FUNCTIONAL OUTCOME OF PROXIMAL FIBULAR GRAFTING AFTER WIDE RESECTION OF DISTAL RADIUS TUMOUR IN HUSM FROM YEAR 2000 TO 2013

By
DR CHOO CHIN YIN

Dissertation Submitted In Partial Fulfillment
Of The Requirements For
The Degree Of Master Of Medicine
(Orthopaedics)

UNIVERSITI SAINS MALAYSIA
MAY 2016

ACKNOWLEDGEMENT

I wish to express my greatest gratitude to the following individuals for helping me in writing this dissertation for my master study.

First and foremost I would like to thank Dr. Norazman Md Zain and Prof. Dr. Wan Faisham Wan Ismail as my supervisor and co-supervisor for introducing this topic, guiding me and gave me full support and confidence in the process of writing this dissertation. I would also like to thank Dr. Najib Majdi Yaacob from the Unit of Biostatistics and Research Methodology (PPSP,USM) for his help in the statistical analysis and calculation.

Not forgetting Miss Nur Hazwany for helping me in understanding and solving the statistical problems arise.

Last but not least, the support from my parents and seniors that has given me the strength and inspiration to complete the dissertation.

TABLE OF CONTENTS

Chapter 3 : Research objectives and hypothesis

Chapter 4 : Methods and Materials

Chapter 5 : Results

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

GCT	Giant cell tumour
Et al.	Et alia
PMMA	Polymethylmethacrylate
MSTS	Musculoskeletal Tumor Society
DNA	Deoxyribonucleic acid
CT	Computerized tomography
MRI	Magnetic resonance imaging
CNB	Core needle biopsy
AJCC	American Joint Committee on Cancer
ISOLS	International Symposium on Limb Salvage
ASHT	American Society of Hand Therapy
HUSM	Hospital Universiti Sains Malaysia
OORU	Orthopaedics Oncology and Reconstructive Unit
HREC	Human Research Ethics Committee
HPE	Histopathological examination
X-ray	X-radiation
SD	Standard deviation
DCP	Dynamic compression plate
ABC	Aneurysmal bone cyst
FDA	Food and Drug Administration
IQR	Inter quartile range

ABSTRAK

PENGENALAN: Pembedahan kanser pada tulang radius pergelangan tangan melibatkan pembedahan rumit mengeluarkan tulang dijangkiti dan rekonstruksi pengantian tulang yang hilang. Terdapat beberapa prosedur rekonstruktif telah digunakan termasuk graf fibular vascular dan bukan vaskular, osteoarticular allograft, penggantian sendi pergelangan tangan dan ulnar translokasi. Graf fibular proximal telah digunakan untuk mengekalkan fungsi pergelangan tangan yang lebih baik kerana persamaan dalam bentuk dan saiz hujung radius. Tujuan kajian ini adalah untuk menilai semula dan membandingkan hasil fungsi antara fusion pergelangan tangan dan rekonstruktif pergelangan tangan menggunakan graf fibular proksimal selepas pembedahan pembuangan luas tumor hujung radius dengan menggunakan sistem markah MSTS.

KAEDAH: Kajian ini merupakan satu kajian keratan rentas di mana hanya satu intervensi dan penilaian dilakukan terhadap sebelas orang pesakit terpilih yang memenuhi kriteria-kriteria inklusi dan exkluusi selepas pembedahan reseksi luas tumor hujung radius dan menggunakn graf fibular proksimal untuk membentuk semula pergelangan tangan. Semua pesakit termasuk dalam kajian ini adalah dari tahun 2000 hingga 2013 dan sampel kepada dua kumpulan, iaitu rekonstruktif pergelangan tangan dan fusion pergelangan tangan. Kebolehan fungsi dinilai dan dibandingkan dengan menggunakan sistem markah MSTS. Kekuatan gengaman tangan dan kadar penyatuan tulang dinilai oleh Jamar dinamometer tangan dan filem-filem radiograf masing-masing.

KEPUTUSAN: Didapati 6 pesakit menjalani prosedur reconstruktif pergelangan tangan dan 5 pesakit menjalani fusion pergelangan tangan. Umur min pesakit ialah 36.55 tahun.

Min susulan tempoh adalah 6.3 tahun. Terdapat 9 kes gred II dan gred III GCT, 1 kes osteosarcoma dan 1 kes ABC dalam kajian ini. Pemjumlahan purata MSTS adalah dalam lingkungan 70% ke 93.3% dengan keputusan 4 baik dan 7 sangat baik. Min MSTS bagi kumpulan rekonstruktif pergelangan tangan adalah 24.83 (82.78%) dan fusion pergelangan tangan adalah 23.4 (78.0%). Purata kekuatan gengaman tangan berbanding dengan tangan sebelah yang normal adalah 60.0% bagi fusion pergelangan tangan di mana keputusannya lebih baik daripada rekonstruktif pergelangan tangan, iaitu 58.07%. Penyatuan tulang di bahagian radiofibular berlaku dalam 8 kes daripada 11 kes. Kadar penyatuan untuk rekonstruktif pergelangan tangan ialah 83.3% manakala bagi fusion pergelangan tangan adalah 60%. Pengecualian 3 kes yang gagal mencapai penyatuan, masa purata bagi cantuman adalah 18.4 minggu untuk rekonstruktif pergelangan tangan dan 18.7 minggu untuk fusion pergelangan tangan. Tiada kes ulangan tumor dan semua pesakit sekarang bebas daripada tumor.

