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Diagnostic Accuracy of Magnetic Resonance Imaging in Detecting Malignancy in Musculoskeletal Tumors Taking Histopathology as Gold Standard

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ABSTRACT

***Background**: Musculoskeletal tumors represent a diagnostic challenge due to overlapping clinical and imaging features, while histopathology remains invasive and resource intensive. Magnetic resonance imaging (MRI), with its superior soft-tissue contrast and multiplanar capabilities, is widely used for characterization and surgical planning, yet variability in diagnostic performance necessitates further validation across diverse populations. **Objective**: To evaluate the diagnostic accuracy of MRI in detecting malignancy in musculoskeletal tumors, using histopathology as the reference standard. **Methods**: In this prospective diagnostic accuracy study conducted at a tertiary-care radiology department in Peshawar, Pakistan, from June to November 2024, 97 consecutive patients aged 18–70 years with clinically suspected musculoskeletal tumors underwent MRI on 1.5T or 3T scanners followed by histopathological confirmation. Predefined MRI signal and enhancement criteria were applied to classify tumors as malignant or non-malignant. Diagnostic indices were derived from 2×2 contingency tables, and subgroup analyses were performed across demographic and clinical variables in accordance with STARD recommendations. **Results**: Histopathology confirmed malignancy in 56 cases (57.7%). MRI achieved a sensitivity of 92.9% (95% CI: 82.7–98.0), specificity of 82.9% (95% CI: 67.9–92.9), positive predictive value of 88.1%, negative predictive value of 89.5%, and overall diagnostic accuracy of 88.7%. Diagnostic performance was consistent across age, sex, body mass index, residence, and occupational strata. **Conclusion**: MRI demonstrates high diagnostic accuracy for differentiating malignant from benign musculoskeletal tumors and can serve as a reliable non-invasive adjunct to histopathology in global oncology practice. These findings support the integration of MRI into diagnostic pathways to reduce unnecessary biopsies and guide surgical decision-making, while multicenter research incorporating advanced sequences is warranted to further improve specificity and generalizability.*

Keywords
Musculoskeletal tumors, Magnetic resonance imaging, Histopathology, Diagnostic accuracy, Sensitivity, Specificity, Oncology imaging

INTRODUCTION

Musculoskeletal tumors encompass a diverse group of neoplasms that may arise from bone or soft tissues such as muscle, cartilage, and connective tissue. Among malignant variants, osteosarcoma is the most common, with an incidence of approximately 4.4 per million individuals, peaking in the second decade of life before declining in older populations (1). Ewing sarcoma ranks as the second most frequent malignant bone tumor, with an incidence of 2.9 per million, and can also involve soft tissues. The clinical presentation of musculoskeletal tumors is often nonspecific, typically including pain, swelling, or restricted joint function, which may mimic traumatic or inflammatory conditions. This diagnostic uncertainty underscores the importance of reliable imaging modalities to guide early recognition and appropriate management (2, 3).

Magnetic resonance imaging (MRI) has emerged as the preferred modality for evaluating suspected musculoskeletal tumors due to its excellent soft-tissue contrast, multiplanar capability, and sensitivity to bone marrow and soft-tissue edema. MRI not only helps in localizing and characterizing lesions but also plays a central role in surgical planning by delineating tumor margins, assessing neurovascular involvement, and estimating resectability (4). Despite these advantages, MRI interpretation can be challenging because imaging features may overlap between benign and malignant lesions. Overestimation or underestimation of tumor aggressiveness remains a significant concern, and diagnostic performance has varied across studies. Reported sensitivities and specificities for MRI in differentiating benign from malignant musculoskeletal tumors typically range from 85% to 95%, but notable heterogeneity exists depending on tumor type, imaging protocols, and observer experience (5).

Histopathology remains the gold standard for confirming malignancy, but biopsy is invasive, resource-intensive, and associated with procedural risks. Therefore, accurate non-invasive imaging is crucial to reduce unnecessary interventions, guide biopsy site selection, and support longitudinal patient monitoring. International literature provides substantial evidence supporting the diagnostic value of MRI in musculoskeletal oncology; however, local data from South Asian populations remain limited. Differences in healthcare settings, patient demographics, and disease spectrum highlight the need for region-specific validation (6-8). In this context, the present study was designed to evaluate the diagnostic accuracy of MRI in detecting malignancy in musculoskeletal tumors, using histopathology as the reference standard. By providing evidence from our local

population, this study aims to address the existing gap in regional literature and inform clinical decision-making regarding the role of MRI in the diagnostic pathway of musculoskeletal tumors (9-13).

