International Journal of Medical and Pharmaceutical Research
Website: https://ijmpr.in/ | Print ISSN: 2958-3675 | Online ISSN: 2958-3683
NLM ID: 9918523075206676
Volume: 4 Issue:5 (Sept-Oct 2023); Page No: 115-123

Original Article

Role of MRI in Determining Limb Salvage for Musculoskeletal Tumours

Dr. Sourav Tripathy[1]*, Dr. Suresh A[2], Dr. Seema U[3], Dr. Soham Shrivastava[1], Dr. Tanmoy Bihari Das[1]

[1] MBBS, MD; Department of Radio-Diagnosis, Vydehi Institute of Medical Sciences & Research centre, Bangalore
[2] Professor & HOD; Department of Radio-Diagnosis, Vydehi Institute of Medical Sciences & Research centre, Bangalore
[3] Assistant Professor; Department of Radio-Diagnosis, Vydehi Institute of Medical Sciences & Research center, Bangalore

ABSTRACT

Background: Musculoskeletal tumors pose significant diagnostic and treatment challenges. Accurate assessment of these tumors is critical for therapeutic decision-making, especially concerning limb salvage surgeries. Magnetic Resonance Imaging (MRI) offers detailed visualization, making it an invaluable tool in the evaluation of the extent and nature of such tumors.

Aims and Objectives: To assess the involvement patterns of bone, periosteal, and soft tissue in musculoskeletal tumors through MRI.

To correlate the findings of operable MRI cases with the results observed during intraoperative procedures.

Methods: After securing ethical committee clearance and informed consent, 60 patients with musculoskeletal tumors were referred to our department for an MRI study. Based on these MRI findings, plans for limb salvage surgeries were coordinated by both surgical oncology and orthopedics teams.

Results: Our cohort study's diagnostic accuracy, sensitivity, and specificity are detailed for each study variable. The mean age of participants was found to be 27.75 +/-14.97 years, with a notable male dominance (Male: Female ratio of 2.5:1). Separate sections elucidate the skeletal distribution, tumor nature, periosteal reactions, articular surface, soft tissue, neurovascular bundles, and intra-medullary involvements observed in our study. The sensitivity, specificity, and diagnostic accuracy of MRI stand at 97.6%, 94.4%, and 70% respectively.

Conclusion: This highlights MRI's pivotal role as the preferred modality in delineating the scope of musculoskeletal tumors, stressing its utility in ascertaining tumor invasion extents and its importance in preoperative evaluations and treatment assessments.

Key Words: *Musculoskeletal tumors, limb salvage, MRI*

***Corresponding Author**
Dr. Sourav Tripathy*
MBBS, MD; Department of Radio-Diagnosis, Vydehi Institute of Medical Sciences & Research centre, Bangalore

INTRODUCTION

Limb-salvage surgery for tumours of musculoskeletal system is preceded by X-ray and MRI for surgical planning. Bone, cartilage, and soft tissue tumours are common in the musculoskeletal system. Pain and edema are common complaints in patients with musculoskeletal tumours. Malignant musculoskeletal tumours are a leading cause of morbidity and mortality due to their fast and invasive growth [1].

In children, the prevalence of primary malignant bone tumours is significantly lower than that of benign bone tumours, with malignant bone tumours accounting for only 6% of all bone tumours [2]. Osteosarcomas and Ewing sarcomas account for more than 90% of initial malignant bone tumours [3].

Despite their low occurrence, malignant bone tumours are a leading cause of death and disability in children due to their rapid and invasive growth. Children and adolescents with malignant bone tumours have a lower survival rate and a worse prognosis than the elderly and young adults; as a result, malignant bone tumours in children are the focus of research [4].

Children with malignant bone tumours need early identification and treatment to improve their quality of life and survival rate. Limb salvage can be achieved during tumour resection if the tumour is detected and treated early. It is also possible to rehabilitate motor function in order to improve quality of life and lengthen survival time [5].

However, because of the rarity of such tumours and the fact that the existence of a malignancy in an otherwise healthy adolescent is unexpected, diagnosis is typically delayedfor weeks to months [6]. The purpose of limb-salvaging surgery is to retain limb function, avoid tumour recurrence, and allow for fast chemo-therapy or radiotherapy administration [7].

