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DIAGNOSTIC ACCURACY OF MRI IN PREDICTING SOFT TISSUE MALIGNANCY OF MUSCULOSKELETAL SYSTEM BY TAKING HISTOPATHOLOGY AS GOLD STANDARD

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Abstract:

Background: *Soft Tissue Malignancies of Musculoskeletal System or sarcomas are a rare and heterogeneous group of malignant tumors of mesenchymal origin that comprise less than 1 percent of all adult malignancies and 12 percent of pediatric cancers. MR imaging is an integral part of the multi-modality approach to the assessment of malignancies of soft tissue musculoskeletal system diagnosis and treatment.*

Objective: *The objective of the study was to evaluate the diagnostic accuracy of MRI in predicting soft tissue malignancy of musculoskeletal system by taking histopathology as gold standard.*

Study Design: *Cross sectional (validation) study*

Sampling Technique: *Non probability consecutive sampling*

Setting: *Department of Radiology and Medical Imaging Allied Hospital Faisalabad.*

Duration of Study: *09 months after the approval of synopsis. From: 01-04-2016 to 31-12-2016*

Results: *In our study, mean age was calculated as 50.21±7.03 years, 48.35%(n=44) were male and 51.65%(n=47) were females, the diagnostic accuracy of mri in predicting soft tissue malignancy of musculoskeletal system by taking histopathology as gold standard shows 85.29% sensitivity, 87.72% specificity, 80.55% positive predictive value, 90.91% negative predictive value and accuracy rate was calculated as 86.81%.*

Conclusion: *We concluded that the diagnostic accuracy of MRI is encouraging for predicting soft tissue malignancy of musculoskeletal system by taking histopathology as gold standard.*

Keywords: *Soft Tissue Malignancy of Musculoskeletal System, MRI, Diagnostic Accuracy*

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INTRODUCTION:

MRI is an excellent modality for evaluating the size, extent, intensity of characteristics, and involvement of surrounding soft tissues [1]. Malignancy is predicted with the highest sensitivity when the lesions have high signal intensity on T2-weighted MRI, larger than 6cm in diameter, have heterogeneous signal intensity on T1-weighted MRI and have peritumoral edema. The highest specificity is noted when the lesions show tumor necrosis, bone or neurovascular involvement and mean diameter of more than 8cm. When a lesion has nonspecific MR imaging appearance, it is useful to formulate a suitably ordered differential diagnosis based on tumor prevalence, patient, age and anatomic location. A systemic approach markedly improves diagnostic results [2].

The clinical presentation of bones and soft tissue sarcomas is varied. Constitutional symptoms are rare, and although bone sarcomas are painful while soft tissue sarcomas are not, there are exceptions to this general rule. A high index of suspicion is required for any unexplained mass with indeterminate findings. Choosing the right imaging modality is critical to diagnosis and management of the patients with suspected sarcoma, and referring clinicians have multitude of imaging options. After discovery of malignant appearing bone lesions by radiography, further imaging is obtained for better characterization of lesion with MRI and for staging with computed tomography of the chest. In contrast, radiographs are rarely helpful for evaluation of soft tissue lesions, which almost always require MRI assessment [3].
The role of MR imaging in monitoring the therapeutic response in soft tissues sarcomas continues to evolve. At present time, MR imaging is part of a more comprehensive process that involves other modalities, such as PET imaging, for assessment of treatment related necrosis. Nevertheless, MR imaging has some unique advantages in study of treatment response. These advantages include the lack of ionizing radiation and its relatively high spatial resolution compared with nuclear imaging studies [4]. Gadolinium enhanced MRI (GeMRI) improves reader confidence, improves reader's concordance and modestly improved accuracy for less experienced observer [5]. Pattern recognition of component characteristics of soft tissue masses can increase the ability of MRI to differentiate benign and malignant soft tissue masses. It has advantage over traditional morphologic and perilesional analysis; however, a combination of these characteristics yields the best results. The parameters favoring malignancy were large lesion size, peritumoral edemas, necrosis and absent fat rim, absent calcification and lack of fibrosis [6].

