability, especially in wide abduction of the upper arm. (2, 12) The weak ligamentous apparatus is the reason for the high risk of dislocation of the shoulder joint. (4) In 95% of cases, dislocation mechanism are anterior translation of the humeral head in relation to the glenoid fossa. (14)

Thus, well-developed, and strong shoulder muscles are particularly important for shoulder stability.

Muscles

Since the movements of the shoulder girdle are complex, muscular support is also provided by many different muscles. A meaningful classification should consider both topographical and functional aspects. First, there are the muscles of the shoulder joint itself, i.e., the scapulohumeral muscles. These muscles, especially those of the so-called rotator cuff, ensure the stability of the humeral head in its socket. Second, the muscles of the shoulder girdle, which extend from the front and back of the trunk to the shoulder, enable complex movements of the upper extremity. (2)

Scapulohumeral muscles

An important component of the shoulder joint is the so-called rotator cuff. The rotator cuff muscles include the supraspinatus muscle, infraspinatus muscle, subscapularis muscle and teres minor muscle. The supraspinatus muscle originates above the spina scapulae and attaches to the greater tubercle of the humerus. Thus, it is the starting muscle of abduction and supports the deltoid muscle in its function. (5) The infraspinatus muscle also inserts at the greater tubercle of the humerus, but

originates below the spina scapulae and is the strongest external rotator of this muscle group. (5) This external rotation is supported by the teres minor muscle, which extends from the axillary border of the scapula to the greater tubercle of the humerus. Furthermore, the teres minor muscle serves as a weak adductor of the humerus. The subscapularis muscle is the only rotator cuff muscle originating from the anterior surface of the scapula, that faces the thorax. It attaches to the lesser tubercle of the humerus and assists in adduction, but may also participate in abduction through its cranial portion. (4) Notably, with its large muscle cross-section relative to the other rotator cuff muscles, the subscapularis muscle is the strongest internal rotator in its main function. (5)

Other muscles of the shoulder joint are the deltoid muscle, the latissimus dorsi muscle, the teres major muscle and the pectoralis major muscle. The deltoid muscle performs various functions due to its three different origins. All muscle parts attach to the superolateral humeral shaft. The posterior part of the deltoid muscle originates from the spina scapulae and thus allows retroversion, external rotation, and adduction. However, when the arm is already abducted, it supports further abduction. (4, 5) The middle portion originates from the acromion and is responsible for most of the abduction movement up to 90°. (7) A particularly interesting part of the deltoid muscle is the clavicular portion. This originates from the lateral third of the clavicle and is responsible for internal rotation, anteversion and adduction. If the arm is already abducted, this part of the muscle also supports further abduction. (4, 5) The partially antagonistic functions of the deltoid muscle provide a powerful abduction to the horizontal. In addition, the weight of the entire arm is supported by the deltoid muscle. (5)

Covering almost the entire back, the latissimus dorsi muscle originates from the lower six thoracic vertebral bodies, the entire lumbar spine, the large iliac crest of the ilium, the lateral 9th-12th ribs, and the inferior angle of the scapula. Together with the teres major muscle, which also originates from the scapula, the latissimus dorsi muscle attaches to the lesser tubercle of the humerus, allowing internal rotation, adduction, and retroversion in the shoulder joint. In fixed arms, it can be used as an assisting respiratory muscle due to its rib involvement. (2, 5)

The pectoralis major muscle is the large pectoral muscle and is divided into three distinct parts according to its origins. The clavicular part originates from the antero-

medial clavicular surface, the sternocostal part from the sternum and the cartilages of the 2nd-6th ribs. The weaker abdominal part originates from the aponeurosis of the external oblique abdominal muscle. (7) All muscle fibers attach to the region of the greater tubercle of the proximal humerus. The tendon fiber bundles of the lower abdominal part attach most proximally and under-cross the fibers of the clavicular part that insert most distally at the greater tubercle of the humerus. As the elevation of the arm increases, the muscle de-torques. This allows the muscle to develop maximum force at its greatest stretch. (2) The pectoralis major muscle is primarily responsible for powerful adduction, internal rotation, and anteversion. (4)

Trunk-shoulder girdle muscles

The large number of shoulder muscles that pull from the trunk to the shoulder girdle can be divided in several ways. A categorization into ventral and dorsal muscles is simple and provides an easy overview. The four muscles on the ventral side of the shoulder girdle are the subclavius muscle, serratus anterior muscle and pectoralis minor muscle. The dorsal side is formed by the trapezius muscle, levator scapulae muscle as well as the major and minor rhomboid muscles.

The subclavius muscle is a small but powerful muscle that extends from the 1st rib to the inferior surface of the clavicle, pulling and securing the clavicle within the SC joint. (5) Like the pectoralis major muscle, the pectoralis minor muscle originates from the ribs of the anterior thorax. It extends from the 3rd to 5th ribs to the coracoid process. In addition to its role of fixing the scapula to the trunk when the arm is fixed, it is responsible for the elevation of the ribs and therefore serves as an auxiliary respiratory muscle. (5) The serratus muscle consists of different parts, i.e., a superior part, intermediate part, and inferior part. They all originate from the 1st to 9th ribs and insert at the front of the medial scapula. As a result, the entire muscle pulls the scapula laterally-ventrally and also assists in breathing by raising the ribs. (2)

The largest muscle of the dorsal side of the shoulder girdle is the trapezius muscle. With its three parts, i.e., the descending part from the occipital bone and the 2nd to 6th cervical vertebral bodies, the transverse part from the 1st to 4th thoracic vertebral bodies and the ascending part from the 5th to 12th thoracic vertebral bodies, this

muscle attaches to the lateral third of the clavicle, the acromion, and the entire scapular spine. As a result, the entire muscle pulls the scapula medially. Especially with the upper and middle parts, it is also responsible for rotation of the scapula. Thus, the glenoid cavity is directed upward-outward and allows elevation beyond 90° . (5, 7)

The three smaller muscles of the posterior shoulder girdle, i.e. levator scapulae muscle as well as the major and minor rhomboid muscles all have the function of pulling the scapula cranio-medially to return the elevated arm to its neutral-null position. (2) They originate from the 1st to 4th, 6th to 7th cervical vertebrae and the 1st to 4th thoracic vertebrae, respectively, and pull on the entire border of the medial scapula. (4)

Biomechanics of the shoulder joint

The entire movement of the upper extremity is basically the result of various individual movements of the involved joints of the shoulder girdle. Movements of the actual shoulder joint, the GH joint, are composed of three degrees of freedom. (2) With the scapula fixed, the humerus can be actively adducted to 30° and abducted to 90° before the greater tubercle collides with the acromion. After external rotation of the humerus by approximately 90° , the greater tuberosity rotates behind the acromion and abduction can continue up to 120° . (3) "Abduction" is often called "elevation" once it exceeds 90° . (2) Anteversion and retroversion (also called flexion and extension) are possible without involving the shoulder girdle by 90° and 30° , respectively. (4) Internal and external rotation (with the arm abducted by 90°) are approximately 90° and 70° , respectively. (2)

If the scapula is not fixed, it is significantly involved in the movement of the upper extremity and especially in the elevation of the arm. Since some sources describe an elevation of the arm of up to 180° but only 120° can be performed by the GH joint itself, the remaining 60° must be performed by the ST joint. (3)

The scapula slides across the back of the thorax within the ST joint and can perform five individual directions of movement, namely elevation and depression in the vertical plane (**a.**), pro- and retraction in the frontal plane (**b.**), and rotation (**c.**). (see **Figure 2**) (2)

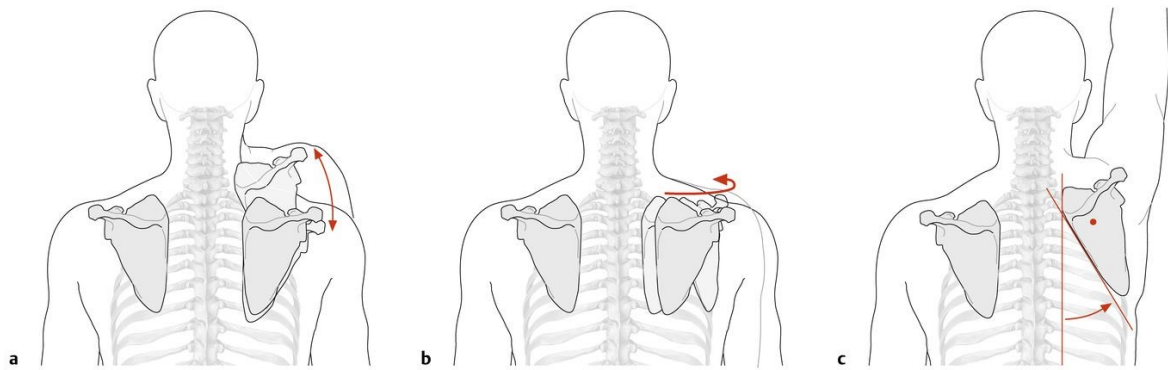


Figure 2 Movement of the scapula. Picture from Prometheus Lernatlas. (2)

These elementary movements usually occur simultaneously in different combinations during the complex movements of the upper extremity. (15)

The elevation movements of the GH joint and the ST joint also occur simultaneously. This coordinated movement between the humerus, and scapula is called the humeroscapular or scapulohumeral rhythm. This implies that there is no isolated elevation of the humerus in one joint and subsequently in the other joint, but rather a simultaneous elevation in a ratio of 2:1. (16) For example, for every 15° of abduction of the humerus, there is 10° coming from the GH joint and 5° from the ST joint, allowing smooth motion. (3) Another important function of scapular motion is to support the humerus in maximum abduction. The glenoid fossa can be moved almost to the horizontal plane by lifting and rotating outward. This minimizes shear forces between the humerus and glenoid fossa, preventing inferior dislocation of the humerus. (3)

While the GH joint is often discussed in biomechanical analyses, the precise importance of the clavicle, its interaction with the scapula, ST joint, and its influences on shoulder movement are less frequently addressed. (16, 17)

Therefore, the characteristics and functions of the clavicle will be described in more detail below to provide a basis for the question of what role can be attributed to the clavicle in shoulder movement and stability.

Characteristics and function of the clavicle

As mentioned earlier, the clavicle is the only bony structure that connects the upper extremity to the trunk via the acromioclavicular or sternoclavicular joint. Due to the close connection of the scapula and clavicle via the AC joint, the mechanics of the SC joint are critical to the movements of the scapula on the thorax. (4)

As already noted above, the scapula performs a rotation of 60° during elevation of the upper limb, which therefore also affects the two clavicular joints due to the close connection with the clavicle. Similar to the scapulohumeral rhythm, there is also a coordinated sequence of elevation between the scapula and clavicle. During the first 90° of upper limb abduction, there is an elevation of the clavicle in the SC joint of approximately 4° for every 10° of abduction. (3) Thus, slightly more than half of the 60° rotation of the scapula occurs in the SC joint. The remaining 25° - 30° take place in the AC joint. These are divided into two movement phases of approximately 15° each at the beginning and end of the abduction movement. (3) The combination of pro-/retraction and elevation/depression allows the clavicle to have a range of motion in the shape of a cone, which tapers proximally and has a slightly oval base with a diameter of about 10 to 13 cm. (see **Figure 3**) (2)

The ability of the clavicle to rotate around its own axis, creating a functional ball-and-socket joint is of particular interest. (2) Thus, despite the tight ligamentous apparatus between the coracoid process and the clavicle, a relatively high degree of motion can be achieved in the AC joint. During full abduction of the arm, the coracoclavicular ligament tenses and pulls down the lateral curve of the clavicle. As a result, the clavicle undergoes a posterior axial rotation of up to 45° . (2, 3) If rotation of the clavicle is blocked or manually prevented, active abduction of the upper extremity is limited to 110° . (18)

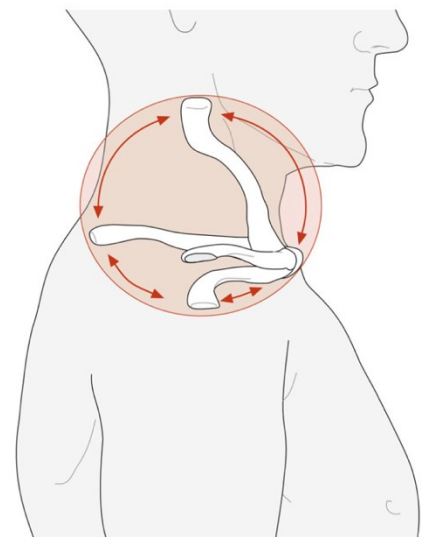


Figure 3 Movement of the clavicle.
Picture from Prometheus Lernatlas. (2)

Loss of function without the clavicle

Based on the aforementioned facts, it is evident that movements of the upper arm are a complex interaction of multiple joints. The tight ligaments that connect the clavicle to the scapula, sternum and 1st rib inhibit movements in the two joints of the clavicle. As a result, there is a reduced freedom of movement, but also a significant amount of stabilization and guidance of the movements of the scapula facilitated by the clavicle. If the muscular stabilization of the scapula is weakly developed, loss of the clavicle could lead to feelings of unsteadiness when moving the upper extremity. This could particularly affect overhead work, in which the scapula supports the humerus with the glenoid fossa during maximal abduction.

For example, one case report on the outcome after clavicle resection in a trained bodybuilder and rower attributes the good functional results to precisely this extremely strong muscular guidance. (19)

Furthermore, malfunction in any of the involved joints of the shoulder complex and thus the absence of the clavicle with the two SC and AC joints is usually reflected in impaired function of the remaining joints. As a result, the coordinated movement of the scapulohumeral rhythm is also lost, resulting in movement changes of the upper extremity. (3)

Tumors of the clavicle, tumor entities and syndromes

In the 5th Edition of the Book "*Soft Tissues and Bone Tumours*", the *World Health Organization* (WHO) distinguishes over 50 histological subtypes of tumors of the bone. (see **Table 1**) (20)

Bone sarcomas are generally rare and account for only 0.2% of all diagnosed malignancies. (20, 21) The clavicle is especially rarely affected, accounting for 1% of all bone tumors. (22)

Two large retrospective studies with a total of 319 cases of clavicle tumors and tumor like lesions have described the frequencies of the individual tumor subtypes. (22, 23) The most common malignant tumors of the clavicle were eosinophilic granuloma, plasmacytoma, bone metastases, osteosarcoma, Ewing's sarcoma, and chondrosarcoma. (22, 23) Notably, only the study by *Priemel et al.*, which analyzed

113 patients with clavicular tumors, reported on secondary bone metastases as well.
(22)

In the next section, these tumor subtypes, as well as Merkel cell carcinoma, spindlecell sarcoma and the so-called Li-Fraumeni syndrome, which are of relevance for this diploma thesis, will be described in more detail.