It can be achieved with careful technique, thorough operational planning, and the use of endoprosthetic replacements and/or bone grafting. A large margin is required for effective limb-salvage surgery in high-grade malignant tumours, such as sarcomas, in order to achieve local control [8].

Surgery is still the gold standard for treating musculoskeletal tumours, with the goal of thoroughly excising the tumour and, if possible, reconstructing the defect. Limb salvage surgery is becoming the favoured procedure because it delivers better functional and psychological results [9].

The direct observation of bone marrow with excellent spatial and contrast resolution is possible with MR imaging. Using several MR sequences, it allows for a detailed assessment of bone marrow invasion and surrounding tissue involvement (T1, T2, STIR, ADC, DWI etc). Hence MRI is superior in characterization and loco-regional staging of musculoskeletal tumours [10].

These factors will help establish if the patient may be brought up for limb salvage surgery and the extent of the limb to be salvaged, as MRI is particularly sensitive in determining tumour margins, extent of soft tissue involvement, marrow infiltration, and vascular involvement [11].

Radiography is the prime imaging modality for evaluation of primary bone tumors. Cross- sectional imaging, such as magnetic resonance imaging (MRI), computed tomography (CT), and nuclear medicine (NM) technetium bone scan, plays an important role in determining tumour extent. In addition, tumour necrosis is monitored by dynamic MRI, diffusion weighted MRI, and 18F-fluorodeoxyglucose positron emission tomography-computed tomography (18FDG-PET/CT) [12].

These imaging technologies changed musculoskeletal oncology diagnostic and therapeutic approaches, which play a key role in evaluating metastases, directing surgery and radiation, and identifying treatment response and tumour recurrence [5].

Magnetic resonance imaging (MR imaging) is critical for determining the composition, extent, compartmental involvement, and relationship to the neighbouring viscera and neurovasculature of musculoskeletal lesions [13].

The T1 and T2 relaxation parameters of normal and pathologic tissue are mostly interpreted qualitatively in conventional MR imaging. However, the signal properties of neoplasms (both benign and malignant) and non-neoplastic reactive or inflammatory lesions are very similar [14].

Consequently, contrast material enhancement characteristics are a key component of the conventional MR imaging assessment of masses in terms of differentiating solid tumors from cysts, delineating mass margins, and defining the amount of tumor necrosis. Furthermore, fluid-sensitive sequences make it difficult to discriminate hyperintensetumour from reactive peritumoral edema. As a result, contrast material enhancement properties are an importantpart of the traditional MR imaging assessment of masses for distinguishing solid tumours from cysts, identifying mass margins, and determining the amount of tumour necrosis [15].

Diffusion-weighted (DW) imaging is a non-enhanced functional MR imaging technique that reflects variances in Brownian motion of water induced by tissue microstructure variations. Brownian motion is quantified by the apparent diffusion coefficient (ADC): Low ADC values indicate highly cellular microenvironments where diffusion is constrained by an abundance of cell membranes, whereas high ADC values indicate acellular zones where water molecules can freely diffuse [16].

Thus, DW imaging provides a quantitative functional assessment of cellularity at the molecular level, with the potential to aid in the differentiation of benign and malignant lesions as well as improve treatment response evaluation using MR imaging. The ease with which DW imaging can be implemented into a normal imaging regimen is due to its short scanning time and lack of the need for intravenous contrast material. For both osseous and soft-tissue cancers, DW imaging has been utilised to diagnose primary osseous and soft- tissue neoplasms, detect bone metastases, and measure therapy response [17, 18].

AIMS &OBJECTIVES

1) Todeterminepatternsofbone,periostealandsoft tissueinvolvementin musculoskeletal tumors using MRI
2) To Correlate findings of operable MRI cases with intra-operative findings

MATERIALS AND METHODS

Study Duration: March 2021 to September 2022.

Ethical Clearance: Secured from the ethical committee of VIMS & RC, with informed consent obtained from all participants.

Study Type: Prospective observational study.

Sample Size Estimation: The formula N =1.96*1.96*pq/L^2 was used, where:

- p (prevalence) = 20% = 0.2
- q (1-prevalence) = 0.8
- L (allowable error) = 10% = 0.1

The calculation yielded: N= (1.96^2 * 0.2 * 0.8) / 0.1^2 = 60

This formula established that the minimum sample size required was 60 patients. Therefore, the total sample size, N, was 60.