KESIMPULAN: Pembedahan graf fibular proksimal selepas reseksi luas tumor tulang hujung radius adalah baik ke sangat baik bagi markah MSTS untuk kedua-dua rekonstruktif dan fusion pergelangan tangan. Satu penemuan penting ialah skor untuk komponen sakit dalam MSTS lebih unggul dalam fusion pergelangan tangan. Walau bagaimanapun, di antara kedua-dua prosedur ini, tidak menghasilkan keputusan yang berbeza bagi jumlah MSTS skor. Komplikasi yang paling biasa yang dihadapi adalah subluxation di pergelangan tangan bagi kumpulan pembedahan rekonstruktif pergelangan tangan.

ABSTRACT

INTRODUCTION : Distal radius bone tumour surgery is a complicated and challenging procedure which includes resection of the affected bone and reconstruction of the bony defect. Several reconstructive procedures have been described including vascularized and non-vascularized fibular graft, osteoarticular allograft, prosthetic replacement and ulnar translocation. The proximal fibular graft was used in order to preserve better wrist function due to its similarity in shape and size to the distal radius. The aim of this study is to evaluate and compare the functional outcome between total wrist fusion and wrist reconstruction with proximal fibular grafting after wide excision of distal radius tumour by using Musculoskeletal Tumor Society scoring system (MSTS).

METHODS : This study was a cross-sectional, single intervention and retrospectively assessed the selected eleven patients with distal radius bone tumour who had wide excision and reconstructive surgery done with proximal fibular autograft that fulfilled the inclusion and exclusion criteria. All the patients recruited in this study were from year 2000 to 2013 and sampled into two groups; the wrist reconstruction and total wrist fusion groups. Functional outcome was evaluated and compared by using Musculoskeletal Tumour Society scoring system (MSTS). Hand grip strength and union rate were assessed by Jamar hand dynamometer and plain radiographs respectively.

RESULTS : There were 6 patients underwent wrist reconstruction procedure and 5 patients underwent total wrist fusion. The mean age of patients was 36.55 years old. Mean follow up period was 6.3 years. There were 9 patients with Campanacci grade II to grade III giant cell tumours, 1 patient with osteosarcoma and 1 patient with aneurysmal bone

cyst in this study. Overall musculoskeletal tumor society (MSTS) score range from 70% to 93.3%, with 4 good and 7 excellent results. The mean MSTS score for wrist reconstruction group was 24.83 (82.78%) and total wrist fusion group was 23.4 (78.0%). Average grip strength compared to the contralateral hand was 60.0% for total wrist fusion which was better than wrist reconstruction, 58.07%. Radiofibular union occurred in 8 out of 11 cases. The union rate for wrist reconstruction was 83.3% whereas for total wrist fusion was 60%. Excluding the 3 non-union cases, average time for union was 18.4 weeks for the wrist reconstruction and 18.7 weeks for the total wrist fusion. There was no tumour recurrence and all the patients were disease free.

CONCLUSION : Proximal fibular grafting after wide excision of distal radius bone tumour had good to excellent MSTS score for both wrist reconstruction and total wrist fusion. The only significant finding was the scoring for pain component in MSTS was more superior in total wrist fusion. However, there was no significant difference for the overall MSTS score between these procedures. The most commonly encountered complication was fibulocarpal subluxation which found in wrist reconstruction group.

Chapter 1: Introduction

Distal radius is not a common site for malignant or aggressive benign bone tumor. Surgical resection of distal radius tumour creates a massive bony defect and it warrants reconstruction in order to achieve functional painless wrist and good hand function. Few options, including resection arthroplasty (Campanacci M. *et al*., 1979), use of a non-vascularised (Aithal V.K. *et al*., 2003; Cheng C.Y. *et al*., 2001; Maruthainar N. *et al.*, 2002) or vascularised autogenous fibular graft (Ferracini R. *et al*., 1999; Koichiro I. *et al*., 1999; Pho R.W., 1981) and allograft replacement (Kocher M.S. *et al*., 1998), prosthetic replacement (Gold A.M., 1965), ulnar translocation (Seradge H., 1982) and arthrodesis (Campbell C.J. *et al*., 1975; Vander Griend R.A. *et al*., 1993; Murray J.A. *et al*., 1986) have been used for reconstruction of this bone defect. Currently, custom megaprosthesis was also used to reconstruct the distal radius osseous defect.

In attempt to preserve better wrist function, the proximal fibular graft (vascularised or nonvascularised) is sometimes used for reconstruction due to its similarity in shape and size to the distal radius. Fibula reconstruction achieves good functional results with satisfying range of motion, but instability and degenerative change of carpofibular joint are frequently observed due to the relatively incongruence of carpofibular articular surfaces. Several authors have advocated arthrodesis rather than arthroplasty in view of high incidence of degenerative changes of carpofibular joint and carpal subluxation in later.

From the literature, only small number of published researches with small sample size or case reports found in related to the reconstruction procedure and

outcomes for distal radius bone tumour. The rationale behind this study is to assess and compare the functional performance in between total wrist fusion and wrist reconstruction and radiofibular union rate with proximal fibular graft after excision of distal radius tumour which involving a larger sample size especially in total wrist fusion group in which the outcome of this procedure was not commonly reported. The use of more rigid fixation with plate and screws especially in total wrist fusion may jeopardize the fibular graft and affect the union rate. We did assess the proximal union rate in between these two procedures. We also assessed grip strength of the operated hand and patients' hand function by using Musculoskeletal Tumor Society scoring system (MSTS). Thus, we can predict the functional outcome and use it as a guide for us to counsel patient prior to surgical procedures.

