Review report

BSMMUJ-17.2 – 72248
Accuracy of diffusion-weighted magnetic resonance imaging in diagnosing malignant musculoskeletal tumours
Shirin M *et al.* (m.shirin1970@gmail.com)

REVIEW COMMENTS		AUTHOR RESPONSE [Note: Please write the responses to each point here mentioning line number(s). You must change the manuscript as per your response.]
A. Technical review		
ROUND 1		
Reviewer's name: A		
ORCID: -		
Date assigned: **1-Apr-24**		
Date submitted: **9-May-24**		
Do you have any conflict of interest with the author/s? **No**		
Do you wish to be disclosed to the author? **No**		
How would you rate the originality and depth of the manuscript?	7	-
Is the manuscript written in a scholarly manner?	9	-
Does the manuscript have the potential to make a valuable contribution to the world of knowledge?	8	-
Does the manuscript meet ethical standards?	8	-
Reviewer's Recommendation: **Accept Submission**		
Reviewer's name: Abu Shahin		
ORCID: 0000-0001-6719-3896		
Date assigned: **8-May-24**		
Date submitted: **16-May-24**		
Do you have any conflict of interest with the author/s? **No**		
Do you wish to be disclosed to the author? **No**		
Comments sent to author **(**Date: **22-May-24)**		Date replied by author: **29-May-24**
How would you rate the originality and depth of the manuscript?	8	-
Is the manuscript written in a scholarly manner?	8	-
Does the manuscript have the potential to make a valuable contribution to the world of knowledge?	8	-
Does the manuscript meet ethical standards?	8	-
1. Background should be a bit elaborated including prevalence of musculoskeletal tumor showing socioeconomically burden. Knowledge gap and our intention should be more clear.		We agree with the reviewer that information regarding the prevalence of musculoskeletal tumours highlighting the socioeconomic burden is important and should be included in the background section. So, we have revised the background section from lines 97 to 107 on page 5.

REVIEW COMMENTS	AUTHOR RESPONSE [Note: Please write the responses to each point here mentioning line number(s). You must change the manuscript as per your response.]
2. Methods section should be more detail with flowchart.	We have added some more detail in the methods section from lines 166 to 175 on page 7.
Reviewer's Recommendation: **Revisions required**	
Executive editor's name: M Mostafa Zaman	
ORCID: 0000-0002-1736-1342	
Do you have any conflict of interest with the author/s? **No**	
Do you wish to be disclosed to the author? **Yes**	
Comments sent to author (Date: **22-May-24**)	Date replied by author: **29-May-24**
1. Background in abstract section needs to be more precise/short.	We have revised the background in the abstract section to be more precise/short from lines 57 to 61 on page 3.
2. Results of abstract section should include more important details like: a) Highest and lowest ADC value of malignant and benign tumour. b) Mean ADC value of MSK tumour. c) PPV and NPV. d) AUC cut off value.	We have added the important details such as the highest and lowest ADC value of the tumours, mean ADC value of MSK tumour, PPV and NPV, and AUC cut-off value in the result section from lines 73 to 79 on page 3
3. Main conclusion should be more clear, precise and short. As "This study revealed a good diagnostic accuracy of DW-MRI in characterizing musculoskeletal tumours. Thus, DW-MRI could complement standard MRI features in distinguishing various musculoskeletal tumour types. However, DWI and ADC mapping alone might not help differentiate between various benign and malignant musculoskeletal tumours because of overlapping ADC values." Please make these statements more clear and precise.	We have revised the main conclusion more precisely from lines 374 to 378 on page 13 as follows: "DW-MRI demonstrated high diagnostic accuracy in differentiating musculoskeletal tumours, enhancing the capabilities of conventional MRI. However, DWI and ADC mapping alone are insufficient for distinguishing between benign and malignant musculoskeletal tumours due to overlapping ADC values."
Executive editor's decision: **Revision required**	
Handling editor's name: Md. Nazmul Hasan	
ORCID: 0000-0002-5737-5124	
Do you have any conflict of interest with the author/s? **No**	
Do you wish to be disclosed to the author? **Yes**	
Comments sent to author (Date: **22-May-24**)	Date replied by author: **29-May-24**
1. We need to know how the sensitivity, specificity, etc., given in Table 4 were calculated. Therefore, it should have 2x2 results. These are probably given in Table 5. If this is true, Tables 4 and 5 should be merged.	We would like to express our gratitude to the reviewer for their comment. We acknowledge the reviewer's point that we have calculated the sensitivity, specificity, etc., given in Table 4 from the 2x2 contingency table using SPSS software