Chondrogenic tumors	Osteoclastic giant cell-rich tumors
Benign	Benign
Subungual exostosis	Aneurysmal bone cyst
Bizarre parosteal osteochondromatous proliferation	non-ossifying fibroma
Periosteal chondroma	Intermediate (locally aggressive, rarely metastasizing)
Enchondroma	Giant cell tumor of the bone NOS
Osteochondroma	Malignant
Osteochondroma NOS	Giant cell tumor of the bone, malignant
Chondromyxoid fibroma	Notochordal tumor
Osteochondromyxoma	Benign
Intermediate (locally aggressive)	Benign notochordal tumor
Chondromatosis NOS	Malignant
Atypical cartilaginous tumor	Chordoma NOS Chondroid chordoma
Malignant	Poorly differentiated chordoma
Chondrosarcoma Grade 1, 2, and 3	Dedifferentiated chordoma
Periosteal chondrosarcoma	Other mesenchymal tumors of bone
Clear cell chondrosarcoma	Benign
Mesenchymal chondrosarcoma	Chondromesenchymal hamartoma of chest wall
Dedifferentiated chondrosarcoma	Simple bone cyst
Osteogenic tumors	Fibrous dysplasia
Benign	Osteofibrous dysplasia
Osteoma NOS	Lipoma NOS
Osteoid osteoma NOS	Hibernoma
Intermediate (locally aggressive)	Intermediate (locally aggressive)
Osteoblastoma NOS	Osteofibrous dysplasia-like adamantinoma
Malignant	Mesenchymoma NOS
Low-grade central osteosarcoma	Malignant
Osteosarcoma NOS Conventional, Telangiectatic, and small cell	Adamantinoma of long bones Dedifferentiated adamantinoma
Parosteal osteosarcoma	Leiomyosarcoma NOS
Periosteal osteosarcoma	Pleomorphic sarcoma, undifferentiated Bone metastases
High-grade surface osteosarcoma	Haematopoietic neoplasms of bone
Secondary Osteosarcoma	Plasmacytoma of bone
Fibrogenic tumors	Malignant lymphoma, non-Hodgkin NOS
Intermediate (locally aggressive)	Hodgkin disease NOS
Desmoplastic fibroma	Diffuse large B-cell lymphoma NOS
Malignant	Follicular lymphoma NOS
Fibrosarcoma NOS	Marginal zone B-cell lymphoma NOS
Vascular tumors of bone	T-cell lymphoma NOS
Benign	Anaplastic large cell lymphoma NOS
Haemangioma NOS	Malignant lymphoma, lymphoblastic NOS
Intermediate (locally aggressive)	Burkitt lymphoma NOS

Epithelioid haemangioma	Langerhans cell histiocytosis NOS
Malignant	Langerhans cell histiocytosis, disseminated
Epithelioid haemangioendothelioma NOS	Erdheim-Chester disease
Angiosarcoma	Rosai-Dorman disease

Table 1 Histological classification of the bone tumors as defined by the World Health Organisation (WHO) in 2020. (20)

Eosinophilic granuloma

Eosinophilic granuloma belongs to the group of Langerhans-cell histiocytosis, characterized by clonal proliferation of Langerhans cells. (24) Within this group it accounts for about 60-80% of all cases and most likely manifests in children or adolescents. (25) The skull, spine, ribs, and long bones, especially the femur, humerus, and clavicle, are commonly affected. (25, 26)

Clinically, the tumor presents variably, most commonly with pain, tenderness, and decreased range of motion depending on location. (25) Biopsy, whether Fine-needle aspiration (FNA), core needle biopsy, image-guided biopsy or open biopsy, reveals cytologic and histologic abundance of Langerhans-cell histiocytes, eosinophilic granulocytes, and in some cases also other inflammatory cells. (27)

Therapy for eosinophilic granuloma ranges from observation, radiofrequency ablation and chemotherapy (CTX), to local excision therapy. Generally, this tumor has a good prognosis with a recurrence rate of less than 20%. (25)

Plasmacytoma

Plasmacytoma is often used as a synonym for multiple myeloma, which is characterized by diffuse monoclonal proliferation of malignant plasma cells in the bone marrow. However, strictly speaking, plasmacytoma is the solitary, extramedullary form of plasma cell proliferation without a systemic component. (28)

Multiple myeloma is rare and accounts for approximately 1% to 2% of all malignancies, with 90% of cases affecting individuals over the age of 50 years. (29, 30)

Clinical manifestation depends on the location of the multiple myeloma or plasmacytoma. Bone pain occurs in almost 60% of cases, with pathologic fractures,

compression fractures, or osteoporotic lesions observed in 20% to 25% of patients. (30)

Therapy is highly dependent on the patient's general condition and clinical manifestation of the disease. Prognosis is generally rather poor, with stem cell transplantation being the only curative treatment approach. Yet, in recent years, new immunotherapies and chemotherapeutic agents increased the 10-year survival rate to about 50%. (31)

Osteosarcoma

Osteosarcoma, which originates from polymorphic mesenchymal cells and predominantly affects the long bones, is the most common primary malignant bone tumor. (32, 33) Although the tumor is most common in young adults, there is a second peak above the age of 65 years. (see **Figure 4**) (34) The two cases in this diploma thesis affected by osteosarcoma were 13 and 14 years old at the time of diagnosis.

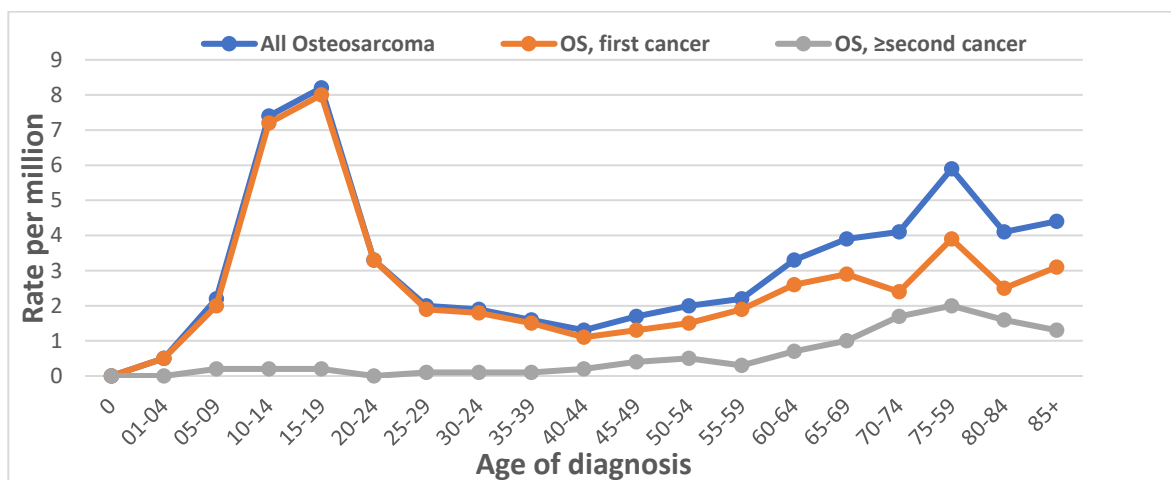


Figure 4 Osteosarcoma incidence based on L. Mirabello et al. (34)

Clinically, patients with osteosarcoma often describe localized pain over several months. A landmark finding on physical examination may be a painful soft tissue mass, although it might not be palpable in bones covered by sufficient soft tissue layers (e.g., the proximal femur). The distal femur, proximal tibia, and proximal humerus are most commonly affected, although theoretically any bone, including the clavicle, may be involved. (35)

After diagnosis by imaging and biopsy, wide resection of the tumor with concomitant neoadjuvant and adjuvant CTX is the mainstay of treatment. (36) The introduction of standardized, high-dose chemotherapeutic protocols has increased the average 5-year survival probability to 60%, with a better prognosis at younger ages. (37)

Chondrosarcoma

Chondrosarcoma is the second most common primary bone sarcoma after osteosarcoma. In contrast to osteosarcoma, it does not arise from bone-forming cells but from cartilage-forming cells. (38) The group of chondrosarcomas can be classified according to histologic appearance into different subtypes such as conventional, dedifferentiated, mesenchymal, clear cell, or myxoid, with the conventional type accounting for approximately 75% of chondrosarcomas. (39) In addition, chondrosarcoma is histologically classified into three grades of differentiation (i.e., grade I, II, and III), depending on mitotic activity, cellularity, and size of the nucleus. (40)

The most commonly affected bones are the proximal femur, pelvis, tibia, humerus, and scapula. (39) Depending on the affected location, chondrosarcoma may cause pain and swelling, which often increases over months (or even years in slow-growing sarcomas). (41)

Due to its often slow growth, the tumor is rather insensitive to conventional radiotherapy (RTX) and CTX, wherefore in most cases, radical surgical therapy is the only curative approach. (42)

The most important factor in terms of prognosis is grading. Former “grade I” chondrosarcomas of the extremities, nowadays referred to as “atypical chondromatous tumors” rarely if ever metastasize, which is why the 5-year, and 10-year survival rates are 90-99% and 83-95%, respectively. (39, 40) In grade III chondrosarcomas, on the other hand, metastases occur in 71% of cases and the 5-year and 10-year survival rates are just 43% and 29%, respectively. (40)

Ewing's sarcoma

First described by James Ewing in 1921, this tumor of the long bones consists of many small undifferentiated cells which, in contrast to osteosarcoma, are radiosensitive. (43) Since then referred to as "Ewing's sarcoma" the tumor most commonly affects children and adolescents before the age of 24 (approximately 76%) and is the third most common primary bone sarcoma after osteosarcoma and chondrosarcoma. (38) Another 22% of patients affected are between the ages of 25 and 59 years of age. Gender distribution is shifted towards males at 60%. (44)

Ewing's sarcoma affects the axial skeleton in more than half of cases, such as the pelvis, ribs, or even the clavicle in 1.2%. In the other cases, long bones such as the femur, tibia, or fibula are often affected. (see **Figure 5**) (1)

Clinically, 70% of all patients present with regional pain that increases over weeks and months, 11% with a palpable mass firmly attached to the bone, and 15% with a combination of both. (45)

As in osteosarcoma, therapy includes wide resection of the tumor with concomitant neoadjuvant and adjuvant CTX. However, postoperative follow-up RTX may also be performed due to good radiosensitivity. (46) The main prognostic factor is the absence of metastases. In the case of a localized tumor only, the long-term survival rate has now been increased up to 75% by multimodal CTX. (47)

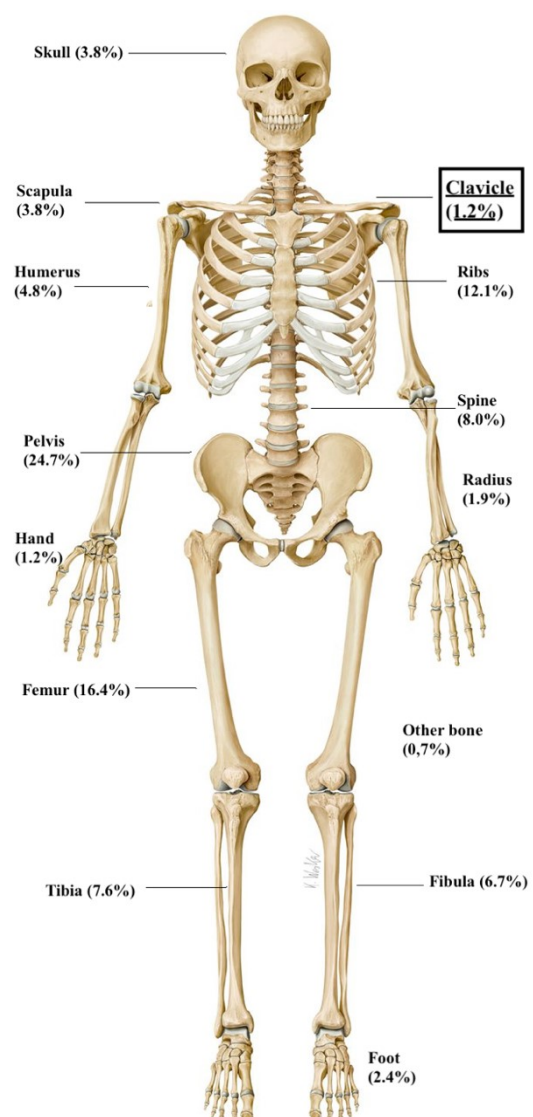


Figure 5 Site of primary Ewing's sarcoma of bone based on Cotterill et al. (1) Picture from Prometheus Lernatlas. (2)

Bone Metastases

Metastases are defined as the systemic spread of malignant cells from a primary tumor. They are therefore so-called secondary tumors. (48) Bones are one of the most common sites affected by distant metastases. These occur in nearly 70% of solid tumors, such as breast or prostate cancer. (49) While primary bone tumors account for less than 1% of all malignancies, clinically relevant skeletal metastases account for approximately 16% of all malignant tumors. (50) In the study involving 113 cases of clavicular tumors and tumor-like lesions already mentioned above, 15% of lesions were metastases. (22)

The changes within the bone caused by metastases can be divided into osteolytic and osteoblastic processes, although a precise separation is not always possible and mixed forms do also occur. (51) Also, the exact cause why some tumors, such as breast or lung cancer, tend to cause osteolytic metastases and other tumors, such as prostate cancer, tend to cause osteoblastic metastases, is not fully understood up to now and is the subject of current research. (51, 52)

If symptomatic, secondary bone tumors, similar to primary bone tumors, most commonly present with pain. Bone metastases are the most common cause of cancer-related pain. However, osteolysis-related hypercalcemia or pathologic fractures may also be caused by bone metastases. (53)

Often, the presence of bone metastases is a chronic condition and a generalized state of the underlying tumor disease. Therefore, the prognosis is therefore rather poor and largely depends on the prognosis of the underlying tumor disease. Therapeutic interventions are primarily palliative and aimed at functional preservation or pain therapy, although in selected cases, singular bone metastases or oligometastases in bones may be treated with curative intent. (54)

Merkel-cell carcinoma

Since one of the patients in this diploma thesis had a Merkel-cell carcinoma (MCC) metastasis to the clavicle, this tumor is briefly described as well.

MCC is a neuroendocrine tumor of the skin, which is rather rare compared to other cutaneous tumors. It mostly affects patients over 65 years of age and particularly

affects sun-exposed skin areas. (55) MCC has a high risk of recurrence and metastasis occurring in 40% to 45% and up to 75%, respectively. In 10-15% of cases, metastases are located within bones. (56) Due to the high risk of recurrence, excision with a wide resection margin and adjuvant regional RTX is usually necessary. The 5-year survival rate is approximately 65%. (57)

Spindle-cell sarcoma

Soft tissue sarcomas (STS) are a rare heterogeneous group of tumors of mesenchymal origin and account for less than 1% of all human malignancies. The WHO distinguishes well over 50 different histological subtypes of STS. (58)

Some examples are liposarcoma (fat tissue cells), leiomyosarcoma (smooth muscle cells), rhabdomyosarcoma (skeletal muscle cells), or myofibroblastic sarcoma (muscle and connective tissue cells). (58, 59)

The so-called spindle cell sarcomas form a heterogeneous group of various such tumors and are characterized by the cytological and histological appearance of fusiform cells. (60) These may also involve the bones and require management similar to osteosarcoma. The 5-year survival rate in patients with high-grade spindle cell sarcoma in the extremities is approximately 60%. (60)

Li-Fraumeni-Syndrome

As one patient of this diploma thesis had the so-called Li-Fraumeni syndrome (LFS), this hereditary tumor predisposition syndrome is briefly described as well. LFS is associated with a germline mutation and inactivation of the p53 tumor suppressor gene. (61) Malfunction of the p53 protein, results in defective DNA repair mechanisms, which predispose to various tumor diseases, such as CNS tumors, leukemias, melanomas or bone and soft tissue sarcomas, from childhood to adulthood. (62, 63)

The lifetime risk of developing any malignant tumor is nearly 100%, with a cumulative probability of 57% to develop a second tumor within 30 years of diagnosis of the first tumor. (64, 65)

Imaging

Today, imaging procedures, together with physical examination, are part of the diagnostic standards in everyday clinical practice. They are especially important in the context of tumor diagnosis, staging, and follow-up. By combining information deriving from the patient's history taking, clinical findings and X-ray examination, a bone tumor may already be correctly diagnosed as such in >80% of the cases. (66)

The classic imaging methods include ultrasound, X-ray, computed tomography (CT) and magnetic resonance image (MRI) scans. While ultrasound plays a rather minor role in bone tumor diagnostics, it may be used as the first diagnostic tool in soft tissue lesions, allowing analysis of size, perfusion, and location in relation to the fascia. X-ray is usually the first step in evaluating a of suspected bone tumors. Based on X-rays, initial parameters such as localization, size, shape, radiographic margins, periosteal reaction or pathological fractures can be assessed in bony lesions. (66) Notably, X-rays may also be of value in suspected soft tissue tumors, enabling identification of soft tissue calcifications, presence of phlebolitis and involvement of adjacent bones (e.g., periosteal reactions, osteolysis).