Chapter 2: Literature Review

2.1 Overview of bone tumour

Primary skeletal neoplasms account for 0.2% of human tumours, whereas involvement of skeletal tissue by metastatic disease is much more common. Bone tumours are neoplastic growth of tissues in the bone. They are rare and heterogeneous group of tumous. Abnormal growths found in the bone can be either benign or malignant.

In the past two decades, survival and the quality of life of patients with bone sarcomas has dramatically improved as a result of the multimodality treatment approach. Surgery, used in combination with chemotherapy and radiation therapy, can achieve cure in the majority of patients with bone sarcomas and resection is performed instead of amputation in more than 90% of all patients.

2.1.1 Classification of bone tumour

Bone tumours may be classified as "primary tumours", which originate in bone or from bone-derived cells and tissues, and "secondary tumours" which originate in other sites and spread (metastasize) to the skeleton. Carcinomas of the prostate, breasts, lungs, thyroid, and kidneys are the carcinomas that most commonly metastasize to bone. Secondary malignant bone tumours are estimated to be 50 to 100 times as common as primary bone cancers. Because these lesions are so rare, not much pathologists have sufficient experience to deal comfortably with their diagnosis. This is further compounded by the steady evolution in the classification of bone tumours, which is based on their biological behaviours, ultrastructure and results of immunohistochemical and cytogenetic studies.

Bone tumours are usually classified according to the type of matrix production for example osseous, cartilaginous, fibrous, cystic, giant cell, round cell and etc. Sarcomas originate primarily from elements of the mesodermal embryonic layer. Osteoid-producing sarcomas are classified as osteosarcomas and chondroid-producing sarcomas are classified as chondrosarcomas. The most common bone sarcomas are osteosarcoma, chondrosarcoma, and Ewing's sarcoma. Common benign bone tumours are endochondroma, osteochondroma, nonossifying fibroma, chondroblastoma, osteoid osteoma, osteoblastoma, giant cell tumour, aneurysmal bone cyst and etc.

Table 2.1 : Classification of primary bone tumours

HISTOLOGIC TYPE	BENIGN	MALIGNANT
Hematopoietic (41.1%)		Myeloma Lymphoma
Chondrogenic (20.9%)	Osteochondroma Chondroma Chondroblastoma Chondromyxoid fibroma	Primary chondrosarcoma Secondary chandrosarcoma Dedifferentiated chondrosarcoma Mesenchymal chondrosarcoma Clear cell chondrosarcoma
Osteogenic (19.3%)	Osteoid osteoma Osteoblastoma	Parosteal osteosarcoma Periosteal osteosarcoma
Unknown Origin (9.8%)	Giant cell tumour Fibrous histiocytoma	Ewing's sarcoma Malignant giant cell tumour Adamantinoma

Fibrogenic (3.8%)	Fibroma Desmoplastic fibroma	Fibrosarcoma Malignant fibrous histiocytoma
Notochordal (3.1%)		Chordoma
Vascular (1.6%)	Hemangioma	Hemangioendothelioma Hemangiopericytoma
Lipogenic (<0.5%)	Lipoma	
Neurogenic (<0.5%)	Neurilemoma	

2.1.2 Biology behaviour of tumour

Tumours arising in bone tissues have characteristic patterns of biological behaviour because of their common mesenchymal origin and anatomical environment. These unique patterns form the basis of the staging system and current treatment strategies. Histologically, sarcomas are graded as low, intermediate or high grade. The grade is based on tumour morphology, extent of pleomorphism, atypia, mitosis, and necrosis. It represents its biological aggressiveness and correlates with the likelihood of metastases.

Sarcomas form a solid mass that grows centrifugally with the periphery of the lesion being the least mature. In contradistinction to the true capsule that surrounds benign lesions, which is composed of compressed normal cells; sarcomas are generally enclosed by a reactive zone or pseudocapsule. The thickness of the reactive zone varies with the histogenic type and grade of malignancy.

Sarcomas respect anatomical borders. Local anatomy influences tumour growth by setting natural barriers to extension. In a later stage the walls of that

compartment are violated (either the cortex of a bone or aponeurosis of a muscle), and the tumour breaks into a surrounding compartment.

The biology behaviour of certain benign bone tumours can be infrequent and unpredictable. Although numerous attempts have been made to predict the behaviour of GCT, there are no definite biologic or histologic parameters to determine the prognosis or aggressiveness of this lesion. Histological grading has proved to be of little value and since there is a great need for indicators of how aggressive the treatment should be in each particular tumour, different promising alternatives had been explored e.g. DNA cytophotometry and proliferation index, gene expression of vascular endothelial growth factor, in-vitro proliferation of neoplastic stromal cell population and etc.

2.1.3 Etiology of bone tumour

Although bone tumour does not have a clearly defined cause, they often occur in areas of rapid bone growth. Researchers have identified several factors that increase the likelihood of developing these tumours.