Sen et al [1] concluded from their study that overall sensitivity and specificity of MRI in detection of malignant soft tissue tumors of musculoskeletal system were 83% and 81% respectively and their prevalence was 42% [1]. The rationale of this study is to evaluate the role of MRI in diagnosing the malignant soft tissue neoplasms of musculoskeletal system before histopathology. This study will show whether we can accurately diagnose soft tissue neoplasms of musculoskeletal system by a noninvasive investigation of MRI before the invasive investigation of histopathology or not, MRI also having the added advantage of predicting the extent and depth of neoplasms. So this study will help both the clinicians and radiologists

METHODOLOGY:

After the approval from ethical committee all patients included in study were taken from OPD of general surgery, oncology and Radiology Allied Hospital Faisalabad after preliminary clinical examination by surgeon in OPD. After taking relevant history of swelling, the patients having a suspected neoplastic lesion was again examined clinically, x-ray and ultrasound examination of the lesion was performed by me under consultant supervision to exclude the patients having superficial and non-neoplastic lesions and primary bone lesions. MRI examination was done in the included patients on 1.5 Tesla ACHIEVA PHILIPS with phase array body coil using T1-weighted (TR/TE 500/16) {repetition time, ms/echo time, ms}, T2weighted (TR/TE3000/100), Short TauInversion Recovery (STIR) (TR/TE2500/100)/fat suppressed sequences and Gd-DTPA-enhanced by Gadavist (gadobutrol) T1-weighted scan (0.1 mmol / kg of contrast was used intravenously). The MRI features of lesions like size, shape (regular, irregular, lobulated), margins (infiltration), isointensity on T1W, slight hyper intensity on T2W, heterogeneous lesion and heterogeneous enhancement, peritumoural edema, intratumoral necrosis, hemorrhage, fascia penetration, bone changes ,neurovascular involvement, absent fat rim, absent calcification and lack of fibrosis was noted and each feature was individually noted by me after discussion with same consultant to reduce observer variation and results regarding final diagnosis was entered in specially designed Performa attached with synopsis and patient followed up for histopathology report [7], which was done in PMC histopathology lab and reported by histopathologic and I entered the findings of histopathology in the Performa.

RESULTS:

A total of 91 cases fulfilling the inclusion/exclusion criteria were enrolled to evaluate the diagnostic accuracy of MRI in predicting soft tissue malignancy of musculoskeletal system by taking histopathology as gold standard. Patients were distributed according to age, it shows that 13.19%(n=12) were between 15-40 years and 86.81%(n=79) were between 41-60 years of age, mean±SD was calculated as 50.21±7.03 years. (Table No. 1). Gender distribution shows that 48.35%(n=44) were male and 51.65%(n=47) were females. (Table No. 2). Frequency of soft tissue malignancy of musculoskeletal system by taking histopathology as gold standard shows was recorded in 37.36 %(n=34) while 62.64%(n=57) had no findings of malignancy. (Table No. 3). The diagnostic accuracy of MRI in predicting soft tissue malignancy of musculoskeletal system by taking histopathology as gold standard shows 85.29% sensitivity, 87.72% specificity, 80.55% positive predictive value, 90.91% negative predictive value and accuracy rate was calculated as 86.81%. (Table No. 4). The data was stratified for age and gender to control the effect modifiers. (Table No. 5 & 6)