Nevertheless, a much more accurate assessment of the lesion and surrounding tissue can be achieved with CT or MRI scans. Particularly when it comes to matrix mineralization, involvement of the cortex, periosteal reactions and pathological fractures, CT is superior MRI. (66) CT is also useful for evaluating the thorax for pulmonary metastases, which is the most important anatomical staging region, considering that the lung is the most common site for metastasis for all sarcomas, with pulmonary lesions accounting for approximately 80% of all metastases. (67, 68)

MRI, on the other hand, facilitates the assessment of different aspects of the tumor and tissue by allowing different MRI sequences. For example, the T1-weighted sequence is the best method for detecting bone marrow involvement of the tumor, whereas bone marrow edema is better seen in the T2-weighted or Short Tau Inversion Recovery (STIR) sequence. (66)

MRI is the optimal imaging technique for surgical planning due to its high accuracy in determining soft tissue, joint, and vascular involvement and in distinguishing healthy tissue from tumor tissue. (69)

In addition to classical imaging, nuclear medicine procedures such as bone scintigraphy can be used. In bone scintigraphy, the patient is administered radioactive tracers, for example methylene diphosphonate (MDP) labeled with technetium-99m (99mTc). These tracers accumulate in particularly metabolically active areas of the skeleton, making them visible on gamma cameras. (66, 70) Whole-body 18-fluorodeoxyglucose positron emission tomography (FDG-PET) works on a similar principle, visualizing tissues with particularly high glucose metabolism and may help distinguish benign from malignant lesions. (71)

Biopsy

Following imaging, biopsy is usually the final and most important step in diagnosing and grading the tumor. The goal is to obtain sufficient and representative tissue for histopathological examination. Specimens are often obtained by open biopsy, which allows for sufficient tissue to be obtained for histopathological examination and additional analyses such as cytology, special immunohistochemical staining, molecular diagnostics, and microbiological examination, if needed (e.g., to identify bacteria in cases of suspected osteomyelitis). In open biopsy, a distinction is made between incisional and excisional biopsy, in which either an easily accessible part of the tumor or the entire tumor is resected, respectively. (72)

A closed biopsy by punch biopsy, core needle biopsy or as FNA is beneficial in terms of low patient morbidity and may be particularly useful in unfavorable anatomical localizations such as the retroperitoneum, vertebral body, or sacrum. As an image-guided biopsy, minimally invasive core needle biopsy or FNA is performed under radiological guidance. However, there is always the risk of obtaining a non-representative tumor tissue. As a result, the accuracy of CT-guided biopsies or FNA is 75% and 63%, respectively, according to a study of 359 patients with musculoskeletal lesions. (73)

Whenever possible, the biopsy tract should be located in the planned surgical area, as this allows the biopsy scar and drainage site to be excised during definite surgery. Therefore, areas potentially contaminated with tumor cells can be removed. Consequently, biopsies should always be planned and thoroughly discussed with the tumor-orthopaedic surgeon in charge. Notably, for bone biopsies it is important

to ensure adequate stability of the remaining bone after the biopsy has been performed because a pathological fracture of the weakened bone would result in tumor cells seeding within the fracture haematoma and thus necessitate significantly larger surgical procedures to obtain clear margins. (72)

Grading and Staging

Prior to planning of the definite treatment options and evaluating patients' prognosis, it is necessary to determine both the dignity or the degree of malignancy (grading) and its type and the extent of spread (staging). (74)

Grading

During histological examination of specimens, the tumor tissue and its cells are compared with the tissue that would be produced by native cells in order to determine the degree of differentiation. If the tumor tissue is very similar to the original tissue, it is referred to as high differentiation. If, on the other hand, there is hardly any similarity, the tissue is said to have a low degree of differentiation or to be de-differentiated. In many cases, however, the primary cell cannot be classified based on histopathological examination alone, wherefore immunohistochemical markers and – more recently – molecular diagnostics are required. For example, Ewing's sarcoma can only be differentiated from other blue, small round-cell neoplasms by identifying one of its specific genomic translocations leading to expression of a characteristic fusion protein as EWS-FLI. (75) In general, the lower the degree of differentiation, the more malignant and high grade is the tumor and the worse the prognosis. (74) Regarding primary bone tumors, a high cell count and irregularities of the nuclear contours, abnormal mitotic figures, and tumor necrosis are indicative of low-differentiated tissue. (76) Grading varies for different tumor entities and may not be applied equally well depending on tumor types. For instance, grading plays a major role in osteosarcomas, whereas it is less reliable in Ewing's sarcoma. As another example, mesenchymal chondrosarcomas are always classified as high grade. Consequently, the significance of histological grading in bone sarcomas is subject to great variability. (20)

Staging

The staging system used by the *Musculoskeletal Tumor Society* (MSTS) was developed by Enneking and co-authors. (77) It classifies malignant bone tumors into stages I-III based on three factors: grade of differentiation (G), considering histological, radiological, and clinical aspects, the site of tumor extension (T) and metastases (M). Stage I and II refer to low- and high-grade tumors without metastases, respectively, and Stage III to metastatic tumors. A further subdivision into A and B specifies anatomical spread intra- or extracompartmentally in the respective stages. (77) (see **Table 2**)

Stage	Tumor
Stage I	Low grade without metastases
IA	Intracompartmental
IB	Extracompartmental
Stage II	High grade without metastases
IIA	Intracompartmental
IIB	Extracompartmental
Stage III	High/low grade with metastases

Table 2 MSTS Staging System based on Enneking et al. (77)

Another staging system has been developed by the *American Joint Committee on Cancer* (AJCC) and is based on the TNM system. The criteria for primary bone tumors of the appendicular skeleton, trunk, skull, and facial bones are tumor extension (T), lymph node metastases (N), distant metastases (M), or histologic grade of differentiation (G). (78) (see **Table 3**)

Primary Tumor (T) - Appendicular skeleton, trunk, skull, and facial bones	
T category	T criteria
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
T1	Tumor ≤ 8cm in greatest dimension

T2	Tumor > 8cm in greatest dimension
T3	Discontinuous tumors in the primary bone site
Regional lymph nodus (N)	
N category	N criteria
NX	Regional lymph node cannot be assessed.
N0	No regional lymph node metastasis
N1	Regional lymph node metastasis
Distant metastasis (M)	
M category	M criteria
M0	No distant metastasis
M1	Distant metastasis
M1a	Lung
M1b	Bone or other distant sites
Histologic grade of differentiation (G)	
G category	G criteria
GX	Grade cannot be assessed
G1	Well differentiated, low grade
G2	Moderately differentiated, high grade
G3	Poorly differentiated, high grade

Table 3 TNM-System used by AJCC to describe bone tumors. (78)

Based on this information, four prognostic stage groups (I-IV) including subgroups A and B (for I, II, and IV) can be distinguished. (78) (see **Table 4**)

Prognostic stage groups				
Appendicular skeleton, trunk, skull, and facial bones				
Stage	T	N	M	G
IA	1	0	0	1 or X
IB	2	0	0	1 or X

	3	0	0	1 or X
IIA	1	0	0	2 or 3
IIB	2	0	0	2 or 3
III	3	0	0	2 or 3
IVA	Any	0	1a	Any
IVB	Any	1	Any	Any
	Any	Any	1b	Any

Table 4 Prognostic stage groups based on AJCC. (78)

Salzer-Kuntschik classification

Rather than being a classification system to determine the tumor's initial dignity, the Salzer-Kuntschik regression grade allows for analysis of a tumor's response to neoadjuvant CTX. (79) Specifically, osteosarcomas and Ewing's sarcomas can be classified into six grades depending on the amount of remaining vital tumor cells. (79) (see **Table 5**)

In case only single or <10% vital tumor cells remain after chemotherapy (grade I-III), these tumors are referred to as responders. If more than 10% or 50% vital tumor cells remain, or if there is no effect of chemotherapy at all (grade IV-VI), these tumors are referred to as non-responders. (80)

Salzer-Kuntschik grade	Vital tumor cells
I	No viable appearing tumor cells
II	Single vital tumor cells or one vital cell cluster < 0,5cm
III	Vital tumor < 10%
IV	Vital tumor 10-50%
V	Vital tumor > 50%
VI	No effect of chemotherapy

Table 5 Grade of regression after CTX based on Salzer-Kuntschik classification. (79)

Therapy of bone tumors

The treatment of bone tumors is challenging due to their rarity. Patients should therefore present to a tumor center with a multidisciplinary team (MDT) when a bone tumor is suspected. At the center, various disciplines such as pediatric, medical and radiation oncologists, orthopedic and surgical oncologists, musculoskeletal pathologists and radiologists are then involved in diagnosis and treatment planning. (81) This center-specific approach ensures a high level of experience due to a large caseload, as well as continuous collection and analysis of data on patients, tumors, treatment and outcome. (81) Usually, this is done in the context of clinical studies and established treatment protocols. (82) Through this tumor-center as well as international and consensus-based approaches, primary bone sarcomas have become a potentially curable disease and prognosis has improved significantly due to improved multimodal treatment strategies using surgery, CTX and RTX. (83) The therapy of individual bone tumor entities varies, as they often differ with regards to chemo- and radiosensitivity. In the following sections, the basic principles of therapy for bone sarcomas will be discussed and the therapeutic approach for some of the most common primary bone tumors will be outlined as examples.

Surgery

The type of surgical resection can be classified, based on the extent of the tumor resected, as intralesional, marginal, wide resection, or radical resection with or without limb preservation. Nowadays, limb sparing procedures are the first choice whenever possible. (84) However, a sufficiently wide resection of the tumor upon limb salvage surgery is not possible in every case. In these cases, primary amputation should be performed, as any residual tumor tissue in bone sarcomas increases risk for local relapse, distant spread, and thus reduces overall prognosis. Moreover, amputation may be chosen in case wide resection can only be achieved by sacrificing important anatomical structures such as major nerves or vessels that would leave the affected limb nonfunctional. Overall, the best possible compromise should be sought sufficiently wide resection of the tumor, the best possible functional outcome, and the lowest risk for local or systemic relapse.

During definite surgery, the intraoperative margin status may be analyzed to ensure sufficiently wide resection. This can be done by frozen section diagnostics, in which a pathologist examines the removed tissue while the operation is still in progress. Even more important is the definite surgical margin that is thoroughly analyzed by pathologists on the resected tumor specimen. Depending on the amount of healthy tissue between tumor and surface, resection margins are defined as R0, R1 and R2, based on the R-classification. (85) (see **Table 6**) Another commonly used classification system for margin status is the UICC-classification, which defines R2, R1 and R0 margins as intralesional margins, margins with < 1 mm of healthy tissue between tumor and surface, and margins with > 1 mm of healthy tissue between surface and tumor. (86)

First and foremost, an R0 resection with simultaneous preservation of the functionality of the affected body region or extremity should be aimed for. If R0 resection is not possible, neoadjuvant therapy, e.g., RTX or CTX, should be considered. This may result in local tumor regression, allowing limb-sparing surgery. (85) Notably, in the case of metastatic osteosarcoma, a curative treatment approach by surgery is also possible by removing all known metastases together with the primary tumor following the same principles. (87)

R-classification	Micro-/Macroscopic resection margin
R0	The surgical margins are macroscopically and microscopically negative for tumor cells
R1	A surgical margin is microscopically contaminated with tumor cells or the tumor was marginally resected along its pseudocapsule
R2	An intralesional tumor resection was performed

Table 6 R-classification for tumor resection margins based on P.U. Tunn et al. (85)

Chemotherapy

The applications of CTX include neoadjuvant, adjuvant, and palliative CTX. Neoadjuvant CTX is performed prior to a planned surgery in order to both reduce systemic tumor burden due to present (micro-)metastases and to achieve a reduction in tumor size to increase the success of planned surgery. Adjuvant CTX

likewise targets (micro-)metastases and thus improves patients' prognosis. The term "palliative" CTX is used when a curable therapeutic approach is no longer possible, but CTX is still applied to reduce local or systemic tumor burden.

During the 1970s, the positive impact on survival of the introduction of systemic CTX on survival was demonstrated, particularly in patients with osteosarcoma. The 5-year survival rate of 20% with surgical therapy alone increased up to 60% after administration of postoperative CTX. (88) In Ewing's sarcomas, 5-year survival improved from <10% in patients without metastases undergoing surgery alone to up to 70% in patients undergoing surgery and CTX, and to up to 40% in patients with metastases treated by surgery and CTX. (89)

However, not every bone tumor is CTX-sensitive. In contrast to the good effectiveness in osteosarcomas and Ewing's sarcomas, most chondrosarcoma subtypes do not respond to conventional CTX. Therefore, the therapeutic decision has to be made individually, depending on the histological subtype. (89) (see **Figure 6**)

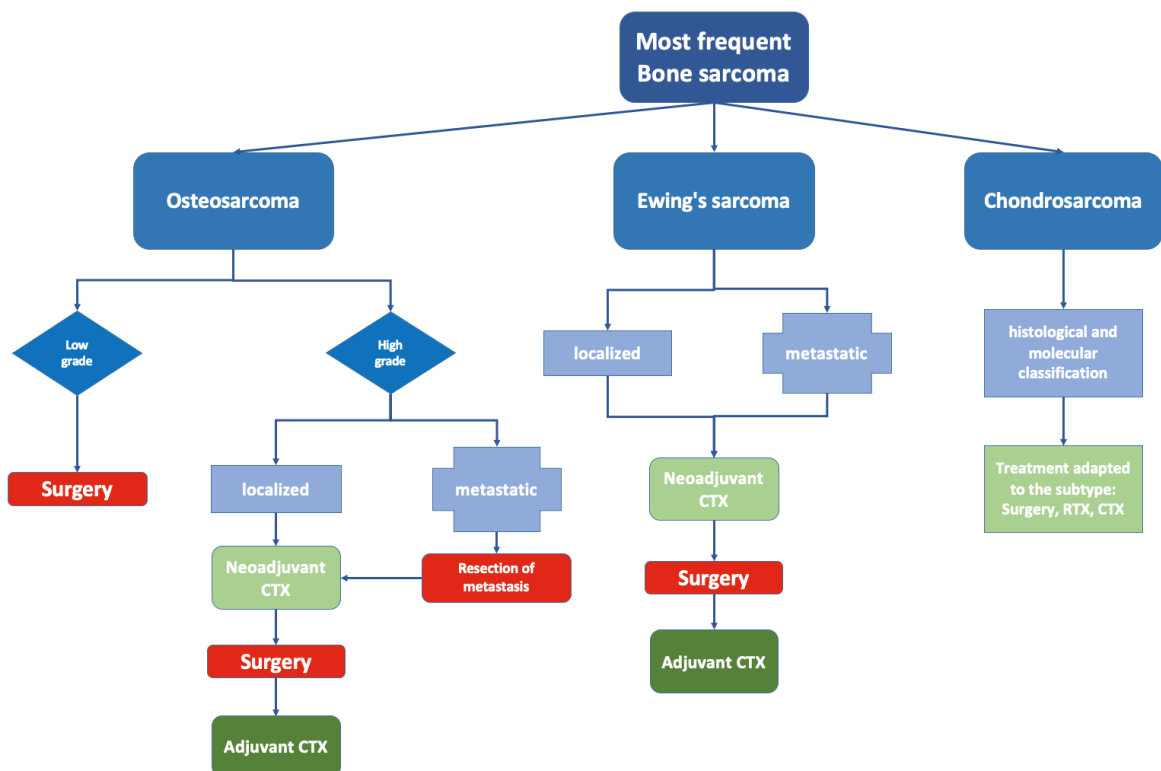


Figure 6 General therapeutic approach for the three most frequent primary bone sarcomas based on the ESMO Guidelines. (82)

Chemotherapy is usually given according to internationally established protocols such as the EURO E.W.I.N.G. 99 (European Ewing Tumor Working Initiative of National Groups) protocol in patients with Ewing's sarcoma or the EURAMOS-1 (European and American osteosarcoma study group) protocol in patients with osteosarcoma. (89)

For example, after Ewing's sarcoma is diagnosed, induction chemotherapy consists of six VIDE (vincristine, ifosfamide, doxorubicin, and etoposide) cycles at 21-day intervals before resection of the tumor may be performed. (90) (see **Table 7**)

Depending on parameters like tumor response to chemotherapy, the size of the tumor, or the presence of metastases, further therapy will vary. For example, in a well-localized, well-resectable tumor with a good response to CTX, treatment may constitute a combination of an additional 8 cycles of CTX consisting of one VAI cycle (vincristine, actinomycin D, and ifosfamide) and seven additional VAC cycles (vincristine, actinomycin D, and cyclophosphamide). (90, 91) (see **Table 8, Table 9**)

VIDE Scheme			
Drug	Dose	Days of the cycle	Dose per cycle
Vincristine	1.5 mg/m ² /d	Day 1	1.5 mg/m ²
Ifosfamide	3,0 g/m ² /d	Day 1,2, and 3	9 g/m ²
Doxorubicin	20 mg/m ² /d	Day 1,2, and 3	60 mg/m ²
Etoposide	150 mg/m ² /d	Day 1,2, and 3	450 mg/m ²

Table 7 VIDE Scheme: One cycle of a 21-day interval. (91)