The risk factors for bone sarcomas include previous radiation therapy, exposure to chemicals (e.g., vinyl chloride, arsenic), immunodeficiency, prior injury (scars, burns), chronic tissue irritation (foreign-body implants, lymphedema), neurofibromatosis, Paget's disease, bone infarcts, and genetic cancer syndromes (hereditary retinoblastoma, Li–Fraumeni syndrome, Gardner's syndrome).

The incidence of bone tumours are also increased in families with familial cancer syndromes. The incidence of bone tumour in children is approximately 5 cases per million children each year. In most patients, however, no specific etiology can be identified.

2.2 Evaluation of bone tumour

2.2.1 Clinical Presentation

An adequate history and physical examination are the first and most important steps in evaluating a patient with a musculoskeletal tumour. Clinically, bone tumours may present in various ways. Patients may present to the orthopaedic oncologist with pain, a mass, or an abnormal radiographic finding detected during the evaluation of an unrelated problem. The more common benign lesions are frequently asymptomatic and are detected as incidental findings. Many tumours, however, produce pain or are noticed as a slow-growing mass. Sometimes, the first hint of a tumour's presence is a sudden pathologic fracture. Radiographic analysis plays an important role in diagnosing these lesions.

Patients with bone tumours most frequently present with pain. The pain initially may be activity related, but a patient with a malignancy of bone often complains of progressive pain at rest and at night. Patients with benign bone tumours also may have activity-related pain if the lesion is large enough to weaken the bone.

Although some tumours show a sex predilection (e.g., female predominance with giant cell tumours), this is rarely of diagnostic significance. Race likewise is of

little significance, with the exception that Ewing sarcoma is exceedingly rare in individuals of African descent. Family history occasionally can be helpful, as in cases of multiple hereditary exostosis (autosomal dominant inheritance) and neurofibromatosis (autosomal dominant inheritance). Age may be the most important information obtained in the history because most benign and malignant musculoskeletal neoplasms occur within specific age ranges.

2.2.2 Physical Examination

The physical examination should include evaluation of the patient's general health and a careful examination of the part in question. A mass should be measured, and its location, shape, consistency, mobility, tenderness, local temperature and change with position should be noted. Atrophy of the surrounding musculature should be recorded, as should neurological deficits and adequacy of circulation. Cafe-au-lait spots or cutaneous hemangiomas also may provide diagnostic clues. Potential sites of lymph node metastases should be palpated. Although lymph node metastases are rare with most sarcomas, they often are present with rhabdomyosarcomas, epithelioid sarcomas, and synovial sarcomas. When metastatic disease is suspected the thyroid gland, lungs, abdomen, prostate and breast should be examined as appropriate.

2.2.3 Radiography

Imaging studies play an important role in providing the exact location and extent of the tumour, detect features that help limit diagnostic possibilities and give clues to the aggressiveness of the tumour.

2.2.3.1 Plain radiograph

Plain radiographs remain the key imaging modality in the evaluation of bone tumours. Based on medical history, physical examination and plain radiographs, accurate diagnosis of bone tumours can be made in more than 80% of cases. Because of the fine trabecular detail revealed by plain radiographs, bone lesions of the extremities can be detected at a very early stage. Whereas lesions of the spine and pelvis are not diagnosed until a large volume of bone has been destroyed.

2.2.3.2 Computerized tomography (CT) scan

Computerized tomography (CT) scan should be performed on a helical scanner that enables improved two-dimensional images and three dimensional reconstruction capability. The field of view should be small enough to allow adequate resolution, particularly of the lesion and the adjacent neurovascular bundle and muscle groups. The slice thickness should be designed in order to allow at least 10–15 slices through the tumour. Intravenous contrast dye is of little value in the evaluation of bone tumours. Once a bone lesion is found on plain radiograph, CT scan is the imaging modality of choice to evaluate the extent of bone destruction.

2.2.3.3 Magnetic resonance imaging (MRI)

MRI is a valuable tool in the evaluation of the medullary and soft-tissue components of bone tumours. The signal intensity of a tumour is assessed by comparing it with that of the adjacent soft tissues, specifically skeletal muscle and subcutaneous fat. MRI also enables one to view a lesion in all three planes (axial, sagittal, and coronal). Contrast- enhanced MRI is useful in evaluating the relationship of a tumour to the adjacent blood vessels and in characterizing cystic lesions. MRI has

been proven to be superior to CT in the evaluation of the intramedullary and extraosseous, extent of bone tumours. The general guidelines regarding narrowing of the field and recommended number of slices per tumour are similar to those of CT scan.

2.2.4 Biopsy

Biopsy is a key step in the diagnosis of a musculoskeletal tumour. In a book published in 1958, Jaffe stated that a biopsy should be regarded as the final diagnostic procedure, not as a mere short cut to diagnosis (Jaffe H. L., 1958). Biopsy must be preceded by careful clinical evaluation and analysis of the imaging studies.

In the past, biopsies were performed routinely through a large incision with significant contamination of the surrounding soft tissues with tumour cells. The contamination however had minimal significance because most malignant tumours of the extremities and pelvis were treated with amputation. Today, limb sparing procedures are performed in 90–95% of patients with musculoskeletal tumours of the extremities, and indications and surgical technique of musculoskeletal biopsy had to be changed to allow these procedures to be performed (Chang A. E., Sondak V. K., 1995; Simon M. A. 1982)

The position of the biopsy site within the lesion has a major significance because bone tumours may have regional morphologic variations (Enneking W. F., 1983; Dorfman H. D. *et al*., 1988; Chang A. E. *et al*., 1995). As a result of that heterogeneity, multiple samples are required to establish a diagnosis. The biopsy incision or the needle puncture hole, and the tract to the tumour, must be made with

the planned surgical incision site so that they will be included within the surgical specimen. Preferably, the surgeon performing the biopsy will be the same person who will perform the definitive procedure.