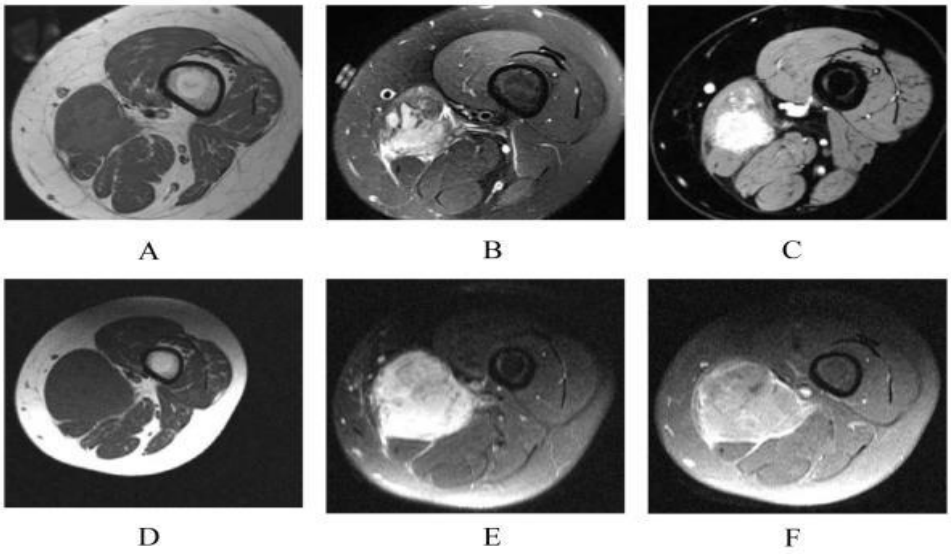

Fig. 1: Pre-treatment and post-treatment Scan

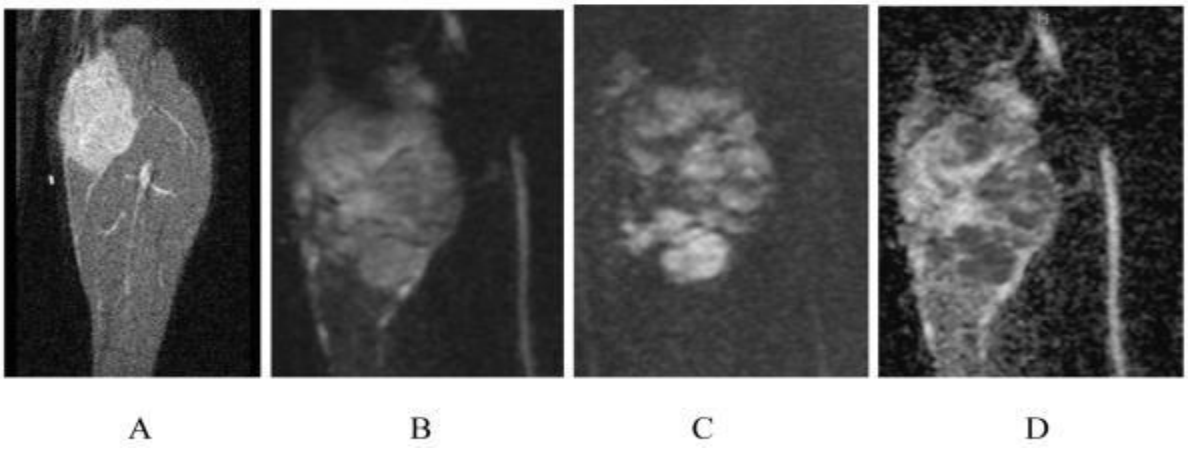

Fig. 2

A. Pretreatment scan in a 15-year-old girl with a high-grade undifferentiated sarcoma. Coronal STIR (TR/TE 1600/5) shows a large mass in the calf with a slightly heterogeneous increased signal. B. Pretreatment scan in a 14-year-old girl with a high-grade undifferentiated sarcoma. Coronal DWI (b=0) shows a heterogeneous calf mass of increased signal. C. Pretreatment scan in a 14-year-old girl with a high grade undifferentiated sarcoma. Coronal DWI (b=500) shows persistent areas of increased signal, implying the presence of viable tumor. D. Pretreatment scan in a 14-year-old girl with a high-grade undifferentiated sarcoma.