VAI Scheme			
Drug	Dose	Days of the cycle	Dose per cycle
Vincristine	1.5 mg/m ² /d	Day 1	1.5 mg/m ²
Actinomycin D	0,75 mg/m ² /d	Day 1 and 2	1.5 mg/m ²
Ifosfamide	3,0 g/m ² /d	Day 1 and 2	6 g/m ²

Table 8 VAI Scheme: One cycle of a 21-day interval. (91)

VAC Scheme			
Drug	Dose	Days of the cycle	Dose per cycle
Vincristine	1.5 mg/m ² /d	Day 1	1.5 mg/m ²
Actinomycin D	0,75 mg/m ² /d	Day 1 and 2	1.5 mg/m ²
Cyclophosphamide	1500 mg/m ² /d	Day 1	1500 mg/m ²

Table 9 VAC Scheme: One cycle of a 21-day interval. (91)

On the other hand, patients with osteosarcoma are usually initially treated with methotrexate 12g/m²/cycle (M), doxorubicin 75 mg/m²/cycle (A) and cisplatin 120 mg/m²/cycle (P). Two preoperative cycles of five weeks which are followed by surgical resection. If the tumor responds well to CTX, two additional cycles of MAP and two cycles of MA will follow. This may be extended in some cases by additional therapy with interferon (IFN) α-2b 0.5–1.0 µg/kg/week for another 75 weeks, depending on the randomization group. In case the tumor's response to CTX is poor, postoperative therapy can be extended to a total of 9 cycles and adjusted using ifosfamide with a total 23 g/m² (I) and etoposide 500 mg/m² (E). (92) (see **Figure 7**)

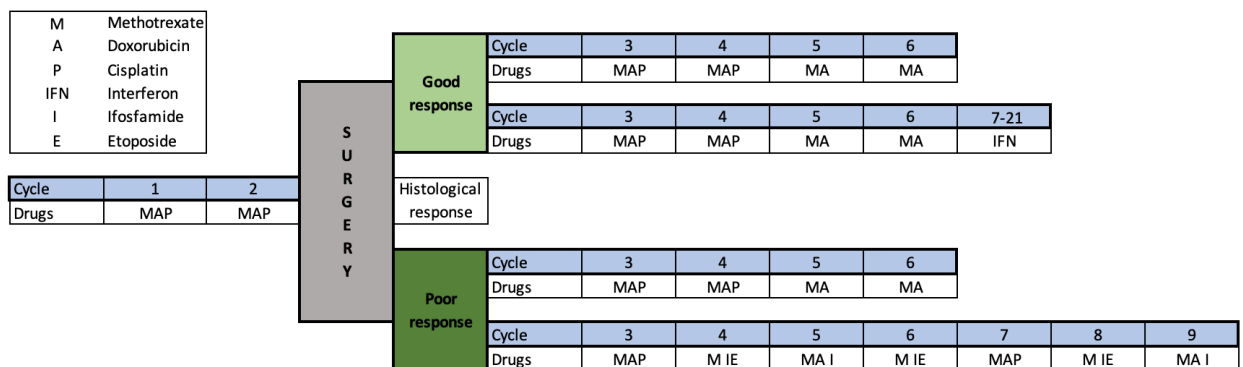


Figure 7 Treatment schedule for Osteosarcoma based on EURAMOS-1. (92)

Radiotherapy

The principle of radiotherapy is to use ionizing radiation in order to eliminate tumor cells. The high-energy radiation damages the DNA in both tumor and healthy cells, stops further proliferation and induces apoptosis. As healthy cells usually proliferate

at a significantly lower rate than tumor cells, the number of cell cycles upon which healthy cells can be disrupted is lower. (93) Consequently, mainly tumor tissue is damaged by RTX. Nevertheless, effects of RTX on surrounding healthy tissue result in short- and long-term radiation-associated side effects. Side effects can be distinguished into short-term side effects such as redness or skin irritation and mostly irreversible long-term side effects such as edema, fibrosis, fractures, or growth disturbances in children. In addition, there is a risk of radiotherapy-induced second malignancies, which may occur especially with relatively high radiation doses above 60 Gy. In addition to the total dose, other factors such as the fraction dose, localization of radiation or the duration of therapy are also indicators for the occurrence of side effects. (94)

Similar to CTX, RTX can be performed in a wide variety of settings. In addition to CTX, RTX can be used to destroy residual tumor cells after surgery to reduce local recurrences. Preoperative RTX may improve surgical therapy by reducing tumor size. In the palliative setting, radiation is used either to prevent further tumor growth and associated complications or to relieve tumor-related pain. However, RTX is also justified as a curative treatment approach on its own, especially in the case of very radiation-sensitive tumors such as lymphomas. (95)

The most common primary bone tumors, i.e., osteosarcoma and chondrosarcoma, tend to be radiation-resistant tumors. In contrast, the good radiation sensitivity of Ewing's sarcoma has already been reported by its first describer, James Ewing. (43) Moreover, multiple myeloma is also treatable by curative radiation. (96)

The total dose of RTX is usually divided into many individual fractions administered over several weeks with fractionated radiation doses of 1.5 to three Gray (Gy). (93)

Aim of the study

Summarizing the previous descriptions, it can be said that there is only a small and heterogeneous number of patients suffering from a tumor of the clavicle.

Both the nature of the tumors with their respective therapies and potential individual differences in the complex, predominantly muscle-guided shoulder joint provide great variability among these patients.

The aim of this study was to describe the clinical, oncological outcome of a comparably large group of six patients after clavicle resection due to tumors in a retrospective case series. Furthermore, the prospective part of the study is intended to contribute to the discussion of whether functionally satisfactory results can be achieved after clavicle resection, or whether the role of clavicle function is so crucial that a reconstruction should be considered. (19, 97)

Material and methods

Retrospective study

Between 2000 and 2018, seven patients with a malignant tumor affecting the clavicle were treated at the *Department of Orthopaedics and Trauma at the Medical University of Graz, Austria*. These seven patients were primarily included in the retrospective analysis. Furthermore, four of these patients who were still alive at initiation of this diploma thesis were potentially eligible for the prospective part of the study taking place between 2019 and 2020. Gender, age at first clinical presentation, and time until the latest representative follow-up or death were documented as epidemiological parameters. In addition, the time to complete tumor removal, histological findings, Salzer Kuntschik grade in case of osteosarcoma and Ewing's sarcoma, extent of tumor resection and intraoperative complications were also assessed. Information on the pre- and postoperative treatment, as well as on neoadjuvant and adjuvant RTX with respective absorbed dose, and CTX, including treatment cycles and chemotherapeutic agents were documented. Moreover, subjective outcome parameters such as subjective pain and mobility after resection were described. Furthermore, the oncological outcome, i.e., overall survival and disease-free survival was documented.

Following the local tumor center's policy, the follow-up examinations followed a distinct scheme: In addition to thorough clinical examination, chest X-rays (CXR) or CT scans of the thorax as well as MRI scans of the affected region were performed every three months after surgery for the first three years. Thereafter, biannual follow-up examinations involving the same image modalities were performed up to the 5th postoperative year. Thereafter, appointments were scheduled annually.

All information was collected and processed by reviewing patient records, tumor boards, the obituary column and through individual interviews with the patients or relatives via telephone. The collected data were summarized by means of descriptive statistics using Microsoft Excel for Windows 2016 and Microsoft Word 2016.

Prospective study

For the prospective part of the study, patients were re-invited to the *Department of Orthopaedics and Trauma*. It consisted of detailed history taking regarding current complaints, pain, handedness, and restrictions in everyday life, as well as physical activities. The functional range of motion of the upper extremity was recorded for both upper limbs. In one patient this examination was additionally documented with photography. The orthopedic clinical examination also included the Apley scratch test for the neck and back to assess combined shoulder mobility. In addition, the muscles of the rotator cuff, which are important stabilizing muscles in shoulder movement, were tested with the Neer test, the empty can test (Jobe's test), the infraspinatus test and the belly press test (Napoleon's test). (98)

Questionnaires:

In the course of this evaluation, patients completed the two following questionnaires:

- Quick-DASH-Score
- MSTS-Score

Pictures of the four questionnaires are shown in the appendix.

Quick-DASH-Score

The original DASH (Disability of arm, shoulder and hand)-Score is a valid and reliable questionnaire for patients with various upper extremity disorders. (99) Due to the simple language, the DASH-Score is also validated for the German language. (100) The Quick-DASH-Score is a shorter version with 11 items of the original 30 item DASH-Score and has the same clinical characteristics such as reliability and validity and the same simple language. (101) Each item has five possible answers with 1 to 5 points, whereby a minimum of 10/11 items must be answered. The score is calculated as follows:

$$\left(\frac{\text{Achieved points}}{\text{Number of answered questions}} - 1 \right) \times 25 = \text{QuickDASH score in \%}$$

The range of the total score is from 0 to 100, with low values for low disability and high values for high disability. The Quick-DASH-Score is thus associated with a lower administrative effort and will therefore become increasingly important in the daily routine of hospitals. (102)

MSTS-Score -Upper extremity

The MSTS-Score has been tested in several studies and is generally a recommended tool for measuring the functionality and quality of life in patients with musculoskeletal cancer. (103, 104) The MSTS-Score for the upper extremity consists of six items, which include pain assessment, function, emotional mood and relative satisfaction of the patient, hand positioning, dexterity and lifting ability. Each item has six possible answers ranging from 0 to 5 points. The score is calculated as follows:

$$\left(\frac{\text{Achieved points}}{\text{Maximum achievable points}} \right) \times 100 = \text{MSTS Score in \%}$$

The range of the total score is from 0 to 100. Unlike the Quick-DASH-Score, low values indicate low functionality and high values high functionality.

In general, these questionnaires constitute subjective measuring methods, wherefore the patients' abilities may be overestimated by physicians. (105) In order to reduce the potential observer bias, the questionnaires in the current study were completed together with the patients during the clinical examination.

The study protocol was approved by the Ethics Committee of the Medical University of Graz (Ethics committee number: 31-543ex18/19) and patients that underwent an additional examination and photo documentation in the prospective part of the study

were informed about the data protection policy in advance and gave their written consent.

Inclusion/exclusion criteria

Each of the seven patients (n=7) included in the analysis was either diagnosed and treated at the *Department of Orthopaedics and Trauma* at the *Medical University of Graz, Austria* or referred by other institutions between 2000 and 2018 due to a malignant tumor with primary or secondary involvement of the clavicle.

In one 20-year old female patient with an extraosseous Ewing's sarcoma involving the left clavicle, the osseous component showed complete regression after preoperative chemotherapy, wherefore initially planned resection of the clavicle was not performed (n= 1). For this reason, she was excluded from retrospective analysis, resulting in six patients eligible for the retrospective part of the study.

All patients that were still alive at initiation of the prospective part, were potentially eligible for clinical examination and questionnaires. This was the case in four of the six patients (n= 4) who were first informed by mail about the possibility to participate in the study, and subsequently reached by telephone in order to schedule further appointments. As one of the potentially eligible four patients was lost to follow-up and another patient did not agree to participate, two patients (n=2) were finally invited to the *Department of Orthopaedics and Trauma, Medical University of Graz, Austria* for another examination.

Results

The six patients included in the retrospective part of the study were analyzed for various demographic, clinical, tumor- and treatment-related parameters. These analyses will be presented in the first part of the results section. In the second part of the results section, the two patients of the prospective part of the study will be described in more detail, focusing on the functional outcome.

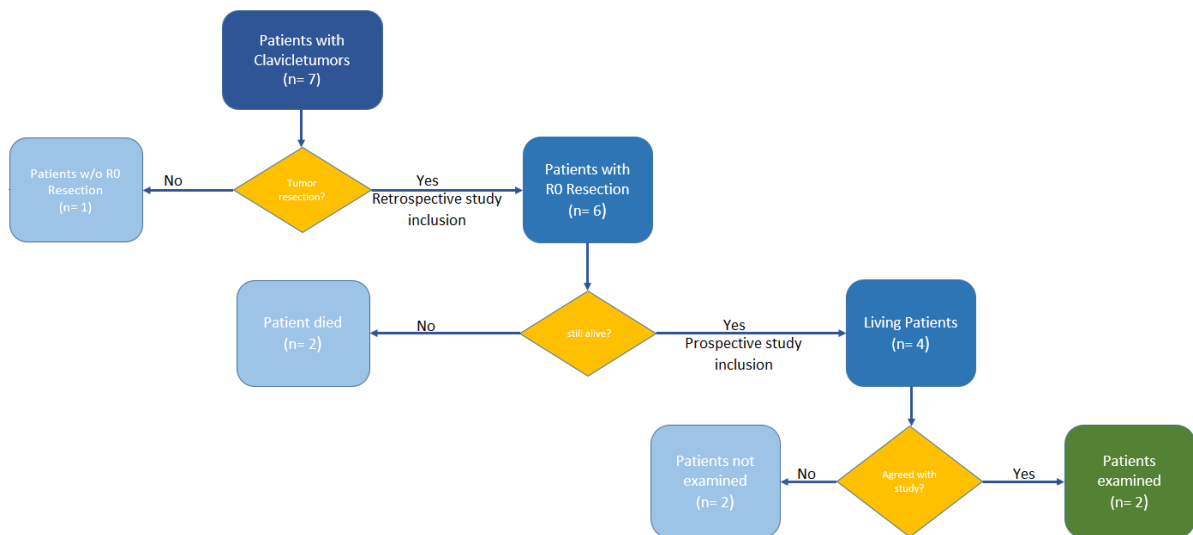


Figure 8 Inclusion/exclusion criteria.

Retrospective part

First clinical presentation and patient demographics

Three patients were male (50%) and three female (50%). The age distribution at time of first clinical presentation at the *Department of Orthopaedics and Trauma* at the *Medical University of Graz, Austria* regarding the clavicle tumor ranged from 13 to 70 years. The average age was 37.3 years with a standard deviation of ± 27 years. All tumors were surgically treated and completely removed one month at the earliest and six months at the latest after first outpatient clinical presentation at the *Department of Orthopaedics and Trauma* at the *Medical University of Graz, Austria*. The average tumor resection was performed after three months with a standard deviation of ± 1.9 months.

Patient 1 (M, 67 years) was referred by an external hospital for re-resection of a previously non-in-sano resected spindle cell carcinoma. Patient 2 (M, 15 years) was referred by an external hospital for further evaluation due to a radiologically visible distension of the right clavicle.

Patient 3 (F, 45 years) presented with an immobile lump at the left shoulder, which had grown to a size of 6 cm x 6 cm over the past three months. Patient 4 (M, 14 years) reported a swelling in the medial aspect of the right clavicle that had been present for one month.

Patient 5 (F, 13 years), with known Li-Fraumeni syndrome, had already been treated several times with chemotherapy, RTX, and surgery due to previous malignant tumors. One of these involved a rhabdomyosarcoma developing in the soft tissues of the left neck that had been treated surgically. Nine years thereafter, she presented to our department for a new solid process in the left clavicle, which was additionally verified by MRI.

Patient 6 (F, 70 years) noticed a supraclavicular node with pain radiating to her right arm a few weeks before presentation to the outpatient clinic. The lump was about 5 cm in size, solid and tightly attached to the surrounding tissues. This patient had previously been diagnosed with a Merkel cell carcinoma on the left cheek, which had been treated by surgery 2.5 years earlier.

Case Number	Sex	Tumor	Age at first clinical presentation	First outpatient clinical presentation	Time until complete tumor removal
1	m	Spindle-cell sarcoma grade 2 with fibroblastic/myofibroblastic differentiation	67	- Previous non-in-sano resection of a spindle-cell carcinoma in an external hospital - Referral from another hospital for further resection	Three months
2	m	Ewing's sarcoma	15	- In MRI apparent prominence in the right clavicle	4,5 months
3	f	Ewing's sarcoma	45	- Soft tissue lesion in the left clavicle increasing in size for three months. 6x6cm not movable	Six months
4	m	spindle-cell, malignant, mesenchymal tumor tissue compatible with high-grade osteosarcoma	14	- Painful swelling in the area of the right medial clavicle. - Simultaneous exanthema with an emphasis on the stem	2,5 months
5	f	Osteoblastic, chondroblastic-differentiated, sclerosed, low-differentiated Osteosarcoma	13	- New MRI apparent lesion in the left Humerus and left clavicle in a patient with known Li-Fraumeni syndrome and previous osteotomy of the left clavicle.	Three months
6	f	Merkel cell carcinoma	70	- 2,5 years after resection of a Merkel cell carcinoma - supraclavicular lump on the right with radiating pain in the right arm	One month

Table 10 Demographics and first clinical presentation.