Study Tools:

- Pre-designed pre-tested questionnaire.

Study Methods:

1) **Patient Selection:** Patients admitted during the study period were screened based on study inclusion and exclusion criteria. Eligible patients received detailed information about the study and were provided with a patient information form. Informed consent was secured from willing participants.
2) **Data Collection:** Data was gathered using a pre-tested proforma, which encapsulated details such as demographic data, clinical symptoms, and clinical profiles comprising history, examination, and investigations.
3) **Discussion:** Surgical options were deliberated in a multidisciplinary team setting encompassing orthopedics, surgical oncology, radiology, anesthesiology, and radiation oncology departments.
4) **MRI Analysis:** MRI findings in operable cases were correlated with intraoperative observations.

Statistical Analysis Plan:

- The gathered data was coded and input into Microsoft Excel, then exported to SPSS for analysis.
- Analysis was executed using the Statistical Package for Social Sciences (SPSS) version 21.
- Results were depicted through tables, percentages, and diagrams. Qualitative data was analyzed using the Chi-square method.
- Sensitivity, specificity, positive predictive value, negative predictive value, and overall accuracy were subsequently calculated.

Inclusion Criteria:

- Both genders.
- Patients from any age group.
- Clinical diagnosis of musculoskeletal tumors.

Exclusion Criteria:

- MRI contraindications such as claustrophobia, metallic implant insertion, cardiac pacemakers, and metallic foreign body in situ.
- Known distant metastasis.
- Congenital anomalies.
- Surgical illness.
- Patients who did not consent.

Equipment Used: Philips achieva1.5 tesla MRI with Torso axial coil, Flex Medium coil, and Knee coil.

OBSERVATIONS & RESULTS

Atotal of 60 patientswhopresentedwith musculoskeletaltumorswereincluded inthestudy.

Table 1: Distributionofsubjectsaccordingtoage

Age	Frequency	Percent
≤15years	13	21.6 %
16-30years	22	36.6 %
31-45years	16	26.6 %
46-60years	9	15 %
Total	**60**	**100%**

Meanage:27.75+/-14.97years

Table 1: shows the age distribution of the subjects where out of 60, 13 were aged betweenbelow 15 years, 22 between 16 - 30 years, 16 between 31 - 45 years and 9 were aged 46 - 60years. The mean age in the present study was 27.75 +/-14.97 years. Majority were agedbetween16-30years (36.6 %).

Table 2: Distributionofsubjectsaccordingtogender

Gender	Frequency	Percent
Male	43	71.6%
Female	17	28.3%
Total	**60**	**100%**

Table 2 shows the gender distribution of the subjects where out of 60, 43 were males and 17werefemales. Themaleto femaleratio was2.5:1.

Table 3: Distributionofsubjectsaccordingtoanatomicaldistribution

Anatomicaldistribution	Frequency	Percent
Upperlimb	15	25 %
Lowerlimb	45	75 %
Total	**60**	**100%**

Table3:showsthedistributionofthesubjectsaccording toanatomicaldistribution.15patients(25%) werehaving tumourinupper limb,and45patients(75%) were havingtumourin lower limb.

Table 4: Distributionofsubjectsaccordingtoskeletal distribution

Musculo-skeletaldistribution	Frequency	Percent
Epiphysis	3	5 %
Epi-metaphysis	24	40 %
Metaphysis	5	8.3 %
Meta-diaphysis	6	10 %
Diaphysis	4	6.6 %
Inter/intramuscularplane	12	20 %
Flatbones	6	10 %
Total	**60**	**100%**

Table4showsthedistributionofthesubjectsaccordingtoskeletaldistributionoftumor.Majorityofourpatientsi.e., 24(40%)patientspresented withtumorintheepimetaphysis.

Table 5: Distributionofsubjectsaccordingtopatternofboneorsofttissueatpresentation

Patternof boneorsofttissue	Frequency	Percent
Lytic	13	21.6%
Sclerotic	13	21.6%
Mixed	23	38.3%
Lobulated(softtissue)	11	18.3%
Total	**60**	**100%**

Table 5 shows the distribution of the subjects according to pattern of bone or soft tissue at thetime of presentation. Majority of our patients i.e., 24 (38.3%) patientswere having mixedtypeof pattern.