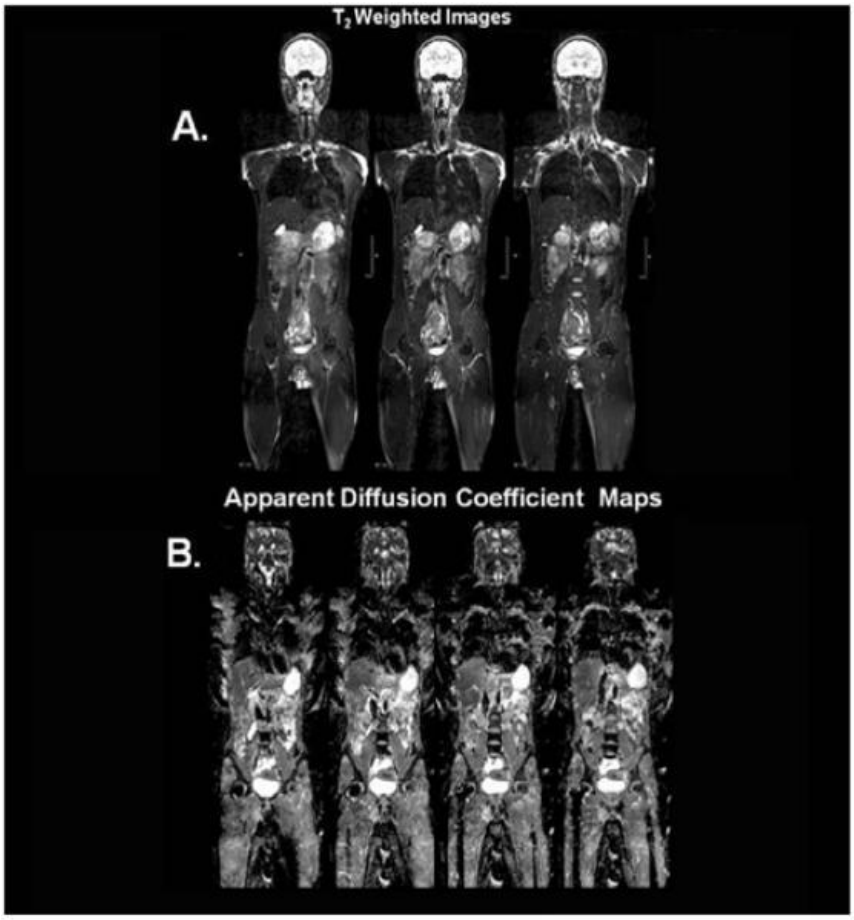

Fig. 3: Representative example of WB-MR and DWI at 1.5T in a normal male volunteer

		histopathology +ve	histopathology -ve
MRI	+ve	a TP	b FP
MRI	-ve	c FN	d TN

Sensitivity = a/a+c x 100
NPV = d/c+d x 100
Specificity = d/b+d x 100
Diagnostic Accuracy= TP+TN/TP+FP+FN+TN x 100
PPV = a/a+b x 100

TABLE No. 1: AGE DSITRIBUTION
(n=91)

Age(in years)	No. of patients	%
15-40	12	13.19
41-60	79	86.81
Total	**91**	**100**
Mean±SD	**50.21±7.03**	

TABLE No. 2: GENDER DSITRIBUTION
(n=91)

Gender	No. of patients	%
Male	44	48.35
Female	47	51.65
Total	**91**	**100**

TABLE No. 3: FREQUENCY OF SOFT TISSUE MALIGNANCY OF MUSCULOSKELETAL SYSTEM BY TAKING HISTOPATHOLOGY AS GOLD STANDARD
(n=91)

Soft tissue malignancy	No. of patients	%
Yes	34	37.36
No	57	62.64
Total	**91**	**100**

TABLE No. 4:DIAGNOSTIC ACCURACY OF MRI IN PREDICTING SOFT TISSUE MALIGNANCY OF MUSCULOSKELETAL SYSTEM BY TAKING HISTOPATHOLOGY AS GOLD STANDARD
(n=91)

MRI	Histopathology		Total
	Malignant (Positive)	Malignant (Negative)	
Positive	True positive(a) 29 (31.87%)	False positive (b) 7 (7.69%)	a + b 36(39.56%)
Negative	False negative(c) 5 (5.49%)	True negative (d) 50 (54.95%)	c + d 55(60.44%)
Total	**a + c** **34 (37.36%)**	**b + d** **57(64.64%)**	**91(100%)**

Sensitivity = a / (a + c) x 100 =85.29%
Specificity = d / (d + b) x 100 = 87.72%
Positive predictive value = a / (a + b) x 100 =80.55%
Negative predictive value = d / (d + c) x 100 =90.91%
Accuracy rate = a + d / (a + d + b + c) x 100 = 86.81%

TABLE No. 5: STRATIFICATION FOR AGE

Age: 15-40 years

MRI	Histopathology		P value
	Malignancy (Positive)	**Malignancy (Negative)**	
Positive	True positive(a) 6	False positive (b) 0	0.01
Negative	False negative(c) 2	True negative (d) 4	
Total	**a + c** **8**	**b + d** **4**	

Sensitivity = a / (a + c) x 100 =75%
Specificity = d / (d + b) x 100 = 100%
Positive predictive value = a / (a + b) x 100 =100%
Negative predictive value = d / (d + c) x 100 =66.67%
Accuracy rate = a + d / (a + d + b + c) x 100 =83.33%

Age: 41-60 years

MRI	Histopathology		P value
	Malignancy (Positive)	**Malignancy (Negative)**	
Positive	True positive(a) 23	False positive (b) 7	0.000
Negative	False negative(c) 3	True negative (d) 46	
Total	**a + c** **26**	**b + d** **53**	

Sensitivity = a / (a + c) x 100 =88.46%
Specificity = d / (d + b) x 100 = 86.79%
Positive predictive value = a / (a + b) x 100 =76.67%
Negative predictive value = d / (d + c) x 100 =93.88%
Accuracy rate = a + d / (a + d + b + c) x 100 =87.34%

TABLE No. 6: STRATIFICATION FOR GENDER

Male

MRI	Histopathology		P value
	Malignant (Positive)	**Malignant (Negative)**	
Positive	True positive(a) 15	False positive (b) 1	0.000
Negative	False negative(c) 0	True negative (d) 28	
Total	**a + c** **15**	**b + d** **29**	