Description of tumor and treatment

Histopathological examinations of biopsy specimens revealed one grade 2 spindle cell sarcoma with fibroblastic/ myofibroblastic differentiation (patient 1), two Ewing's sarcomas (patients 2 and 3), two high-grade osteosarcomas (patients 4 and 5), and one bone metastasis of Merkel cell carcinoma (patient 6). All malignant tumors were subsequently treated by surgical resection aiming at wide margins.

In patient 1 the lateral third of the right clavicle was resected and the remaining clavicle and acromion were stabilized with intraosseous sutures. (see **Figure 12**) All surgeries could be performed without intra- and postoperative complications. In patient 5 with osteosarcoma and underlying Li-Fraumeni syndrome wide resection of the entire clavicle was indicated as a palliative measurement to prevent exulceration. Patients 2 and 4 underwent a resection of the entire right clavicle (see **Figure 14, Figure 19**), patients 5 and 6 underwent a resection of the entire left clavicle, (see **Figure 21, Figure 24**) and patient 3 underwent a resection of the entire left clavicle plus the tip of the coracoid process. (see **Figure 17**)

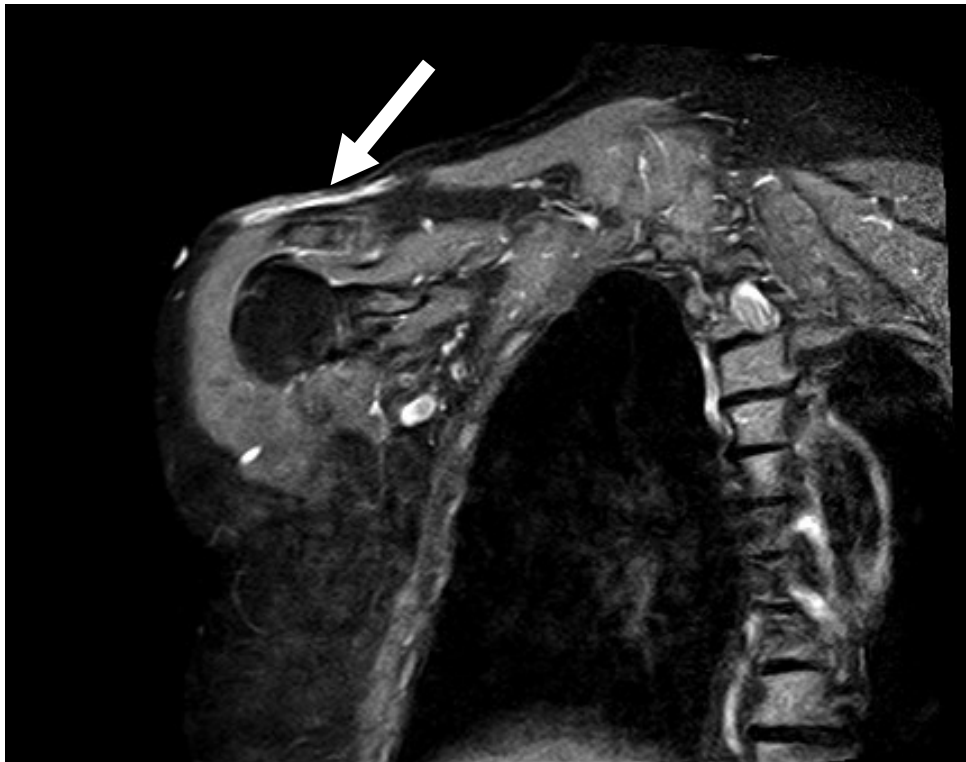


Figure 9 Case 1 – Coronal MRI scan T1 weighted STIR TSE sequence of the lateral right clavicle one month prior to resection. Note the soft-tissue alteration above the AC joint following non in sano resection.



Figure 10 Case 1 – A.p. X-ray of the right shoulder one day prior to resection of the lateral third of the right clavicle.

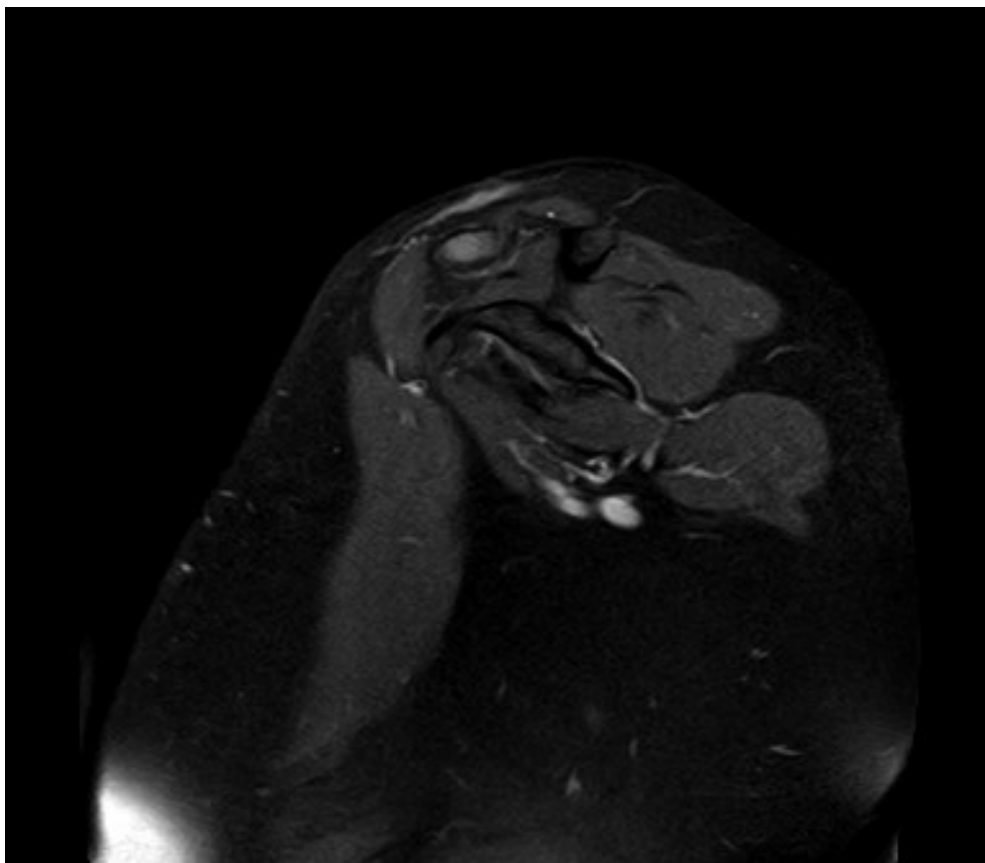


Figure 11 Case 1 – MRI scan T1 weighted TSE FS sequence of the right clavicle at height of AC-joint three months after resection of the lateral third of the right clavicle.



Figure 12 Case 1 – A.p. X-ray of the right shoulder 1,5 years after resection of the lateral third of the right clavicle.

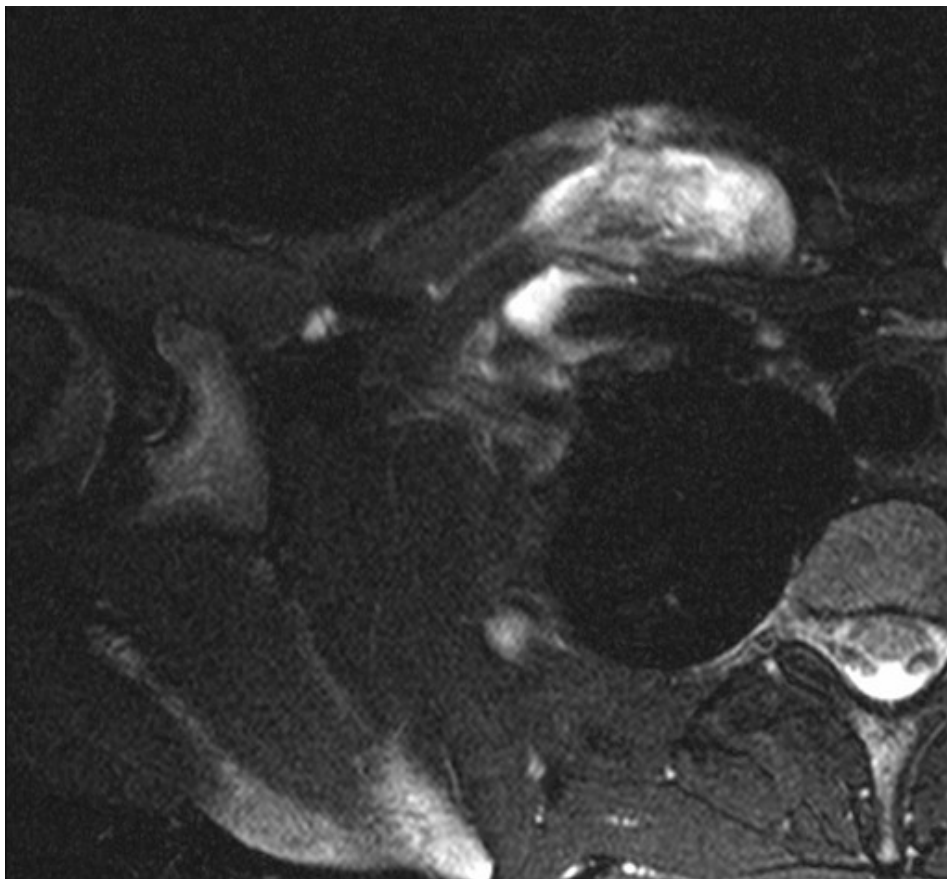


Figure 13 Case 2 – Transverse T2-weighted FS MRI scan of the right shoulder showing a large tumor mass at the medial aspect of the clavicle with soft tissue involvement.



Figure 14 Case 2 – A.p. X-ray of the right shoulder 6 months after resection of the entire right clavicle.

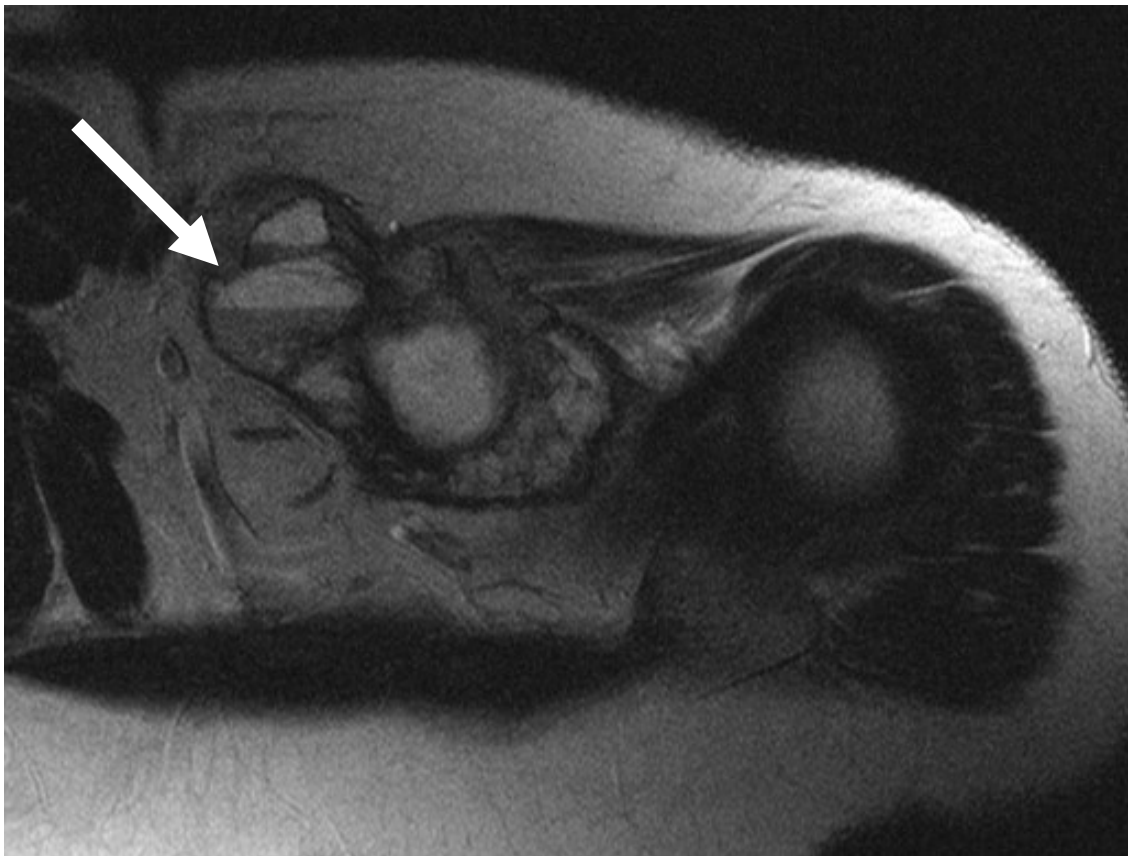


Figure 15 Case 3 – Transverse MRI scan T2 weighted TSE sequence of the left clavicle two months prior to resection. Note the fluid-fluid levels.

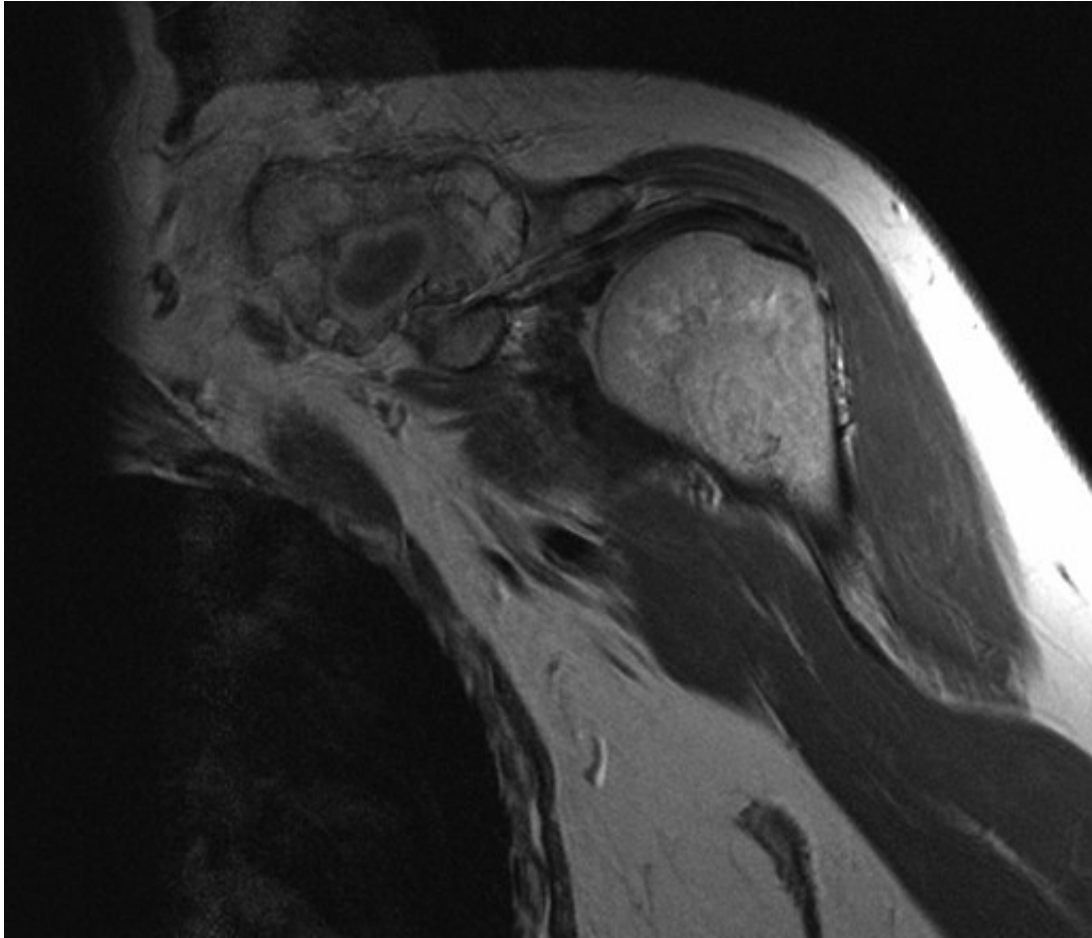


Figure 16 Case 3 – Coronal MRI scan T1 weighted SE sequence of the left clavicle two months prior to resection.