Open incisional biopsy is a reliable diagnostic method because it allows the pathologist to evaluate cellular morphologic features and tissue architecture from different sites of the lesion.

Needle biopsy of mesenchymal tumours was criticized because the quantity of biopsy material was often insufficient for routine histopathologic evaluation and ancillary studies that require tissue. It has been shown to be a reliable technique only for the diagnosis of soft-tissue tumours when the cell type of the tumour is homogeneous.

Core needle biopsy (CNB) provides a core of tissue with a maximum length of 20 mm, was shown to be more than 90% accurate in differentiating malignant from benign lesions (Heslin M. J. *et al.,* 1997). In most patients with suspected bone sarcomas it is the biopsy performed before initiation of treatment. It should be performed under CT or fluoroscopy guidance, and multiple cores should be obtained.

Open biopsy is performed when the pathologic diagnosis either is inconclusive or does not correlate with the clinical presentation and radiologic findings.

Poorly performed biopsy remains a common issue in patients with musculoskeletal tumours who are referred to orthopaedics oncology centers. An

inadequately performed biopsy may fail to allow proper diagnosis, have a negative impact on survival and ultimately necessitate an amputation to accomplish adequate margins of resection.

2.3 Staging of bone tumours

Staging is the process of classifying a tumour with respect to its degree of differentiation, as well as its local and distant extent, in order to plan the treatment and estimate the prognosis. Staging allows the surgeon to determine the type and the extent of the operation that is necessary for a specific type of tumour in a particular anatomical location, as well as the indication for neoadjuvant treatment modalities. Staging of a musculoskeletal tumour is based on the findings of the physical examination and the results of imaging studies. Biopsy and histopathological evaluation are essential components of staging, but should always be the final step. (Barry Schmookler *et al*., 2001)

The Musculoskeletal Tumour Society adopted staging systems that were originally described by Enneking *et al.* (Enneking W. F. *et al*., 1980; Enneking W. F., 1983), for benign and malignant bone tumours, and the American Joint Committee on Cancer developed, with few changes, a staging system for malignant bone tumours (Fleming I. D. *et al.,* 1997).

Enneking staging system of benign tumours are designated by Arabic numbers, and malignant tumours are designated by Roman numerals. Enneking's staging system is based on three factors: histological grade (G), site (T) and the presence or absence of metastases (M). The anatomical site (T) may be either intracompartmental (A) or extracompartmental (B). This information is obtained preoperatively on the basis of

the data gained from the various imaging modalities. A tumour is classified as intracompartmental if it is bounded by natural barriers to extension such as bone, fascia, synovial tissue, periosteum or cartilage. An extracompartmental tumour may be either a tumour that violated the borders of the compartment from which it originated, or a tumour that originated and remained in the extracompartmental space. A tumour is assigned to stage III (M1) if a metastasis is present at a distant site or in a regional lymph node.

Enneking also described a staging system of benign bone tumours, which remains the one that is most commonly used (Enneking W. F., 1983) (Table 2.2). This system is based on the biological behaviour of the tumours as suggested by their clinical manifestation and radiological findings. Benign bone tumours grow in a centrifugal fashion and a rim of reactive bone is typically formed as a response of the host bone to the tumour. The extent of that reactive rim reflects the rate at which the tumour is growing. It is usually thick and well-defined around slowly growing tumours, and barely detectable around fast-growing, aggressive tumours.

Latent benign bone tumours are classified as stage 1. Such tumours are usually asymptomatic and are commonly discovered as an incidental radiographic finding. The natural history is it grows slowly during normal growth of the individual and then to stop, and in most cases it heals spontaneously. These lesions usually heal following simple curettage.

Active benign bone tumours are classified as stage 2 lesions. These tumours grow progressively but do not violate natural barriers. Associated symptoms may occur. Curettage and burr drilling are curative in most cases.

Aggressive benign bone tumours are classified as stage 3. It may cause destruction of surrounding bone and usually break through the cortex into the surrounding soft tissues. Local control can be achieved only by curettage and meticulous burr drilling with a local adjuvant such as liquid nitrogen or by resection of the lesion with a margin of normal tissue (i.e., wide resection).

Table 2.2 : Enneking's System for Staging Benign and Malignant Bone Tumours

Enneking's System for Staging Benign and Malignant Bone Tumours			
BENIGN			
1. **Latent**—low biological activity, remains static or heals spontaneously. Well marginated; often incidental findings. (i.e., nonossifying fibroma)			
2. **Active**—Progressive growth, limited by natural barriers. Symptomatic, limited bone destruction may present with pathological fracture (i.e., aneurysmal bone cyst)			
3. **Aggressive**— Progressive growth, invasive, not limited by natural barriers. Bone destruction/soft tissue extension; do not respect natural barriers (i.e., giant cell tumour)			
MALIGNANT			
STAGE	**GRADE**	**SITE**	**METASTASES**
IA	Low	Intracompartmental	None
IB	Low	Extracompartmental	None
IIA	High	Intracompartmental	None
IIB	High	Extracompartmental	None
III	Any	Any	Regional or distant metastases