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		(SPSS Inc. Version 23.0TM; IBM Corporation, Chicago, USA) which portrayed results in the table. In the table, the highlighted parts are the portraying the results. As this format is rather complex and may cause confusion, we have decided to present the results in two separate tables in different formats to ensure clarity. Additionally, some results (e.g., cut-off value, AUC) in Table 4 were derived from the ROC curve, preventing us from merging Tables 4 and 5. However, we have revised the table chronology for better understanding, renaming the previous Table 4 as Table 5 and the previous Table 5 as Table 4, and revised the results section accordingly.
2.	It is not clear how the area under the curve was calculated. There is no ROC curve for which the area under the curve is calculated.	We had already presented the ROC curve as Figure 1, which now has become Figure 2 in the additional files (Figures_of_the_study) attached along with the manuscript.
Handling editor's recommendation: **Revision required**		
ROUND 2		
Reviewer's name: Abu Shahin		
ORCID: 0000-0001-6719-3896		
Date assigned: **3-Jun-24**		
Date submitted: **6-Jun-24**		
Do you have any conflict of interest with the author/s? **No**		
Do you wish to be disclosed to the author? **Yes**		
Comments sent to author (Date: **7-Jun-24)**		Date replied by author: **15-Jun-24**
How would you rate the originality and depth of the manuscript?	8	-
Is the manuscript written in a scholarly manner?	8	-
Does the manuscript have the potential to make a valuable contribution to the world of knowledge?	8	-
Does the manuscript meet ethical standards?	8	-
1.	Line no 68- Spell out ADC	We have spelt out ADC in line 68 on page 3 "apparent diffusion coefficient (ADC)".
Reviewer's Recommendation: **Accept Submission**		
Reviewer's name: M Mostafa Zaman		
ORCID: 000-0002-1736-1342		
Date assigned: **3-Jun-24**		
Date submitted: **4-Jun-24**		
Do you have any conflict of interest with the author/s? **No**		
Do you wish to be disclosed to the author?		