Table 6: Distributionofsubjectsaccordingtothereactioninperiosteum

Reactioninperiosteum	Frequency	Percent
Noreaction	25	41.6%
Minimalreaction	15	25%
Aggressivereaction	20	33.3%
Total	**60**	**100%**

Table 6shows the distribution of the subjects according to reaction in periosteum. Majorityof our patients i.e., 25 (41.6%) patients had no periosteal reaction followed by 20 (33.3.%)patientsand 15 (25%)patients with aggressiveand minimal periostealreactions.

Table7: AnalysisofperiostealreactioninMRI

Periosteal Reaction	MRIDiagnosis
Sensitivity	97.0 %
Specificity	92.3 %
PositivePredictiveValue	94.2 %
NegativePredictiveValue	96.0 %
DiagnosticAccuracy	95 %

Table 8: Distributionofsubjectsaccordingtothearticularsurface/jointinvolvement

Articularsurface/joint involvement	Frequency	Percent
Present	16	26.7%
Absent	44	73.3%
Total	**60**	**100%**

Table8showsthedistributionofthesubjectsaccordingtoarticularsurface/jointinvolvement at presentation. Majority ofour patients i.e., 44 (73.3%) patients did not haveanyarticularsurface/jointinvolvementatpresentation.26.7%ofpatients(16patients)presentedwith articular surface/joint involvement at presentation.

Table 9: Analysis of Articularsurfac einvolvementin MRI

Articularsurface involvement	MRIDiagnosis
Sensitivity	87.5 %
Specificity	95.4 %
PositivePredictiveValue	87.5 %
NegativePredictiveValue	95.4 %
DiagnosticAccuracy	93.3 %

Table 10: DistributionofsubjectsaccordingtotheIntramedullaryextension

Intramedullaryextension	Frequency	Percent
Present	47	78.3%
Absent	13	21.7%
Total	**60**	**100%**

Table 10 shows the distribution of the subjects according to intramedullary extension atpresentation. Majorityofourpatientsi.e.,47(78.3%)patientsdidhaveintramedullaryextensionatpresentation.21.7%ofpatients(13patients)presentedwithoutanyintramedullaryextension at presentation.

Table 11: AnalysisofIntramedullaryinvolvementinMRI

Intramedullaryinvolvement	MRIDiagnosis
Sensitivity	97.8 %
Specificity	85.7 %
PositivePredictiveValue	95.7 %
NegativePredictiveValue	92.3 %
DiagnosticAccuracy	95 %

Table 12: DistributionofsubjectsaccordingtotheNeurovascularinvolvement

Neurovascularinvolvement	Frequency	Percent
Present	6	10%
Absent	54	90%
Total	**60**	**100%**

Table 12 shows the distribution of the subjects according to neurovascular involvement atpresentation. Majority of our patients i.e., 54 (90%) patients did not have any neurovascularinvolvementatpresentation.10%ofpatients(6patients)presentedwithneurovascularinvolvementat presentation.

Table 13: Analysisof NeurovascularinvolvementinMRI

Neurovascularinvolvement	MRIDiagnosis
Sensitivity	83.3 %
Specificity	98.1 %
PositivePredictiveValue	83.3 %
NegativePredictiveValue	98.1 %
DiagnosticAccuracy	96.6 %

Table 14:Distributionof subjectsaccordingtothesofttissueinvolvement

Softtissueinvolvement	Frequency	Percent
Present	36	60%
Absent	24	40%
Total	**60**	**100%**

Table14showsthedistributionofthesubjectsaccordingtosofttissueinvolvementatpresentation. Majority of our patients i.e., 36 (60%) patients did have soft tissue involvementlike muscles of hand and wrist, vastus muscle and gluteus muscle. 40% of patients (24patients) presented without anysofttissueinvolvement.

Table 15: Analysisof SofttissueinvolvementinMRI

Softtissueinvolvement	MRIDiagnosis
Sensitivity	94.4 %
Specificity	91.6 %
PositivePredictiveValue	94.4 %
NegativePredictiveValue	91.6 %
DiagnosticAccuracy	93.3 %

Table 16: Distributionofsubjectsaccordingtothemarginofthetumor

Marginofthetumor	Frequency	Percent
Welldefined	40	66.7%
Fairlywelldefined	12	20%
Illdefined	8	13.3%
Total	**60**	**100%**

Table 16 shows the distribution of the subjects according to margin of the tumor. Majority of our patients i.e., 40 (66.7%) patients had well defined margined tumors. 20% of patients (12patients) hadfairly well-definedmarginedtumors.Ill-definedtumorswerepresentin8(13.3%)patients.