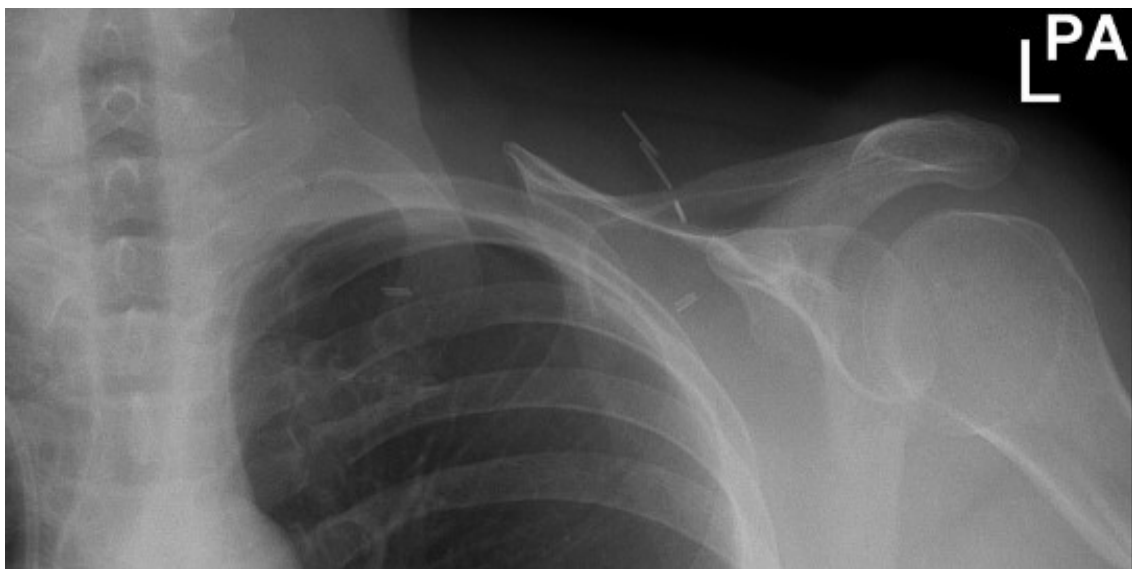


Figure 17 Case 3 – A.p. X-ray of the right shoulder 8 years after resection of the entire left clavicle and the tip of the coracoid process.

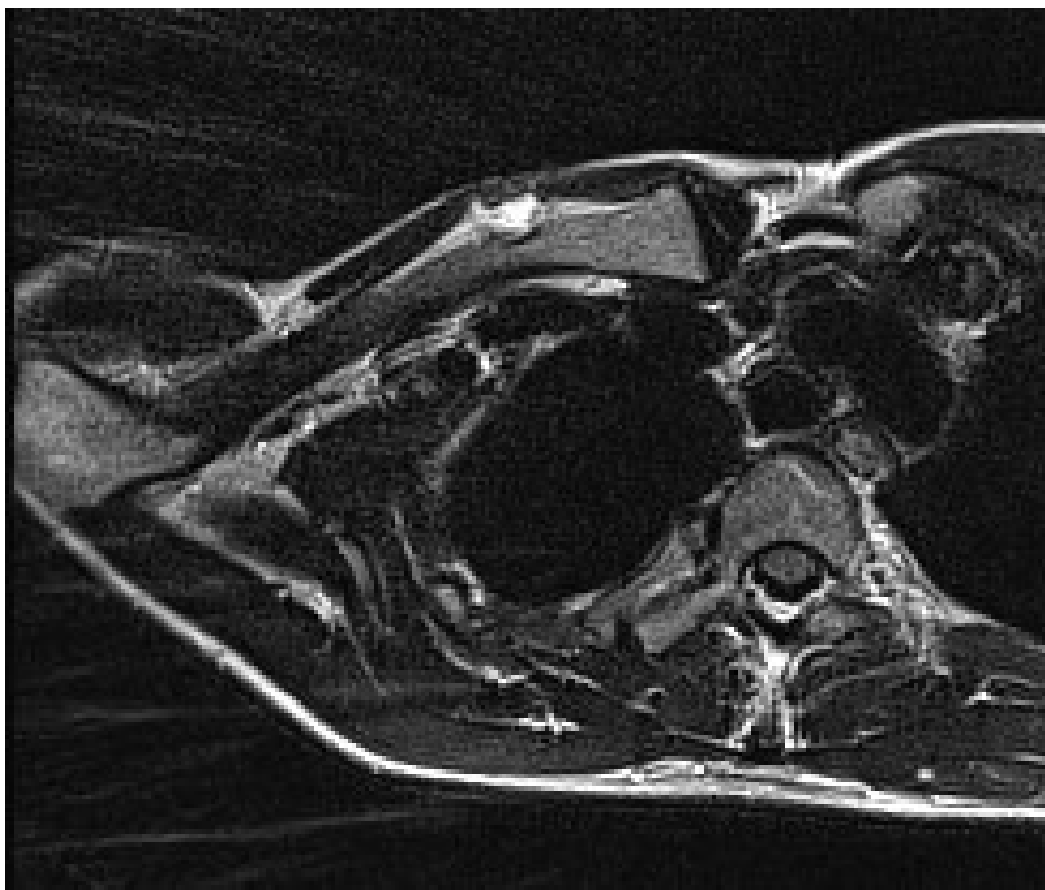


Figure 18 Case 4 – Transverse T2 weighted MRI scan of the right shoulder one week prior to resection revealing tumor in the right clavicle.

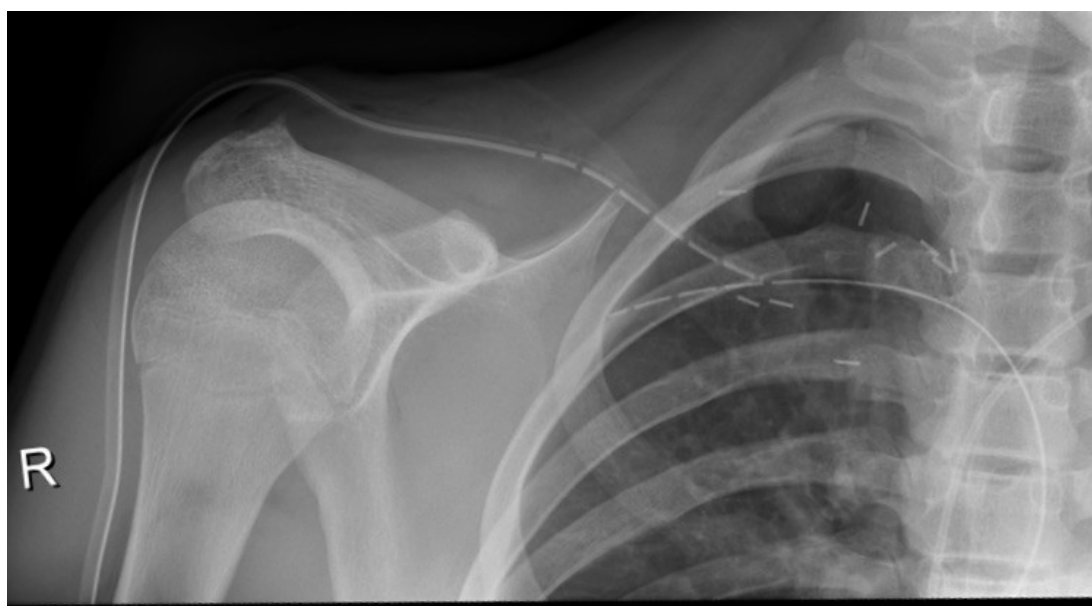


Figure 19 Case 4 – A.p. X-ray of the right shoulder immediately after resection of the entire right clavicle.

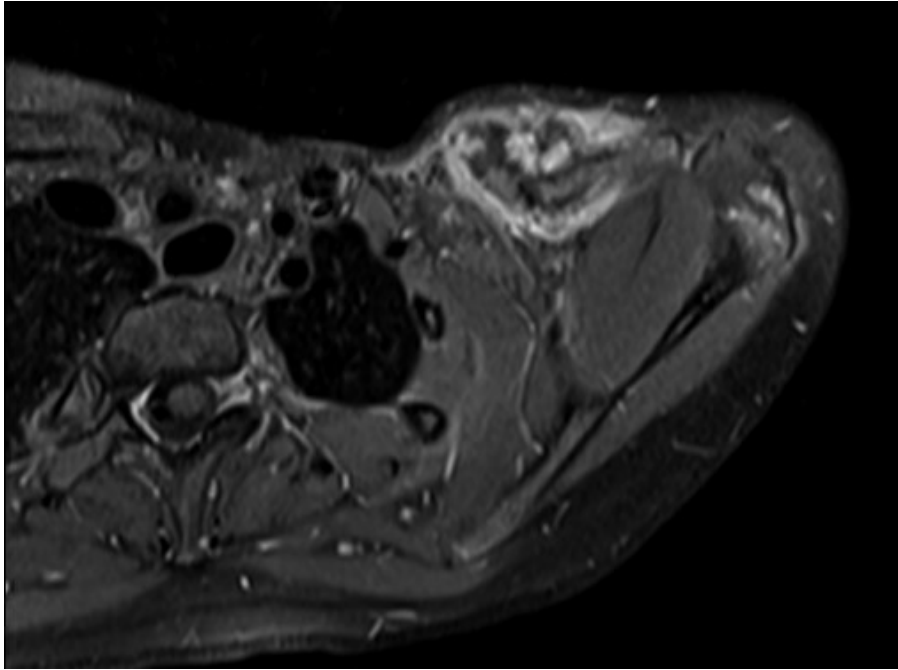


Figure 20 Case 5 – Transverse T1 weighted MRI scan with contrast agent of the left shoulder two weeks prior to resection showing a tumor mass in the left clavicle with soft tissue involvement.



Figure 21 Case 5 – A.p. X-ray of the left shoulder three and a half years after resection of the entire left clavicle. Note the rib plate bridging the large thoracic defect.

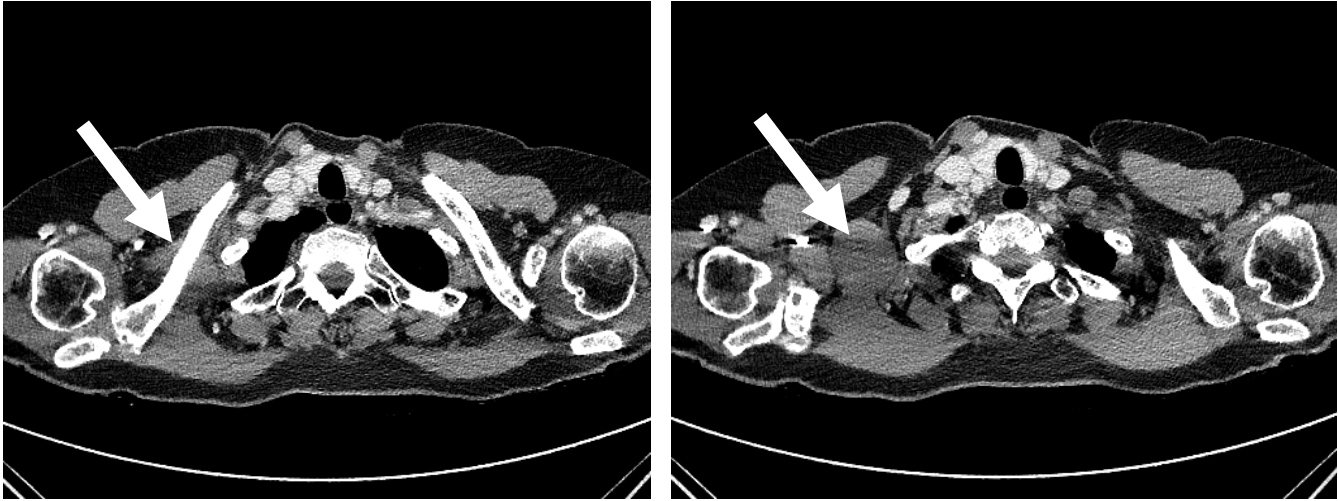


Figure 22 Case 6 – Transverse CT scan of the shoulder girdle three weeks prior to resection. Note the soft tissue swelling at the level (left) of and directly below (right) the right clavicle.

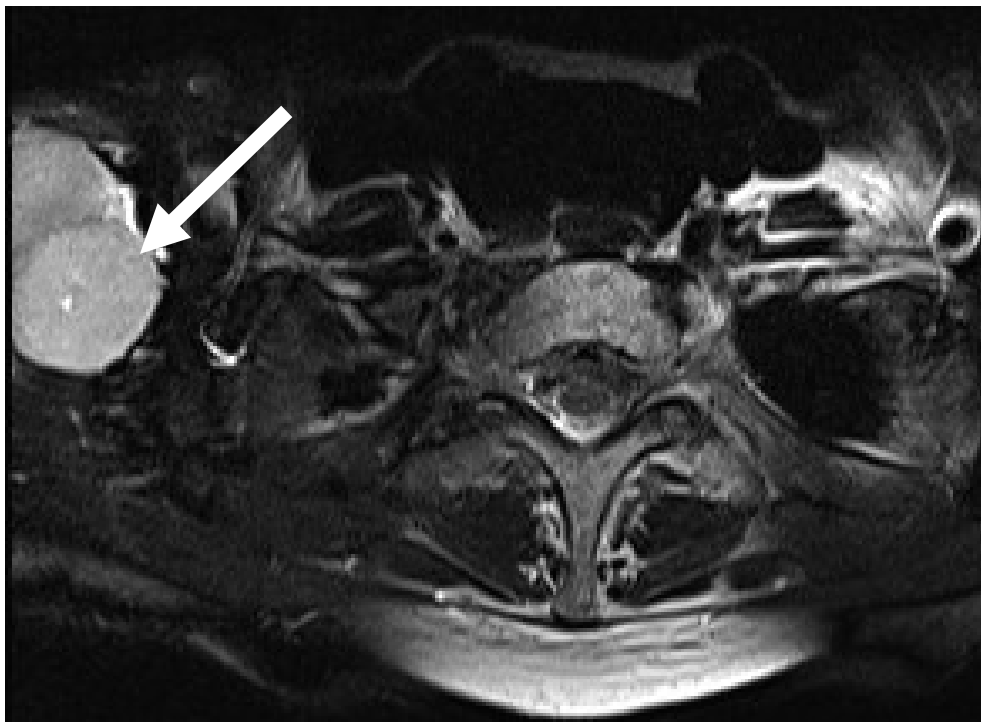


Figure 23 Case 6 – Transverse MRI scan T2 weighted TSE sequence of the shoulder girdle two weeks prior to resection depicting a large soft tissue mass directly below the clavicle.

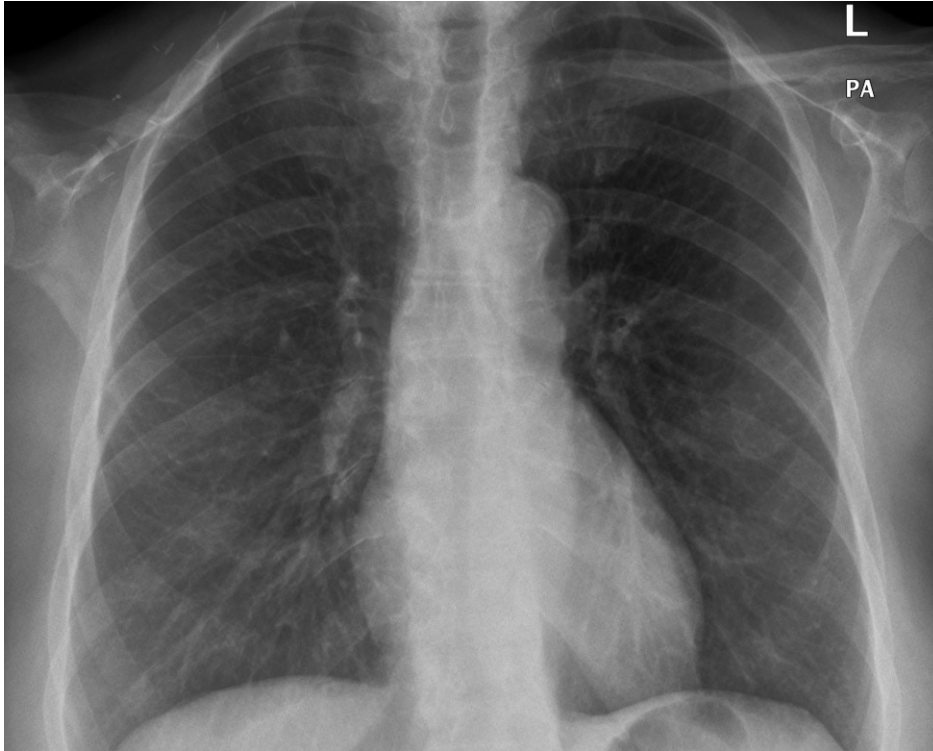


Figure 24 Case 6 – A.p. X-ray of the thorax three years after resection of the entire right clavicle. Note the relatively lower position of the right shoulder girdle in comparison to the unaffected left side.