Alternatively, many orthopaedic oncologists stage musculoskeletal malignancies according to the American Joint Committee on Cancer (AJCC) system (Fleming I. D. *et al.*, 1997). The AJCC staging system for bone sarcomas is based on tumour grade, size, and presence and location of metastases. Stage I tumours, which are low grade; and stage II tumours, which are high grade, are subdivided based on

tumour size. Stage I-A and II-A tumours are 8 cm or less in their greatest linear measurement; stage I-B and II-B tumours are larger than 8 cm. Stage III tumours have "skip metastases," which are defined as discontinuous lesions within the same bone. Stage IV-A involves pulmonary metastases, whereas stage IV-B involves non-pulmonary metastases.

Table 2.3 : American Joint Committee on Cancer System for Staging Bone Sarcomas

American Joint Committee on Cancer System for Staging Bone Sarcomas			
STAGE	**GRADE**	**SIZE**	**METASTASES**
I-A	Low	≤8 cm	None
I-B	Low	>8 cm	None
II-A	High	≤8 cm	None
II-B	High	>8 cm	None
III	Any	Any	Skip metastasis
IV-A	Any	Any	Pulmonary metastases
IV-B	Any	Any	Nonpulmonary metastases

However for giant cell tumour (GCT), besides Enneking's grading system for benign bone tumour, Campanacci (Campanacci M. *et al.*, 1987) had also designed a staging system based on radiological appearance of cortical involvement.

Stage 1 : Intraosseous lesion. Radiographically well-circumscribed lucent lesion with no aggressive features (eg, periosteal reaction, soft-tissue mass, cortical breach).

Stage 2 : Intraosseous lesion with cortical thinning. Relatively well-defined radiographic borders without a radiopaque rim

Stage 3 : Extraosseous lesion. Indistinct or ill-defined borders with radiographic demonstration of cortical bone destruction, and a soft-tissue mass.

A high grade tumour and evidence of tumour metastasis are associated with poor prognosis for all malignant bone tumours regardless of the staging system that is used.

2.4 Overview management of bone tumour

The management of bone tumours has made vast strides in the last few decades. The advent of better imaging modalities, more effective chemotherapy, improved radiotherapy techniques, a better understanding of anatomy with continuous refinement in surgical techniques and advances in prosthesis design and materials have all played a part in increasing the incidence of limb salvage surgery. Limb salvage surgery includes all of the surgical procedures designed to accomplish removal of a tumour and reconstruction of the limb with an acceptable oncologic, functional and cosmetic result. From an era where amputation was the only option, the current day function preserving resections and complex reconstructions have been a major advance.

Though the number of limb salvage surgeries undertaken for malignant bone tumours of the extremity has increased, the principles that govern surgical resection of bone tumours remain unchanged. Tumour recurrence, metastasis and a generally dismal prognosis were a powerful deterrent to progress in limb salvage treatment.

2.4.1 Types of surgical resections

There are four basic types of excisions, each is based on the relationship of the dissection plane to the tumour and its pseudocapsule.

i. An **intralesional** excision is performed within the tumour mass and results in removal of only a portion of it, the pseudocapsule and macroscopic tumour are left behind.

ii. In a **marginal** excision, the dissection plane passes through the pseudocapsule of the tumour. Such a resection may leave microscopic disease.

iii. **Wide** (en-bloc) excision entails removal of the tumour, its pseudocapsule, and a cuff of normal tissue peripheral to the tumour in all directions. This is the desired margin for sarcoma resection, however the adequate thickness of the normal tissue cuff is a matter of controversy. For bone sarcomas, it is generally believed to be a few centimetres.

iv. **Radical** excision involves removal of the tumour and the entire anatomical compartment within which it is located (Figure 2.1). This excision can achieve a marginal or a wide margin, depending on how close the tumour is to the border of the compartment. However, radical excision excludes the possibility of skip metastases.

Depending on the pathology and aggressiveness of the lesion, it is important to plan a surgical procedure capable of obtaining the desired margins for local control. A benign giant cell tumour can be adequately managed with an intralesional procedure whereas an aggressive giant cell tumour would require a wide excision in order to gain adequate local disease clearance.