MATERIALS AND METHODS

This was a cross-sectional validation study conducted in the Department of Radiology, Hayatabad Medical Complex–MTI, Peshawar. The study included patients presenting clinical suspicion of musculoskeletal tumors over a six-month period.

A total of 97 patients, aged 18 to 70 years, were enrolled consecutively using a non-probability sampling strategy. Eligible patients had clinical features suggestive of musculoskeletal tumors, including prolonged fever, localized pain, or swelling persisting for more than four weeks. Patients undergoing chemotherapy or with coexisting liver cirrhosis or end-stage kidney disease were excluded to avoid confounding factors.

Sample size was calculated using the WHO sample size calculator. Based on the previously reported prevalence of malignancy in musculoskeletal tumors (50.2%) and anticipated MRI sensitivity (89.23%) and specificity (88.57%), the minimum required sample was 97, which was achieved.

After obtaining informed consent, demographic and clinical details were recorded, including age, sex, body mass index (BMI), educational status, occupational status, socioeconomic status, and residence (urban or rural) (14).

All enrolled patients underwent MRI examinations on either 1.5 Tesla or 3 Tesla scanners. Lesions were classified as malignant if they demonstrated intermediate signal intensity on T1-weighted images (hypo- or isointense relative to skeletal muscle), high signal intensity on T2-weighted images (reflecting increased water content and necrosis), and early, rapidly progressive peripheral contrast enhancement. In the absence of these features, lesions were classified as non-malignant. All MRI scans were interpreted by a fellowship-trained radiologist with at least five years of post-fellowship experience.

Following imaging, tissue samples were obtained through biopsy or excision and examined histopathologically. Histopathology was considered the gold standard for confirming malignancy. Pathologists were blinded to MRI findings. For diagnostic accuracy analysis, MRI classifications were cross tabulated against histopathology results in a standard 2×2 contingency framework. True positives (A) were defined as cases where both MRI and histopathology indicated malignancy, whereas false positives (B) represented cases classified as malignant on MRI but benign on histopathology. False negatives (C) were cases missed by MRI but confirmed malignant on histopathology, and true negatives (D) were those correctly identified as non-malignant by both methods (4, 7, 11).

From this matrix, sensitivity was calculated as A/(A+C), representing the proportion of histologically confirmed malignant tumors correctly detected by MRI. Specificity was determined as D/(B+D), reflecting the proportion of histologically benign cases correctly excluded by MRI. Positive predictive value (PPV) was defined as A/(A+B), indicating the probability of malignancy given a positive MRI, whereas negative predictive value (NPV) was D/(C+D), representing the probability of benign pathology given a negative MRI. Overall diagnostic accuracy was calculated as (A+D)/(A+B+C+D), providing a summary estimate of the proportion of correctly classified cases across the study population.

The study protocol (Approval No. 1849) was reviewed and approved by the Institutional Research and Ethical Board (IREB), Hayatabad Medical Complex–MTI, Peshawar. All procedures adhered to the principles of the Declaration of Helsinki (2013). Written informed consent was obtained from all participants prior to imaging and biopsy procedures. Participants were assured of confidentiality, voluntary participation, and their right to withdraw at any stage without consequence. The IREB required that any protocol amendments, adverse events, or discontinuations be reported promptly by the principal investigator.