Sensitivity = a / (a + c) x 100 =100%
Specificity = d / (d + b) x 100 = 96.55%
Positive predictive value = a / (a + b) x 100 =93.75%
Negative predictive value = d / (d + c) x 100 =100%
Accuracy rate = a + d / (a + d + b + c) x 100 =97.73%

Female

MRI	Histopathology		P value
	Malignant (Positive)	**Malignant (Negative)**	
Positive	True positive(a) 14	False positive (b) 6	0.0004
Negative	False negative(c) 5	True negative (d) 22	
Total	**a + c 19**	**b + d 28**	

Sensitivity = a / (a + c) x 100 =73.68%
Specificity = d / (d + b) x 100 =78.57%
Positive predictive value = a / (a + b) x 100 =70%
Negative predictive value = d / (d + c) x 100 =81.48%
Accuracy rate = a + d / (a + d + b + c) x 100 =76.60%

DISCUSSION:

This study was planned to evaluate the role of MRI in diagnosing the malignant soft tissue neoplasms of musculoskeletal system before histopathology, so that it may be determined whether we can accurately diagnose soft tissue neoplasms of musculoskeletal system by a noninvasive investigation of MRI before the invasive investigation of histopathology or not, MRI also having the added advantage of predicting the extent and depth of neoplasms [8]. In our study, out of 91 cases presenting with a lump (swelling) which seems to be arising from subcutaneous/muscle plane on clinical ,x- ray and ultrasound examination after taking a detailed history, 13.19% (n=12) were between 15-40 years and 86.81%(n=79) were between 41-60 years of age, mean±SD was calculated as 50.21±7.03 years, 48.35%(n=44) were male and 51.65%(n=47) were females, frequency of soft tissue malignancy of musculoskeletal system by taking histopathology as gold standard shows was recorded in 37.36%(n=34), the diagnostic accuracy of MRI in predicting soft tissue malignancy of musculoskeletal system by taking histopathology as gold standard showed 85.29% sensitivity, 87.72% specificity, 80.55% positive predictive value, 90.91% negative predictive value and accuracy rate were calculated as 86.81% [9].

We compared our results with Sen et al [1] who concluded from their study that overall sensitivity and specificity of MRI in detection of malignant soft tissue tumors of musculoskeletal system were 83% and 81% respectively and their prevalence was 42% [1]. These findings correspond to our results. Another study determined the accuracy of MRI in determining the characteristics of musculoskeletal tumors, [including both skeletal (primary/secondary) and soft tissue tumors] and correlation of MRI findings with histopathological study and recorded that a correct histological diagnosis is reached on the basis of imaging studies alone is 66% of cases. The sensitivity for a MRI diagnosis of bone and soft tissue tumour was 100% and accuracy was 98% [10]. Specificity of detecting benignity and malignancy is 94.7%. These findings are better than our results. This difference may be due to the difference in sinologist experience [10]. They concluded that the diagnosis of musculoskeletal tumors is best made by a combination of clinical and plain picture imaging parameters rather than by any single MR characteristic, except lipomas. When a lesion has a non-specific MR imaging appearance, it is useful to formulate a suitably ordered differential diagnosis based on tumour prevalence, age [7].

Berquist et al in 1990 conducted a study on 95 consecutive patients with soft tissue mass lesions and observed that 87% of malignant tumours were larger than 5 cm. 85% of malignant tumours had irregular margins. Moulton et al in 1995 showed that size criteria of >5cm had a sensitivity of 85% and irregular margins had a sensitivity of 74%. Gielen et al performed a prospective non-quantified MR parameter evaluation in patients with soft tissue tumors. It showed that differentiation between malignant and benign lesions (dignity), a sensitivity of 93%, specificity of 82%, negative predictive value (NPV) of 98% and positive predictive value (PPV) of 60% with accuracy of 85% [5].
In summary, a combination of MRI features of size more than 6 to 8 cm, ill-defined margins, heterogeneous intensity signals on T1-W images,

hyperintense signals on T2-W images, heterogeneous contrast enhancement, absent fat rim and fascia penetration, absent calcification, intratumoral hemorrhage and necrosis and bone and neurovascular involvement suggested malignancy whereas features like peritumoral edema and lack of fibrosis if present were suggestive but if absent did not rule out malignancy of soft tissues of musculoskeletal system [8]. However, taking these parameters, the MRI may be used in our population for accurate evaluation of malignancy of soft tissues of musculoskeletal system.

CONCLUSION:

We concluded that the diagnostic accuracy of MRI is encouraging for predicting soft tissue malignancy of musculoskeletal system by taking histopathology as gold standard.

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