Preoperatively, patients 2, 3 and 4 were administered CTX (see **Table 11**). In osteosarcoma or Ewing's sarcoma, the classification according to Salzer-Kuntschik et al. (79) has become generally accepted in the German-speaking countries for the assessment of the tumor's response to CTX. (106) Thus, in case 2 and 4 a Salzer Kuntschik grade 1 (without vital tumor tissue) and in case 3 a Salzer Kuntschik grade 3 (with less than 10% vital tumor tissue) could be achieved. The other patients did either not suffer from osteosarcoma or Ewing's sarcoma, or did not receive preoperative CTX.

Postoperatively, CTX was continued and successfully completed in patient 2 after a total of 14 cycles (with vincristine, actinomycin D and cyclophosphamide). Patient 4 underwent four postoperative cycles of CTX (with cisplatin, adriablastine (Doxorubicin), high dose methotrexate; see **Table 11**).

Patient 3 underwent 8 cycles of postoperative CTX (with vincristine, actinomycin D, ifosfamide). During follow-up, 7.8 years post-surgery, osteolytic areas in the left ilium

were detected on routine staging CT-scan and confirmed on MRI. Biopsy was performed, revealing Ewing's sarcoma metastasis in the left iliac bone. Neoadjuvant polychemotherapy (topotecan and cyclophosphamide), consisting of 8 cycles, and a RTX of the iliac bone with a total of 54 Gy were initiated. However, wide resection of the ilium was not performed in the further course.

Patient 1 was administered postoperative RTX to the operated area with a total of 60 Gy (see **Table 11**).

Case Number	Preoperative treatment (CTX/RTX)	Operation	Tumor characteristics	Postoperative treatment
1	Not performed	<ul style="list-style-type: none"> - Wide resection in the right clavicle w/o intra-/postoperative complications - Intraosseal sutures between remaining clavicle and acromion for stabilization 	<ul style="list-style-type: none"> - Expansion to the lateral end of the clavicle 	<ul style="list-style-type: none"> - Local RTX with 60 Gy in total - No complications during RTX, except from small skin changes
2	Biopsy CTX good response to CTX	<ul style="list-style-type: none"> - Wide resection of the right clavicle w/o intra-/postoperative complications 	<ul style="list-style-type: none"> - medial clavicle 4 cm longitudinal extension. Salzer Kuntschik grade I 	<ul style="list-style-type: none"> - CTX to complete 14 cycles (Vincristin, Actinomycin D, Cyclophosphamid)
3	Biopsy CTX six cycles VIDE (Vincristin, Ifosfamid, Doxorubicin and 50% Etoposid)	<ul style="list-style-type: none"> - Wide resection of the left clavicle with the tip of the coracoid process w/o intra-/postoperative complications 	<ul style="list-style-type: none"> - Salzer Kuntschik grade 3 70% necrosis 	<ul style="list-style-type: none"> - CTX to complete 8 cycles VAI (Vincristin, Actinomycin D, Ifosfamid) - Then neoadjuvant again due to metastases
4	Biopsy and Scintigraphy CTX HD- MTX (Euramos/COSS Protocol)	<ul style="list-style-type: none"> - Wide resection of the right clavicle w/o intra-/postoperative complications 	<ul style="list-style-type: none"> - Salzer Kuntschik grade 1 	<ul style="list-style-type: none"> - CTX four cycles of (Cisplatin, Adriblastin (Doxorubicin), High dose Methotrexate)
5	Multiple CTX before because of known Li-Fraumeni syndrome	<ul style="list-style-type: none"> - Wide resection of the left clavicle w/o intra-/postoperative complications - (High frequency radiation of the left humerus) - Prevention of exulceration 	<ul style="list-style-type: none"> - Infiltration of the soft tissue 1 mm to resection margins without reaching it 	<ul style="list-style-type: none"> - Not performed

6	Not performed	- Wide resection of the left clavicle w/o intra-/postoperative complications.	-	- Gilchrist bandage for six weeks
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Table 11 Tumor and Treatment.

Clinical and oncological outcome

The average patient follow-up was 5.3 years (standard deviation: 3.2 years), ranging from 1.6 years to 9.4 years. At the time of writing this diploma thesis, patients 1, 2, 4 and 6 were alive and free of metastases, whereas patients 3 and 5 had died due to their disease at 9.4 and 4.6 years after surgery for clavicular sarcoma.

In patient 3 with Ewing's sarcoma and wide resection of the entire clavicle and the tip of the coracoid process, osteolysis of the left iliac bone was detected on MRI 9.4 years after surgery. A biopsy was performed, and the diagnosis of an Ewing's sarcoma metastasis made. During the following months, additional metastatic lesions were diagnosed in the skull, the greater tubercle of the left humerus, the left thoracic wall, the cervical and thoracic vertebrae, and the left proximal femur. Subsequently, the patient's general condition worsened significantly. Eventually, she developed paraplegia due to progressive vertebral metastases in the C7/Th1 region, wherefore palliative RTX was discontinued. At final follow-up 9.4 years after surgery for Ewing's sarcoma involving the clavicle, the patient was in a critical general condition, with multiple metastases and in palliative care.

In patient 5 with known Li-Fraumeni syndrome and osteosarcoma involving the left clavicle, contrast medium-enhancing lesions in the second rib on the left side were detected on MRI 3.7 years after wide resection of the left clavicle. A biopsy was performed, histologically revealing the diagnosis of another osteosarcoma. A resection of the left upper thoracic aperture (1st-3rd rib) with reconstruction using rib plates was performed. During the following year, the patient's general condition steadily worsened due to the systemic tumor load, and a progressive reduction of left upper extremity functionality with strength grade 3/5 and reduced abduction ability of 150° was observed.

Additionally, a de-novo left-sided Horner's syndrome with ptosis of the left eyelid, persistent pain in the left shoulder, and weight loss of 10 kg within the last six months

were noticed, all indicative of local and systemic tumor progression. Indeed, MRI scans revealed masses in the paravertebral soft tissue on the left side from the upper margin of C6 to upper margin of Th3 with consecutive absolute spinal stenosis in the C1/C2 area. At that time, the patient had already developed a paraplegia. At final follow-up 4.6 years after surgery for osteosarcoma involving the clavicle, the patient was in a critical general condition, with multiple metastases and in palliative care.

Patient 1 reported normal motor skills of the affected upper limb with no subjective symptoms 17 days after surgery for clavicular sarcoma. Regarding mobility, a slight restriction of mobility with reduced abduction ability of the right shoulder joint was observed in comparison to the unaffected upper limb. In the last representative follow-up 1.6 years after surgery, the patient reported no movement restrictions or pain in daily life and achieved full range of motion of both upper extremities. Occasionally, the patient reported tingling, and mild pressure pain in the area of the AC joint, especially after tennis training.

Postoperatively and at the follow-up 2.4 and 3.2 years after surgery, patients 2 and 3, respectively, were subjectively symptom free. However, having good upper limb mobility 3.2 years after surgery, patient 3 reported progressive pain during prolonged work and movement in the course of the next four years of follow-up appointments. At the time of the latest follow-up appointment 9.4 years after surgery, shortly before the death of this patient, active abduction and ventral elevation of the left arm was no longer possible due to osteolytic fractures and metastases involving the chest wall and left humerus.

Patient 4 was subjectively free of complaints as early as three days after surgery except for side effects of CTX and mild hypesthesia in the ventral right shoulder region. After initial restrictions of the active elevation of the right arm, he regained full range of motion of the upper extremity in the further postoperative course. At the latest follow-up, he reported no restrictions in his daily life and had full range of motion of the affected shoulder, despite a visible anatomical difference due to the resected clavicle compared to the unaffected side.

Patient 5 with known Li-Fraumeni syndrome was subjectively free of complaints until 3.7 years after surgery, with slight restrictions in the mobility of the upper left

extremity and pain on overstraining. Thereafter, however, symptoms became more severe due to the development of metastases in the second left rib and the consecutive resection of the left thoracic wall (1st to 3rd rib). Shortly before the death of this patient, she merely achieved a motor strength of 3/5 and an abduction ability of 150° of the upper left extremity.

Patient 6 complained of problems with lifting heavy everyday objects and pain in her left shoulder even 5.6 years after resection. Notably, this patient was free of any metastases and or local recurrence.

Case Number	Time from Operation to last representative follow up	Clinical Outcome	Oncological Outcome
1	One year and seven months after resection	<ul style="list-style-type: none"> - 17 days after operation the patient is free of subjective complaints with normal motor skills. Slight restrictions in mobility with reduced abduction in lateral comparison - At latest follow-up subjectively free of complaints and symptoms - Plays Tennis again. No pain in everyday life. Occasionally pain while playing Tennis. Mild tenderness over the AC-joint - Full range of motion in the upper limbs 	- Alive and free of recurrence
2	Two years and five months after resection	- subjectively symptom free	- Alive and free of recurrence
3	9 years and five months after resection	Three years and two months after resection <ul style="list-style-type: none"> - No subjective complaints - Occasionally pain in context of increased exercise - Good mobility of upper extremity - Normal motor skills 	<ul style="list-style-type: none"> - 9 years and five months after resection pain the in left shoulder with no possible abduction or elevation of the arm, due to multiple metastases in the chest wall, cranial bones, hips and left upper arm. - Dead of disease (date unknown)
4	8 years and four months after resection	<ul style="list-style-type: none"> - Three days after operation Patient subjectively free of complaints except from CTX side effects - Some Hypoesthesia at the frontal part of the shoulder - No Pain. Normal motor skills - Extremities passively freely movable - Slight reduction of active elevation movement in lateral comparison, otherwise freely movable 	- Alive and free of recurrence

		<ul style="list-style-type: none"> - At latest follow up visible malposition of the shoulder with no subjective complaints or restrictions in the everyday life - No pain or restrictions in mobility. Full range of motion 	
5	Four years and seven months after resection	<ul style="list-style-type: none"> Three years and 8 months after resection - Subjectively free of complaints. Pain only in context of increased physical stress - Restricted Mobility in the left upper limb. 	<ul style="list-style-type: none"> - Four years and seven months after resection the underlying disease causes further resections of the chest wall with loss of strength in the left upper limb - Dead of disease (date unknown)
6	Five years and seven months after resection.	<ul style="list-style-type: none"> - Pain in the left shoulder and problems with lifting objects 	<ul style="list-style-type: none"> - Alive and free of recurrence

Table 12 Clinical and oncological outcome.

Prospective part

The number of published case reports of the functional outcome after clavicular resection is limited and rather refers to trauma-related resections of the clavicle than tumor-related resections. (107, 108) In addition, the existing literature regarding clavicular resections consists of individual case reports or studies with low case numbers. (19, 109) As in previously published case reports (108, 110), we used the Quick-DASH- and MSTS-Score to prospectively assess the mobility of the effected upper extremity.

We were able to include two of the patients in the prospective part of this study, thus evaluating the functional outcome years after treatment of a clavicular tumor by wide resection. The detailed description of the clinical examination and the objectification through questionnaires will help to better understand the role of the clavicle regarding the functionality of the upper extremity, eventually justifying its scarification during tumor surgery.

The two subsequently presented cases have already been introduced in the retrospective part as case numbers 1 and 4.

Case 1

Case 1 describes a male patient who presented to the *Department of Orthopaedics and Trauma* at the *Medical University of Graz, Austria* for the first time at the age of 67 years. Two months earlier, a non-in-sano resection of a spindle cell sarcoma of the right shoulder had been performed at an external hospital. Imaging prior to that initial resection was unfortunately unavailable for review. At the time of the first presentation to our department, an X-Ray and MRI of the right shoulder showed a high-grade AC joint arthrosis with osteophytic narrowing of the supraspinatus outlet. (see **Figure 25**)



Figure 25 Case 1 at first presentation at our department. Cortical irregularities at the lateral clavicle, adjacent to the acromioclavicular joint, visible on X-ray.

After multidisciplinary tumor board evaluation, a wide re-resection of the surgical field was planned along with the right clavicle, followed by postoperative radiation. Patient history revealed a preceding excision of a dermatofibroma of the right shoulder four years earlier, and a non-insulin-dependent diabetes mellitus.

After preoperative X-ray control, a wide resection with removal of the lateral part of the clavicle was performed five weeks after the first presentation to our department. The resection was performed just below the periosteum and under the AC joint

capsule. Intraosseous sutures between acromion and the remaining medial part of the clavicle were used for stabilization.



Figure 26 Case 1 – X-ray of the right shoulder 1,5 years after resection of the lateral third of the right clavicle. As a comparison, the inset shows the preoperative image with the region of interest (i.e. tumor-bearing zone) marked with a red circle.

Histological examination revealed morphological results corresponding to the previously resected spindle cell sarcoma with fibroblastic/myofibroblastic differentiation. The resection margins were free of tumor cells, wherefore no further resection had to be performed. Routine follow-up appointments were scheduled according to the in-house follow-up protocol. These included MRI scans of the affected region every three months for the first three years, regular CXR and thoracic CT scans. Postoperative RTX of the operated area was performed with a total of 60 Gy.

The patient showed uneventful recovery and could be discharged after three days of inpatient stay. Seventeen days later, the patient was subjectively symptom-free, there were no signs of wound dehiscence or inflammation. Peripheral blood circulation, motor and sensory function were normal. Local RTX with a total of 60 Gy was initiated 1.5 months following surgery and continued for a period of six weeks. During the follow up appointment after three months, only a slight reduction

in abduction ability was noted compared to the other limb. However, another six months later, this restriction had disappeared completely, and the patient was free of complaints with regained unrestricted mobility of the right shoulder. An Apley scratch test for the neck and back was possible without any restrictions. Imaging also showed no evidence of local recurrence or metastases. At the next follow-up appointment 1.1 years after surgery the patient reported that he was able to play tennis on a regular basis and only experienced a mild tingling sensation in the surgical area, but no restrictions in mobility.

Nineteen months after surgery, the patient was re-examined at the *Department of Orthopaedics and Trauma* at the *Medical University of Graz, Austria* within the prospective part of this study.

A short history taking confirmed findings from previous follow-up examinations, with subjective no complaints. The patient reported having no complaints in everyday life and being able to perform all everyday tasks to the same extent as before the onset of the disease. Although he was right-handed, the patient was able to play tennis with his right arm without any restrictions. The previously mentioned tingling over the scar was now only rarely felt when playing tennis.

Regarding the two questionnaires, the patient achieved 2.27% for the Quick-DASH-Score and 100% for the MSTS-Score. The deductions in the Quick-DASH-Score were due to the slight tingling sensations occasionally experienced by the patient.

Range of motion (ROM) was documented once with and once without a fixed scapula and compared with the unaffected side, using the neutral-null-method. Deviations from the respective reference values in the last column were highlighted in bold (see **Table 13**, **Table 14**). (111)

Movement	Right	left	Reference
Ante/ Retroversion	90°/0°/30°	90°/0°/30°	(90°/0°/30°-50°)
Ad-/ Abduction	20°/0°/90°	20°/0°/90°	(20°-40°/0°/90°)
Inner/outer rotation (90°)	70°/0°/70°	70°/0°/70°	(70°/0°/70°)

Table 13 Case 1: Movement with fixed scapula.

Movement	Right	left	Reference
Ante/ Retroversion	170°/0°/30°	170°/0°/30°	(150°-170°/0°/30°-50°)
Ad-/ Abduction	20°/0°/170°	20°/0°/170°	(20°-40°/0°/180°)

Table 14 Case 1: Movement without fixed scapula.