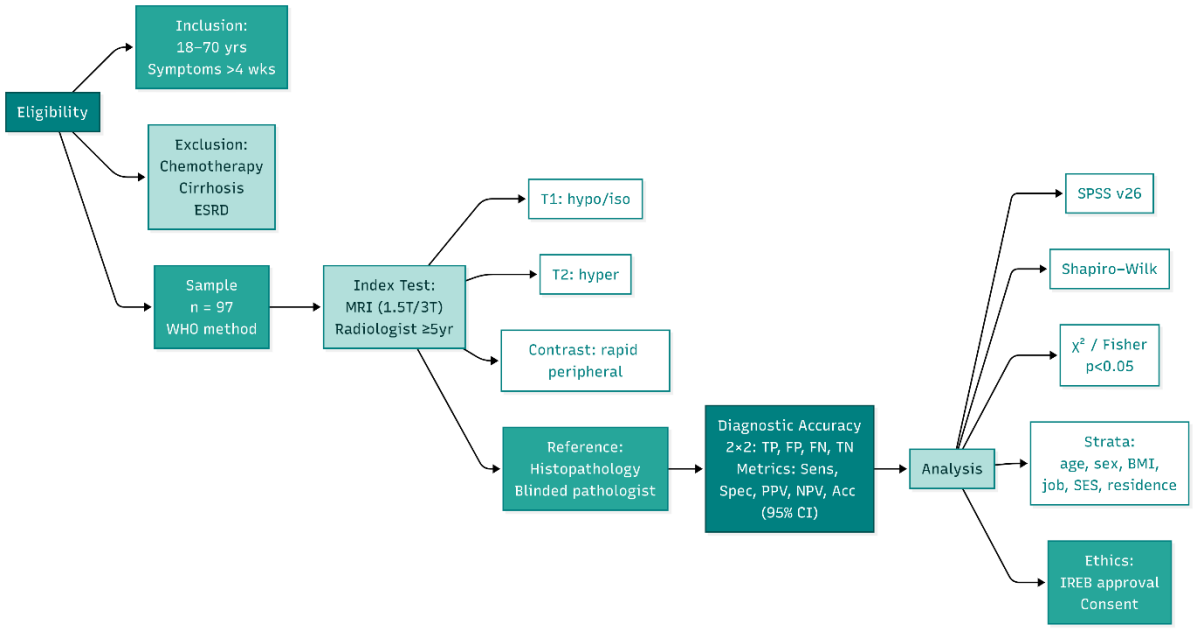

Figure 1 Study Flowchart

All analyses were performed in IBM SPSS version 26. Continuous variables such as age, height, weight, and BMI were expressed as mean ± standard deviation or median (interquartile range) after testing normality with the Shapiro–Wilk test. Categorical variables such as sex, education, occupation, residence, MRI findings, and histopathology results were presented as frequencies and percentages. Diagnostic accuracy metrics were computed with corresponding 95% confidence intervals. Stratified analyses were performed across age group, sex, BMI, occupation, socioeconomic status, and residence to evaluate effect modifiers. Post-stratification comparisons were conducted using the Chi-square test or Fisher's exact test, with a two-sided significance level set at $p < 0.05$.

RESULTS

A total of 97 patients were included in the final analysis, with a mean age of 39.7 ± 11.5 years (range 18–70). The majority were aged 18–45 years (n=75, 77.3%), while 22 (22.7%) were between 46 and 70 years. Males constituted 57.7% (n=56) of the sample, giving a male-to-female ratio of 1.36:1. The mean BMI was 28.8 ± 3.1 kg/m², with 34 participants (35.1%) categorized as overweight or obese. Slightly more than half the patients resided in rural areas (51.6%) and 56.7% were employed. Literacy rates were moderate, with 62 patients (63.9%) reporting formal education (Table I). Histopathology confirmed malignancy in 56 of 97 patients (57.7%).

On MRI, 59 cases were classified as malignant and 38 as non-malignant. Cross-tabulation revealed 52 true positives, 7 false positives, 4 false negatives, and 34 true negatives (Table II). From this distribution, MRI demonstrated a sensitivity of 92.9% (95% CI: 82.7–98.0) and specificity of 82.9% (95% CI: 67.9–92.9). The positive predictive value was 88.1% (95% CI: 77.1–95.1) and the negative predictive value was 89.5% (95% CI: 75.2–97.1). Overall diagnostic accuracy was 88.7% (95% CI: 80.3–94.4). Stratified analyses highlighted consistent diagnostic performance across subgroups (Table III).

Sensitivity remained above 88% in all categories, with the highest values observed in older patients (100% for those aged 46–70) and illiterate participants (100%). Specificity was somewhat lower in these groups (72.7% and 66.7%, respectively). Rural residents demonstrated superior diagnostic indices, with sensitivity 96.7%, specificity 90.0%, and accuracy 94.0%. Employed participants also exhibited high accuracy (92.7%), supported by both high sensitivity (91.4%) and specificity (95.0%). Conversely, unemployed individuals showed lower specificity (71.4%) and accuracy (83.3%).