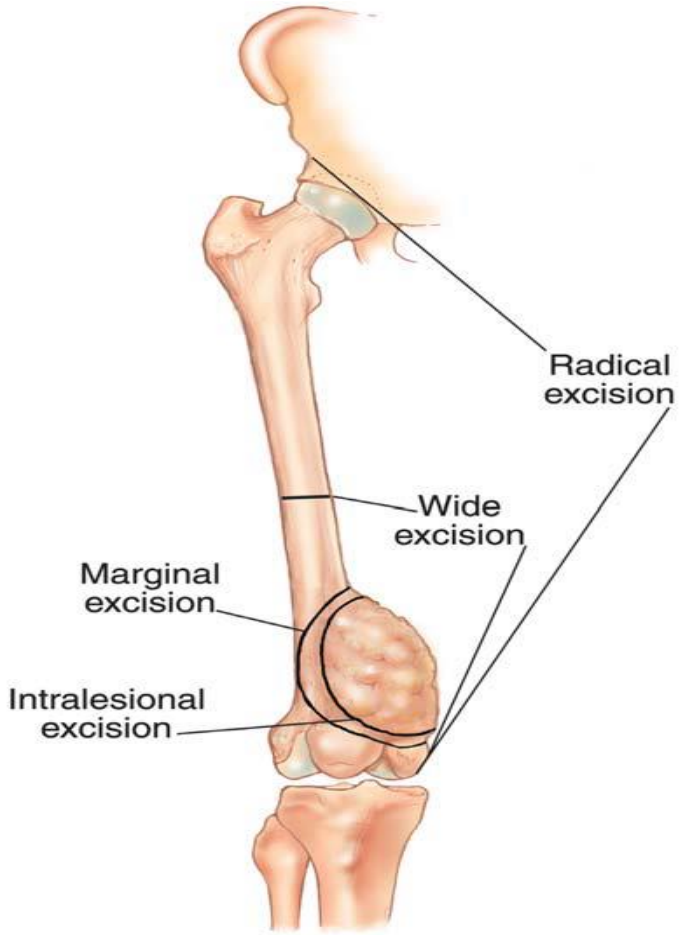

Figure 2.1 : Various excision types for bone tumour (Musculoskeletal Cancer Surgery, 2001)

Any of these excision types may be accomplished by a limb-salvage procedure or by amputation. An amputation is not necessarily an adequate cancer operation, but it is a method of achieving a specific margin. It may entail a marginal, wide or radical excision, depending upon the plane in which it passes. Staging studies are used to assess local tumour extent and relevant local anatomy, and thereby determine how a desired surgical margin may be achieved.

2.5 Overview of distal radius tumours

2.5.1 Giant cell tumour (GCT)

Giant cell tumors of bone are benign lesions that can be locally aggressive. It is a type of giant cell-rich lesion of bone. This benign mesenchymal tumor has characteristic multinuclear giant cells. Mononuclear stromal cells are the physiologically active and diagnostic cell type. Most GCTs are located in the epiphyseal regions of long bones. Although the distal radius is an untypical location, about 10 percent of all giant cell tumour (GCT) affects this part of the skeleton (Campanacci M. *et al.*, 1987; Dahlin D.C. *et al.*, 1970; Goldenberg R.R. *et al.*, 1970; Eckardt J. J. *et al.*, 1986; McDonald D. J. *et al.*, 1986). It represents the third most common location after the distal part of the femur and the proximal part of the tibia (Campanacci M. *et al.*, 1987).

These tumors are typically treated with local resection and/or curettage. Radiation therapy is selectively used for tumors in difficult to resect locations (i.e. spine). Intralesional curettage with or without adjuvant therapy (eg. phenol, bone graft or polymethylmethacrylate) is the procedure of choice for less aggressive lesions over distal radius without marked bone or joint destruction (Apichat A. *et al.*, 2009). There is a high rate of local recurrence after most methods of local treatment for aggressive benign bone tumour. Therefore wide resection of the tumour and reconstruction in this location might be necessary in aggressive cases which exhibit extraosseous extension or recurrence after previous treatment.

Metastatic spread to the lungs is rare, about 2 to 5%. Risk factors for lung metastasis include local recurrence, the location of the primary giant cell tumor (distal radius, proximal femur, and sacrum), Stage 3 GCT and an immunocompromised state.

The clinical course is marked by indolence in character in which some are self-limiting in nature while others may have spontaneous regression but about 25% can caused death by pulmonary failure (Rock M.G.,1984 ; Kay R.M. *et al.*, 1994). Therefore, early detection is important with plain x-ray of primary site and chest, CT-thorax and bone scan. These imaging studies are repeated during follow-up for further evaluation.

2.5.2 Osteosarcoma

Osteosarcoma, the most common bone sarcoma, affects children and adolescents. It is a mesenchymally derived, high-grade bone sarcoma. The incidence of new diagnoses peaks in the second decade of life. Twenty percent of patients present with clinically detectable metastases, with micrometastases presumed to be present in many of the remaining patients.

The most frequent sites of origin are the distal femur, proximal tibia and proximal humerus. Patients typically present with pain, swelling, localized enlargement of the extremity and, occasionally, pathologic fracture. Most patients present with localized disease. Radiographs commonly demonstrate a mixed sclerotic and lytic lesion arising in the metaphyseal region of the involved bone. Computed tomography and bone scanning are recommended to detect pulmonary and bone metastases, respectively.

The wrist is uncommon sites for osteosarcomas. Less than 1% of osteosarcomas arise in the distal radius (KK Unni, 1996). Patients with wrist osteosarcomas are older than those with osteosarcomas in other sites and have a better prognosis (K Okada et al., 1993).

The treatment of osteosarcoma requires a multidisciplinary approach involving the family physician, orthopedic oncologist, medical oncologist, radiologist and pathologist. Before 1970, osteosarcomas were treated with amputation. Survival was poor: 80 percent of patients died from metastatic disease. With the development of induction and adjuvant chemotherapy protocols, advances in surgical techniques and improvements in radiologic staging studies, 90-95 percent of patients with osteosarcoma can now be treated with limb-sparing resection and reconstruction.

Limb-salvage procedures with wide surgical margins are the mainstay of surgical intervention. A combination of advances in surgical technique, improved imaging modalities to accurately document tumor extent, and the effect of neoadjuvant chemotherapy has made limb salvage procedures a safe alternative to amputation. Adjuvant chemotherapy plays an essential role in the control of subclinical metastatic disease. In some patients for whom complete surgical excision is impossible, the addition of radiation therapy may allow local tumor control.