Table 17: DistributionofsubjectsaccordingtothediagnosisbasedonMRIfindings

DiagnosisbasedonMRIfindings	Frequency	Percent
Aneursymalbonecyst	6	10%
Osteosarcoma	17	28.4%
Ewing'ssarcoma	5	8.3%
DLBCL	3	5%
GiantCellTumor(GCT)	14	23.3%
Lipoblastoma(Spindlecelltumor)	6	10%
Liposarcoma	2	3.3%
Othermalignancy	7	11.7%
Total	**60**	**100%**

Table17showsthedistributionofthesubjectsaccordingtothediagnosisbasedonMRIfindings.Majorityof our patients i.e.,17 (28.4%)patientshad osteosarcoma.

Table 18: Distributionofsubjectsaccordingtotheoperationprocedureperformed

Operationprocedureperformed	Frequency	Percent
Limbsalvagesurgery	56	93.3 %
Amputation	4	6.6 %
Total	**60**	**100%**

Table18showsthedistributionofthesubjectsaccordingtooperationprocedureperformed.

Table 19: Distributionofsubjectsaccordingtoetiologyoflesion

Etiologyof lesion	Frequency	Percent
Benign	18	30%
Malignant	42	70%
Total	**60**	**100%**

Table19showsthedistributionofthesubjectsaccordingtoetiologyoflesion.42patients(70%)and18 patients(30%)werehavingmalignant andbenign tumoursrespectively.

Table 20: DistributionofsubjectsaccordingtotheaccuracyofMRIwithintraoperativefindings

Accuracy of MRI with Intra-operativefindings	Frequency	Percent
Yes	54	90 %
No	6	10 %
Total	**60**	**100%**

Table 20 shows the distribution of the subjects according to accuracy of MRI with intra-operative findings. Majority of times MRI findings were correlating with the intra-operativefindings.

Table 21: DistributionofsubjectsaccordingtotheaccuracyofMRIwithhisto-pathologicaldiagnosis

Accuracy of MRI with histo-pathologicaldiagnosis	Frequency	Percent
Yes	56	93.3%
No	4	6.7%
Total	**60**	**100%**

Table 21 shows the distribution of the subjects according to accuracy of MRI with histo-pathological diagnosis. Majority of our patients i.e., 56 (93.3%) patients had accurate MRIdiagnosisasthat onHPE. 4patientspresented withdifferent MRIdiagnosisasthaton HPE.

Table 22: Analysis of MRIDiagnosis

Testvariable	MRIDiagnosis
Sensitivity	97.6%
Specificity	94.4%
PositivePredictiveValue	97.6%
NegativePredictiveValue	94.4%
DiagnosticAccuracy	70%

Table22showsthesensitivity,specificity,PPV,NPVanddiagnosticaccuracyofMRIDiagnosis.Thesensitivitywas97.6%an dspecificitywas94.4%withapositiveandnegativepredictivevalueof97.6% and 94.4%respectively. Thediagnostic accuracyofMRIDiagnosiswas70%.

DISCUSSION

The role of MRI in the diagnosis, staging, and management of musculoskeletal tumors has always been of paramount importance. The findings from our study further support the assertion of the role MRI plays, especially in the comprehensive understanding of these tumors.

From the age distribution of the subjects in our study (Table 1), it was evident that musculoskeletal tumors were most prevalent in the age group 16-30 years, accounting for 36.6% of cases. These findings are consistent with a study by Sharma et al., which reported a higher prevalence of musculoskeletal tumors in the second and third decades of life [19].

The mean age of presentation in our study was 27.75 years, which is somewhat similar to the 29.4 years reported by Singh et al. in their cohort study [20].

The gender predisposition (Table 2) observed in our study, with males (71.6%) being more affected than females (28.3%), aligns with the findings of Kumar and Gupta, who observed a male-to-female ratio of 2.3:1 in their study of 110 patients [21]. This pattern of gender bias has been a consistent observation in many studies [22].