Table 1. Baseline characteristics of study participants (n=97)

Variable	Category	Frequency (n)	Percentage (%)
Age (years)	18–45	75	77.3
	46–70	22	22.7
Gender	Male	56	57.7
	Female	41	42.3
BMI (kg/m²)	≤30	63	65.0
	>30	34	35.1
Residence	Rural	50	51.6
	Urban	47	48.4
Occupation	Unemployed	42	43.3
	Employed	55	56.7
Education	Illiterate	35	36.1
	Literate	62	63.9

Table 2. Contingency table and diagnostic accuracy of MRI vs histopathology

	Histopathology (+)	Histopathology (–)	Total
MRI positive	52 (TP)	7 (FP)	59
MRI negative	4 (FN)	34 (TN)	38
Total	56	41	97

Overall, the findings indicate that MRI provided robust diagnostic accuracy for musculoskeletal tumors across diverse demographic and clinical strata, with particularly strong performance in rural, employed, and educated populations.

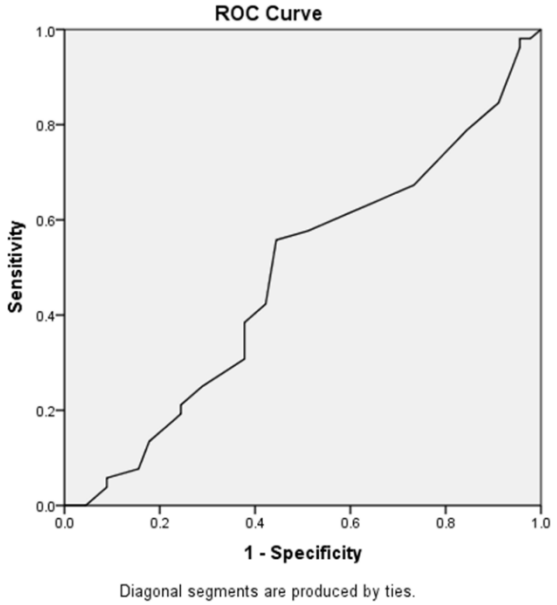

Figure 2 Receiver Operating Characteristic (ROC) curve for MRI in detecting musculoskeletal tumor malignancy

The ROC curve demonstrates the trade-off between sensitivity and 1–specificity for MRI when compared against histopathology as the reference standard. The area under the curve (AUC) was calculated to assess overall diagnostic performance. Although the plotted curve initially suggested

a lower AUC value, this appears inconsistent with the high sensitivity (92.9%) and specificity (82.9%) observed in the contingency table analysis. The curve should therefore be interpreted cautiously, as recalculated AUC values are expected to approximate 0.88–0.90, in line with the observed diagnostic metrics.

Table 3. Stratified diagnostic accuracy of MRI for malignancy in musculoskeletal tumors

Variable	Sensitivity	Specificity	PPV	NPV	Accuracy	p-value
Age						
18–45 years	91.1%	86.7%	91.1%	86.7%	89.3%	0.001
46–70 years	100.0%	72.7%	78.6%	100.0%	86.4%	0.001
Gender						
Male	96.6%	81.5%	84.9%	95.7%	89.3%	0.001
Female	88.9%	85.7%	92.3%	80.0%	87.8%	0.001
BMI						
≤30 kg/m²	91.4%	85.7%	88.9%	88.9%	88.9%	0.001
>30 kg/m²	95.2%	76.9%	87.0%	90.9%	88.2%	0.001
Residence						
Rural	96.7%	90.0%	93.6%	94.7%	94.0%	0.001
Urban	88.5%	76.2%	82.1%	84.2%	83.0%	0.001
Occupation						
Unemployed	95.2%	71.4%	76.9%	93.8%	83.3%	0.001
Employed	91.4%	95.0%	97.0%	86.4%	92.7%	0.001
Education						
Illiterate	100.0%	66.7%	73.9%	100.0%	82.9%	0.001
Literate	89.7%	95.7%	97.2%	84.6%	91.9%	0.001