Advances in chemotherapy protocols have led to a 5-year survival rate of 60% to 78%. The most effective chemotherapy agents currently in use include high-dose methotrexate, doxorubicin, cisplatin, and ifosfamide/etoposide. Among the goals of future treatment regimens are improved chemotherapeutic agents with higher specificity and lower toxicity.

2.5.3 Ewing's sarcoma

Ewing's sarcoma is a primitive malignant bone tumour consisting of small, blue, round malignant cells that may show varying degrees of neural differentiation. It accounts for approximately 5% of all malignant bone tumours. Ewing sarcoma of bone

represents the second most common primary malignant tumor of bone in children and adolescents, exceeded in prevalence only by osteosarcoma. It is the fourth most common primary bone tumour following myeloma, osteosarcoma and chondrosarcoma. It is rare in patients younger than 5 or older than 30 and the highest frequency of this malignancy occurs in patients between 10 and 15 years old. Ewing's sarcoma is more frequent in males than females (3:2) and is rare in Blacks and Asians.

There is a wide skeletal distribution for Ewing sarcoma. The long bones and the pelvis are most commonly affected. The femur is affected in 20-27% of tumours, the tibia and fibula in 15-23% and the humerus in 8-11%. Lesions are classically located in the diaphysis of long bones but can be metaphyseal-epiphyseal with almost equal frequency. The pelvic girdle accounts for 20-26% of the tumours and the ribs 7-11%. Any portion of any bone can be affected but hand or foot (3-6%), radius or ulna (3-5%), skull (1%) or sternum (0.2%) is rarely reported.

Modern combined modality therapies with multiagent chemotherapy have given a significant improvement in the prognosis of Ewing's sarcoma of bone (5-year survival rates have increased from 10-15% to 65-70% in the last 40 years). However, lesser improvements have been seen for patients with metastatic or recurrent disease with a 5-year survival rate of less than 10-35%. Small, distal extremity lesions have a good prognosis, whereas patients with metastatic disease at presentation, large lesions, proximal or axial lesions or recurrent disease have a less favourable prognosis.

The treatment of Ewing's sarcoma of bone is currently based on combined therapy with neoadjuvant chemotherapy, radiation therapy and surgical resection of the primary tumour. Due to the complexity of treatment, it is mandatory for the members of the multidisciplinary team (oncologists, surgeons, radiation oncologists as

well as pathologists and radiologists) to cooperate closely to customize treatments to the histologic response and tumour volume and site, in order to offer the best treatment for each patient. Neoadjuvant chemotherapy is effective for shrinking the primary tumour and management of potential metastatic disease. Standard therapy for localized Ewing's sarcoma includes preoperative induction chemotherapy (4-5 cycles) and local treatment with surgery and/or radiotherapy.

. The role of surgery for local control has gained importance. Surgical resection with adequate margins remains one of the most important prognostic factors for Ewing's sarcoma. The role of surgery and radiation for local disease is still controversial but surgery gives better disease free survival (DFS) than radiotherapy alone. Early results from the EICESS92 study show that significantly better DFS and overall survival (OS) occur with multimodality treatment, i.e. a combination of chemotherapy, surgery and radiotherapy. (Paulussen M. *et al*., 2008)

Many centres advocate resection of the lesion after neoadjuvant chemotherapy, and radiation for positive or inadequate surgical margins. Currently, limb salvage surgery is recommended whenever possible.

Lesions arising in the pelvis or centrally located (sacrum, spine) remain surgically challenging and should be carefully evaluated by the multidisciplinary team: radiotherapy may be the best choice for large volume axial bone tumours or unresectable lesions, in order to avoid unacceptable mutilating surgery.

Metastases are predominantly haematogenous. The lung is the most common site of metastasis, followed by bone and bone marrow. The incidence of metastatic disease at the time of diagnosis ranges from 15% to 35%. The risk of distant

metastasis with a localized tumour is around 40-50%. Metastasis to regional or distal lymph nodes is unusual.

2.6 Overview of surgical treatment of wrist bone tumours

The wrist is uncommon area for bone tumours. Large series of limb salvage procedures in these areas are available. In general, benign bone tumours are adequately treated by either an intralesional procedure (eg. curettage and burr drilling, cryosurgery) or by marginal excision. For aggressive benign bone tumours or recurrence cases, wide resection of tumour and reconstruction, with or without medical therapy (eg. Bisphosphonate or Denosumab) is the treatment option. Primary bone sarcomas, multidisciplinary treatment with wide surgical resection and reconstruction, radiation and/or chemotherapy is used to maximize local and systemic control. Metastatic tumour are treated according to the general intent of the surgery. When a palliative surgery is performed, metastatic lesions are treated by an intralesional procedure. If a curative procedure is performed, as in the case of solitary breast metastasis, for example, the lesion is treated as if it was a primary bone sarcoma (ie, wide excision).

2.6.1 Distal radius anatomy

The wrist is a complex joint that bridges the hand to the forearm. It is actually a collection of multiple bones and joints. The bones comprising the wrist include the distal ends of the radius and ulna, 8 carpal bones, and the proximal portions of the 5 metacarpal bones.

All of these bones participate in complex articulations that allow variable mobility of the hand. Relative to the forearm, the hand is capable of 3 degrees of