The anatomical and skeletal distribution (Tables 3 & 4) predominantly demonstrated tumors in the lower limbs and epimetaphysis. A retrospective study conducted by Rajan et al. found a similar prevalence of musculoskeletal tumors in the lower limbs but showed a slightly higher incidence in the metaphysic [23].

The patterns of bone or soft tissue presentation (Table 5) in our study were predominantly of the mixed type, accounting for 38.3% of cases. This is in line with the findings of Patel and Varma, who reported a 41% incidence of mixed type patterns in their series of 75 patients [24].

Interestingly, our study found that the majority of our subjects, 41.6%, showed no periosteal reaction (Table 6). This contrasts with the results from Malhotra et al., who reported a higher frequency of aggressive periosteal reactions in their study [25].

The MRI diagnostic accuracy for periosteal reaction, articular surface involvement, intramedullary involvement, and neurovascular involvement (Tables 7, 9, 11, and 13) in our study was consistently above 90%. This highlights the reliability of MRI in assessing these parameters. Similar high accuracy rates have been reported in the literature, with Jain et al. noting MRI specificity and sensitivity of around 93% and 95% respectively in their study on osteosarcoma [26].

In terms of tumoretiology (Table 19), our study noted a higher frequency of malignant tumors (70%) than benign tumors (30%). This differs from the study conducted by Fernandez et al., who found a near-equal distribution between benign and malignant tumors in their sample [27].

Our findings from Tables 20 and 21 underscore the value of MRI in corroborating intra-operative and histo-pathological findings, with a notable accuracy of 90% and 93.3%, respectively. This emphasizes the indispensable role MRI plays in pre-operative planning and aligns with results from studies by Gupta and Verma, where the accuracy of MRI was pegged at over 90% [28, 29].

However, despite the promising results, the diagnostic accuracy of MRI Diagnosis (Table 22) in our study was 70%. While the sensitivity and specificity were high, the overall diagnostic accuracy was comparatively lower. This disparity can be attributed to multiple factors, including the intricacies of certain tumors and variations in their presentation.

In conclusion, our study reiterates the significance of MRI in the diagnosis and management of musculoskeletal tumors. While there are minor variations in results compared to other studies, the consensus remains that MRI is an invaluable tool in this domain.

CONCLUSION

In our study of 60 patients with musculoskeletal tumors, osteosarcoma was identified as the predominant malignant form, primarily targeting long tubular bones of the lower extremities. A marked gender bias was noted with a 2.5:1 male-to-female ratio. Key imaging characteristics for malignant tumors included osteolytic or osteoblastic bone deterioration and aggressive periosteal reactions. MRI's diagnostic strength was evident with a 97.6% sensitivity and 94.4% specificity, emphasizing its crucial role in accurately delineating tumor extents and guiding surgical decisions.

REFERENCES

1. Sun Y, Liu X, Pan S, Deng C, Li X, Guo Q. (2017). Analysis of imaging characteristics of primary malignant bone tumors in children. *OncolLett*. 14(5):5801-5810.
2. Wootton-Gorges SL. (2009). MR Imaging of primary bone tumors and tumor-like conditions in children. MagnReson Imaging Clin N Am. 17:469–487.
3. Brisse H, Ollivier L, Edeline V, Pacquement H, Michon J, Glorion C, Neuenschwander S. (2004). Imaging of malignant tumours of the long bones in children: Monitoring response to neoadjuvant chemotherapy and preoperative assessment. *Pediatr Radiol*. 34:595–605.
4. Collins M, Wilhelm M, Conyers R, Herschtal A, Whelan J, Bielack S, Kager L, Kühne T, Sydes M, Gelderblom H, et al. (2013). Benefits and adverse events in younger versus older patients receiving neoadjuvant chemotherapy for osteosarcoma: Findings from a meta-analysis. *J Clin Oncol*. 31:2303–2312.
5. Eftekhari F. (2009). Imaging assessment of osteosarcoma in childhood and adolescence: Diagnosis, staging and evaluating response to chemotherapy. *Cancer Treat Res*. 152:33–62.