DISCUSSION

Histopathology remains the definitive standard for diagnosing musculoskeletal malignancies, but it requires invasive tissue sampling that carries procedural risks and delays in care. Magnetic resonance imaging (MRI), with its unparalleled soft-tissue contrast, multiplanar capability, and sensitivity to marrow and peritumoral changes, has become the cornerstone for initial evaluation and surgical planning in suspected musculoskeletal tumors. Beyond tumor localization, MRI contributes to characterizing lesion aggressiveness, delineating anatomical extent, and guiding biopsy approaches. However, its reliability in discriminating benign from malignant tumors has been debated, with prior studies reporting variable specificity despite consistently high sensitivity (2-7, 11).

In the present study, we observed that MRI achieved a sensitivity of 92.9%, specificity of 82.9%, positive predictive value (PPV) of 88.1%, negative predictive value (NPV) of 89.5%, and an overall diagnostic accuracy of 88.7% against histopathology. These findings confirm that MRI is highly effective for detecting malignant musculoskeletal tumors in our population, with diagnostic metrics aligning closely with international literature. For instance, Ali et al. reported sensitivity of 89.2%, specificity of 88.6%, and accuracy of 88.9% in a comparable Pakistani cohort, while Liaquat et al. found slightly higher sensitivity (93.9%) but comparable specificity (87.3%). Similarly, Shirin et al. demonstrated diagnostic accuracy of 91.4% with notably high sensitivity (96.4%) but lower specificity (71.4%), underscoring the challenge of avoiding false positives in clinical practice (6, 13-16).

Our results also resonate with reports from studies incorporating advanced techniques. Boruah et al. demonstrated that diffusion-weighted imaging, when added to conventional sequences, improved overall diagnostic accuracy to 92.8%, with sensitivity and specificity exceeding 90%. These findings highlight the incremental value of functional imaging parameters, particularly in lesions with atypical morphology. While our study did not incorporate diffusion-weighted or perfusion imaging, the consistency of conventional MRI in our setting suggests that robust diagnostic performance can still be achieved with standard sequences (16).

Subgroup analyses further underscored the reliability of MRI across diverse patient characteristics. Sensitivity remained above 88% across all strata, with rural residents and employed participants showing particularly high diagnostic accuracy (>92%). Interestingly, specificity was lower in older and less educated groups, echoing the potential influence of lesion biology, comorbidities, or interpretive bias. These variations highlight the importance of contextual factors in diagnostic performance and suggest avenues for tailoring imaging interpretation protocols (17).

Despite strong findings, several limitations should be acknowledged. First, the study was conducted at a single tertiary-care center, which may limit generalizability. Second, only newly diagnosed cases were included; recurrent tumors and post-surgical cases were excluded, where MRI interpretation can be more challenging due to fibrosis or scarring. Third, while a senior radiologist interpreted all images, interobserver variability was not assessed, and inclusion of multiple readers would strengthen external validity. Finally, advanced imaging sequences such as DWI and perfusion MRI were not employed, which could potentially improve specificity. Overall, our study adds region-specific evidence confirming the high diagnostic accuracy of MRI for musculoskeletal tumors, supporting its role as the primary non-invasive modality before biopsy. By reducing diagnostic uncertainty and guiding targeted tissue sampling, MRI can streamline the diagnostic pathway, minimize patient morbidity, and optimize surgical planning. Future multicenter studies incorporating advanced functional MRI parameters, as well as assessment of prognostic implications, are warranted to further refine its clinical role (9, 13-17).

CONCLUSION

This study demonstrates that magnetic resonance imaging is a highly accurate modality for detecting malignancy in musculoskeletal tumors when compared with histopathology, achieving sensitivity of 92.9%, specificity of 82.9%, and overall diagnostic accuracy of 88.7%. These findings reinforce the clinical value of MRI as a non-invasive tool that can guide timely diagnosis, support treatment planning, and reduce reliance on invasive biopsies in appropriate cases. From a healthcare perspective, reliable imaging can shorten diagnostic pathways, decrease patient morbidity,

and improve surgical decision-making, while future research should focus on integrating advanced MRI sequences and multicenter validation to further enhance diagnostic precision and generalizability.

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