After the abovementioned, almost unrestricted ROM, the Apley scratch test for both the neck and the back showed normal results. The previously mentioned tests of shoulder mobility and rotator cuff functionality, i.e., Neer test, Jobe test, infraspinatus test and belly press test (or Napoleon test) were all negative and did not differ from the unaffected side.

Case 4

Case 4 describes a male patient who presented to the *Department of Orthopaedics and Trauma* at the *Medical University of Graz, Austria* for the first time at the age of 14 years. At that time, the patient reported having noticed a painful swelling in the medial third of the right clavicle for about one month. The performed X-Ray and MRI scan revealed a 1.4 cm sized lesion of the medial clavicle with periosteal reaction and contrast enhancement of the surrounding soft tissues. (see **Figure 27**, **Figure 28**)

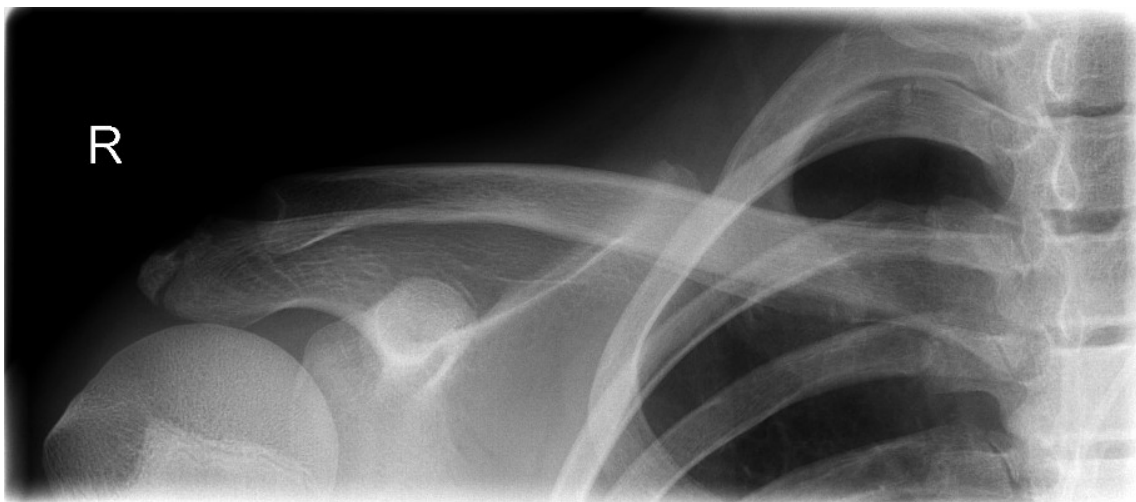


Figure 27 Case 4 – A.p. X-ray of the right clavicle at time of the first presentation at our department. Onion-skin phenomenon visible as periosteal reaction visible at the medial clavicle.



Figure 28 Case 4 – preoperative 3D Imaging of the right clavicle.

A few days later, a skeletal scintigraphy revealed increased tracer uptake in the area of the clavicular lesion. No further conspicuous areas of increased tracer uptake were identified. Histological analysis of the biopsy specimen revealed malignant mesenchymal spindle-cell tumor tissue compatible with high-grade osteosarcoma.

After tumor board evaluation, a wide resection with neoadjuvant and adjuvant CTX according to the EURAMOS-1 (European and American Osteosarcoma Studies) protocol using high-dose methotrexate, cisplatin and adriablastine (Doxorubicin) was planned.

Following completion of preoperative CTX, and 2.5 months after initial presentation, a wide resection of the entire right clavicle was performed. The lateral clavicle was disarticulated from the AC joint. The medial end of the clavicle was disarticulated from the SC joint and removed with parts of the large pectoral muscle and the subclavius muscle in order to obtain clear surgical margins. (see **Figure 29**) Histological examination of the surgical specimen confirmed the diagnosis of the preceding biopsy and revealed tumor-free margins. Furthermore, Salzer-Kuntschik regression grade 1 was diagnosed, with no vital tumor cells left after preoperative CTX.

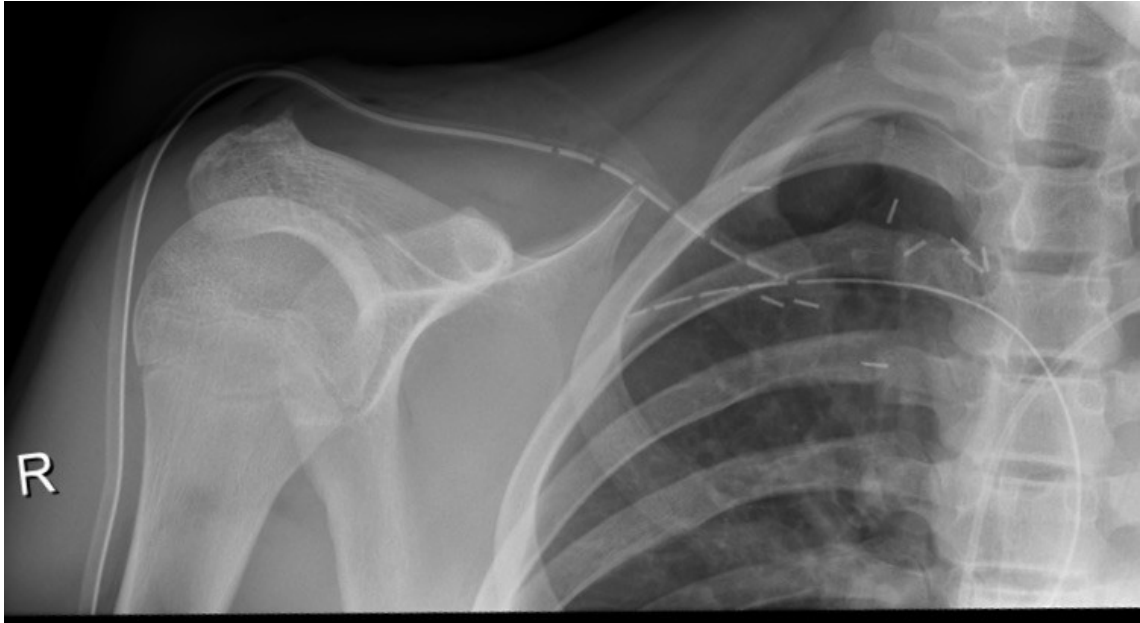


Figure 29 Case 4 – A.p. X-ray of the right shoulder after resection of the entire right clavicle.

As in case 1, routine follow-up appointments were scheduled according to the inhouse follow-up protocol.

Surgery and postoperative recovery were uneventful. Three days after surgical resection of the clavicle, adjuvant CTX was started according to the EURAMOS-1 regimen, consisting of a total of six cycles of cisplatin 70 mg per cycle, 8 cycles of adriablastin (Doxorubicin) 65 mg per cycle, and 8 cycles of high-dose methotrexate 20 g per cycle. The patient initially suffered from side effects from CTX but was otherwise symptom-free. In addition to mild hypesthesia in the ventral right shoulder region, motor, and sensory function, as well as peripheral circulation of the right arm and hand were normal. After three months, the affected upper limb could already be moved passively in all directions. Upon active motion, only a slight restriction in the elevation of the right arm in lateral comparison was noted. However, another two months later, this restriction had resolved completely, and the patient was free of subjective complaints full range of motion.

Five months after surgery, the last cycle of CTX was completed without major complications and the patient was discharged from hospital. During hospitalization, the patient had received Granulocyte-Colony Stimulating Factor (G-CSF)

subcutaneously several times in addition to six red cell concentrates and six platelet concentrates due to depletion of the hematopoietic system caused by CTX.

1.4 years after surgery, the patient presented with unrestricted mobility despite visible deformity of the shoulder contours due to resection of the right clavicle. The patient complained of mild pain at the cervical region, which was diagnosed as cervical spine syndrome due to muscular imbalance. MRI scans and scintigraphy showed no evidence of local recurrence or secondary lesions at this appointment.

A total of 8 years and four months after surgery, the patient could be re-examined at the *Department of Orthopaedics and Trauma* at the *Medical University of Graz, Austria* within the prospective part of this diploma thesis.

History taking confirmed the findings of previous reports, with the patient being free of complaints. Furthermore, he reported being very satisfied with the long-term outcome of his condition. Although the patient is right-handed, and the right clavicle had been resected, he did not complain of any limitations in upper extremity movements in his everyday life. However, the patient reported not being able to perform fast-paced sports involving hitting and throwing movements, such as handball, or performing heavy physical labor, such as working on a construction site.

The patient reported that he spent much of his free time at the computer and had little interest in sports both at the time of the examination and at the time before surgery. The patient further stated that he occasionally suffered from mild muscular stiffness in the cervical spine, which he himself attributed in part to the malposition of the right shoulder, but for the most part to physical inactivity and his poor posture when playing the computer.

In the questionnaires, the patient achieved 34.09% for the Quick-DASH-Score and 86.67% for the MSTS-Score. On the one hand, the higher Quick-DASH-Score was due to the reported mild pain due to muscle stiffness and a rare tingling sensation over the scar of the right shoulder. On the other hand, however, it was due to the moderate restriction in leisure activities involving impact sports. The slight reduction in MSTS-Score were due to the pain mentioned above, which however did not require pain medication, and a very slight functional limitation during heavy physical work.

ROM of the left and right shoulder were documented once with and once without a fixed scapula according to the neutral-null-method. Deviations from the respective reference values in the last column were marked in bold. (see **Table 15**, **Table 16**). (111) In addition, some of the movements could be documented with photography (see **Figure 30**).

Movement	Right	left	Reference
Ante/ Retroversion	90°/0°/30°	90°/0°/30°	(90°/0°/30°-50°)
Ad-/ Abduction	20°/0°/90°	20°/0°/90°	(20°-40°/0°/90°)
Inner/outer rotation (90°)	70°/0°/70°	70°/0°/70°	(70°/0°/70°)

Table 15 Case 4: Movement with fixed scapula.

Movement	Right	left	Reference
Ante/ Retroversion	180° /0°/40°	180° /0°/30°	(150°-170°/0°/30°-50°)
Ad-/ Abduction	20°/0°/180°	20°/0°/ 170°	(20°-40°/0°/180°)

Table 16 Case 4: Movement without fixed scapula.



Figure 30 Case 4: Range of motion in follow up studies.

As in case 1, in addition to the abovementioned ROM, Apley scratch test for both the neck and back were performed, revealing normal results. Tests for rotator cuff functionality, Neer test, Jobe test, infraspinatus test, and belly press test (or Napoleon's test) were all negative and showed no differences to the unaffected left shoulder.

Discussion

As stated at the beginning of this diploma thesis, the aim of this study was to retrospectively describe and analyze the clinical and oncological outcome after clavicle resection due to malignant tumors. In addition, the prospective part of the study aimed at investigating the extent to which the functional outcome after clavicle resection without consecutive reconstruction is impaired.

The current study revealed a favorable oncological outcome after wide resection of the clavicle in 66.7% (4/6) of patients with malignant bone tumors. All of these four patients (one with Ewing sarcoma, one with osteosarcoma, one with spindle-cell sarcoma and one with Merkel cell carcinoma metastases) achieved a complete remission by wide resection of the clavicle and multimodal therapeutic approach with CTX and RTX. On the other hand, two patients, one with metastatic Ewing's sarcoma and one with osteosarcoma due to an underlying hereditary tumor syndrome died within 10 years after resection of the clavicle.

Regarding postoperative shoulder function, there was a good overall outcome after clavicle resection, as indicated by the fact that five of the six patients were subjectively free of symptoms and without major limitations in upper extremity mobility at the time of the last follow-up examination.

The prospective part of this study revealed that a quite satisfying result of the upper extremity functionality can be achieved despite the resection of the clavicle. In particular Quick-DASH and MSTS-Scores, as well as negative tests for impairments of the shoulder muscle functions indicated of minor or even no limitations in everyday movements. Notably, however, these observations were made in only two patients.

To our knowledge, this is one of only few reports of outcome after clavicle resection for malignant bone tumors. A case report by R. Gaulke et al. described the case of a rower with Ewing sarcoma. (19) Although the Constant score was used to objectify functionality rather than the Quick-DASH or the MSTS-Score as in our study, the patient achieved comparable values, also indicating good functionality of the upper extremity. In part, the success was attributed to the well-developed musculature and back- and shoulder-training effect of rowing. It has been speculated that throwing and striking sports could lead to ventralization of the shoulder joint and consequent problems in movement due to increased stress on the pectoralis muscle. (19) Thus, ventral destabilization of the shoulder joint, as happening after clavicle resection, may cause significant restrictions, which could not be confirmed, at least in the course of Case 1, who was able to play tennis regularly again without movement restrictions after approximately one year after the resection and who increasingly recovered from the surgery.

Another case study by Nota et al. evaluated 20 patients with scapula and/or clavicle resection due to chondrosarcoma and used the DASH score to assess functionality. (112) Three of these patients underwent complete resection of the clavicle, with one of them additionally requiring resection of the scapula. While the DASH-Score of all 20 patients after resection ranged from 0 to 47 with an average value of 16, the two patients with clavicle resection only achieved values of 0.83 and 3.3. The patient with both scapula and clavicle resection achieved a DASH-Score of 19. (112) In comparison, the Quick-DASH-Scores of our two patients with complete clavicle resection were similar to slightly worse, being 2 and 34.

There are only few single case reports of patients comparable to ours with resection and consecutive reconstruction of the clavicle. In one case of a 27-year-old female patient with benign bone tumor of the clavicle, reconstruction was performed with an autologous fibula graft. (113) In another case report, an 11-year-old female patient underwent clavicular resection for malignant bone tumor followed by reconstruction using the 5th rib. (97) In both cases, a satisfactory functional and cosmetic outcome was reported, but only 80° of abduction was achieved in the first case 14 months after surgery. (113) Contrary to our hypothesis, the authors of the second case-report supposed that preservation of functionality was attributed to reconstruction of the clavicular defect. (97) However, objective comparability based

on standardized scores such as the Quick-DASH-Score or MSTS-Score was not possible, since these reports did not present results of functional or QoL-based questionnaires did not depict results of questionnaires.

A study by A. Van Tongel et al., in which 30 patients with partial or complete absence of the clavicle due to cleidocranial dysplasia were examined, provides an additional indication of the extent to which shoulder function is impaired by a missing clavicle. (114) It was shown that these patients in general do not seem to have any important limitation of shoulder girdle function. (114) In addition to describing the patients' lack of movement restriction and the functionality of the affected upper extremity, shoulder function was quantified – among other scores – by the Quick-DASH score, with an average value of 11. Although a minority of patients achieved poor scores, no significant difference could be observed between partial or complete absence of the clavicle. (114) This supports our assumption that patients can expect satisfactory functional results even after partial or complete resection of the clavicle due to tumors.

The results of this study should always be considered in light of their limitations. One major limitation of this study is its retrospective design, with results strongly dependent on the quantity and quality of medical records. Functional documentation in particular is often based on subjective observations and only briefly described in records, so that no definite conclusions can be drawn. Nevertheless, by prospectively re-examining two patients, comparable and objective statements regarding functionality after clavicle resection could be made. Another limitation, however, is the problem of obtaining a sufficiently large number of patients due to the rarity of clavicular tumors in general, as well as the restricted follow-up due to loss to follow-up or patient death. Therefore, as with any individual case report, it should be noted that the results of two patients with clavicle resection are not necessarily representative of other patients with the same disease. Furthermore, our group of six patients is rather heterogeneous regarding several factors such as age, underlying diseases or tumor entities, a well-known issue in studies about rare medical conditions.

Conclusion

In summary, by a thorough retrospective analysis of six patients with (partial) clavicle resection for malignant tumors, and the prospective evaluation of two patients, we were able to contribute to the discussion of whether the clavicle is an indispensable part of the shoulder function. According to our findings, although the clavicle is an integral component of the complex interaction between joints and movements of the upper extremity, resection may be associated with quite satisfactory results and without severe loss of function. Therefore, reconstruction after resection may not be necessary to improve functionality. However, as none of our patients underwent reconstruction after (partial) resection of the clavicle, we could only compare results from scarce previous studies with reconstruction of clavicular defects.

For everyday clinical practice, especially in such rare conditions, each individual case report represents a valuable contribution to provide potential patients the best possible evidence-based medicine. To be able to make further statements or an implication for other patients, more patient reports remain to be described in the future, especially using established questionnaires such as the Quick-DASH- and the MSTS-Score.

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