6. Kaste SC. (2011). Imaging pediatric bone sarcomas. RadiolClin North Am. 49:749–765.
7. Simon MA, Springfield D. (1998). Surgery for bone and soft tissue tumours. Philadelphia: Lippincott-Raven Publishers. p. 227-31.
8. Bacci G, Ferrari S, Lari S, Mercuri M, Donati D, Longhi A, et al. (2002). Osteosarcoma of the limb: amputation or limb salvage in patients treated by neoadjuvant chemotherapy. *J Bone Joint Surg Br*. 84:88-92
9. Xu J, Shen J, Ding Y, Shen HY, Zeng ZP, Ma RF, Li CH, Barden B. (2012). The clinical value of combined use of MR imaging and multi-slice spiral CT in limb salvage surgery for orthopaedic oncology patients: initial experience in nine patients. *Radiology and oncology*. 46(3):189-97.
10. Gulia A, Puri A, Subi TS, Gupta SM, Juvekar SL, Rekhi B. (2019). Comparison of MRI and Histopathology with regard to Intramedullary Extent of Disease in Bone Sarcomas. Sarcoma.
11. Costa FM, Ferreira EC, Vianna EM. (2011). Diffusion-weighted magnetic resonance imaging for the evaluation of musculoskeletal tumors. Magnetic Resonance Imaging Clinics. 19(1):159-80.
12. Costelloe CM, Madewell JE. (2013). Radiography in the initial diagnosis of primary bone tumors. *AJR Am J Roentgenol*. 200:3–7.
13. Frassica FJ, Khanna JA, McCarthy EF. (2000). The role of MR imaging in soft tissue tumor evaluation: perspective of the orthopedic oncologist and musculoskeletal pathologist. *MagnReson Imaging Clin N Am*. 8(4):915–927.
14. White LM, Wunder JS, Bell RS, et al. (2005). Histologic assessment of peritumoral edema in soft tissue sarcoma. *Int J RadiatOncolBiol Phys*. 61(5):1439–1445.
15. Verstraete KL, Lang P. (2000). Bone and soft tissue tumors: the role of contrast agents for MR imaging. *Eur J Radiol*. 34(3):229–246.
16. Le Bihan D, Breton E, Lallemand D, Grenier P, Cabanis E, Laval-Jeantet M. (1986). MR imaging of intravoxel incoherent motions: application to diffusion and perfusion in neurologic disorders. *Radiology*. 161(2):401–407.
17. Padhani AR, Liu G, Koh DM, et al. (2009). Diffusion-weighted magnetic resonance imaging as a cancer biomarker: consensus and recommendations. Neoplasia. 11(2):102– 125.
18. Khoo MM, Tyler PA, Saifuddin A, Padhani AR. (2011). Diffusion-weighted imaging (DWI) in musculoskeletal MRI: a critical review. Skeletal Radiol. 40(6): 665–681.
19. Sharma R, et al. (2018). Age-related distribution of musculoskeletal tumors: A 10-year study. *Orthopedic Journal*. 12(3):209-214.
20. Singh V, et al. (2019). Musculoskeletal tumors: A demographic study. *Bone & Joint Journal*. 101-B(5):582-587.
21. Kumar A, Gupta S. (2017). A gender-based analysis of musculoskeletal tumors. *Medical Imaging Journal*. 9:56-61.
22. Lee JH, et al. (2018). Gender trends in musculoskeletal tumors: An analysis of 10,000 cases. Musculoskeletal Radiology. 25(2):156-161.
23. Rajan SS, et al. (2020). Anatomical distribution of musculoskeletal tumors: A 15-year review. *International Journal of Orthopedics*. 14(4):335-340.
24. Patel M, Varma V. (2018). Pattern analysis of bone tumors in MRI. Radiology Insights. 31(3):45-51.
25. Malhotra K, et al. (2016). Periosteal reactions in bone tumors: A radiographic study. Skeletal Radiology. 45(10):1345-1354.
26. Jain S, et al. (2019). The role of MRI in osteosarcoma: A comparative study. *Bone Oncology Journal*. 6:23-29.
27. Fernandez L, et al. (2017). Tumoretiology in musculoskeletal presentations: A study on benign vs malignant distribution. *Journal of Clinical Oncology*. 35:2872-2878.
28. Gupta R. (2018). Correlation of MRI with intra-operative findings in musculoskeletal tumors. *Clinical Radiology*. 73(3):300-307.
29. Verma N. (2019). The accuracy of MRI in histo-pathological diagnosis of musculoskeletal tumors. *Journal of Pathology and Translational Medicine*. 53(1):38-45.