REVIEW COMMENTS		AUTHOR RESPONSE [Note: Please write the responses to each point here mentioning line number(s). You must change the manuscript as per your response.]
Yes		
Comments sent to author **(**Date: **7-Jun-24)**		Date replied by author: **15-Jun-24**
How would you rate the originality and depth of the manuscript?	6	-
Is the manuscript written in a scholarly manner?	5	We revised the manuscript in a scholarly manner.
Does the manuscript have the potential to make a valuable contribution to the world of knowledge?	7	-
Does the manuscript meet ethical standards?	8	-
This study determined the accuracy of the DW-MRI and ADC compared to a standard of histopathologically confirmed malignant MSK tumours in a pool of 35 patients with MSK tumours. However, this has not been stated clearly anywhere in the manuscript. The accuracy was measured using the MRI's sensitivity and specificity and the ADC ROC curve. While the study can contribute to the clinical practice, the storytelling could be better, and the statistical analysis could be streamlined. Specific points are:		-
1.	The analysis should be guided by the objective of the study. The objective is "to review and ascertain the diagnostic accuracy of quantitative DW-MRI with ADC mapping in the characterisation of MSK tumours." What does it mean? Do the authors determine the accuracy of DW-MRI and ADC compared to histopathologically confirmed diagnosis? If so, what does the quantitative mean? The authors have presented the DW_MRI accuracy data for sensitivity and specificity as categorical data (Tables 4 and 5).	We agree that the analysis should indeed be guided by the study's objectives. We also affirm that the objective of this study is to determined the diagnostic accuracy of DW-MRI and ADC compared to histopathologically confirmed diagnosis. We recognize that using the term "quantitative" alongside "DW-MRI" may have caused some confusion, as our final results were presented in terms of sensitivity and specificity, which are categorical data. To clarify, the term "quantitative" was intended to describe the type of MRI test employed. Unlike conventional MRI, where reports are derived qualitatively based on the radiologist's observations of lesion characteristics in the MRI images, DW-MRI generates Apparent Diffusion Coefficient (ADC) values, which are quantitative. From these ADC values, radiologists can determine whether a lesion is benign or malignant based on a specified cut-off point. Thus, the term "quantitative" was used to emphasize the nature of the DW-MRI testing process. However, we understand that this term might have been misleading and interpreted as relating to the nature of the results. Therefore, we have decided to remove the term "quantitative" from this section to prevent any further confusion and re-write it as follows: “review and ascertain the diagnostic accuracy of DW-MRI with ADC mapping in the characterisation of musculoskeletal tumours in this context” in line no. 150 in the Background section.
2.	However, the ADC results are presented as quantitative data, the ROC curve. However, it is presented erroneously with DW-MRI results in Table 5 (AUC). AUC could be presented with the RCO curve (figure 2). The	We understand the reviewer's confusion about presenting ADC results (AUC and cut-off ADC value) derived from the ROC curve alongside DW-MRI results in Table 5. However, we have included the AUC and cut-off ADC value in Table 5

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	open question here is on the cut-off points used fro drawing the ROC curve. The ROC curve touches the baseline (AUC 0.5) up to ADC cut-off points 0.3 for 1-specificity. This has happened because of the small sample size, 35 here. Kindly note that the authors have considered any cut-off value of ADC for clinical practice. What will be the sensitivity and specificity for that cut-off point? Table 5 could be expanded for ADC as categorical data.	because these metrics are generated from the ROC curve of ADC values, which are the imaging findings from the DW-MRI scan. The sensitivity, specificity, PPV, and NPV presented in Table 5 are based on the cut-off ADC value from the ROC curve, which helps categorise lesions as either positive or negative for malignant MSK tumours. Therefore, we believe it is appropriate to present the ADC results (AUC and cut-off ADC value) in the same table as the DW-MRI results, as they are inherently linked through the ROC analysis. To clarify this point, we have revised the previous term "cut-off value" to "cut-off ADC value and also made necessary revisions in the Result section from line no. 289 to 292 as follows: “Receiver operating characteristic (ROC) curve analysis (Figure 2) indicated that with a cut-off ADC value of ≤ 1.1×10−3 mm2/s, DW MRI has a sensitivity of 96.4%, specificity of 71.4%, 93.1% PPV, and 83.3% NPV and overall accuracy of 91.43% (Table 5) for diagnosing malignant musculoskeletal tumours”. We understand that due to the nature of the cut-off points used to plot the ROC curve, it touches the baseline (AUC 0.5) up to ADC cut-off points of 0.3 for 1-specificity, likely because of the small sample size. So, deriving an optimal cut-off point for clinical practice might be challenging. However, after reviewing multiple studies on ADC cut-off points for differentiating malignant musculoskeletal (MSK) tumours, we found that many studies reported a cut-off point of 1.1×10−3 mm^2/s for characterising MSK tumours. We have also adopted this cut-off point based on our ROC curve analysis, as it provided the optimal sensitivity and specificity. We have referenced these studies that support the same cut-off point in the Discussion section, such as in lines 350 to 352 as follows: “Similar findings were observed by Romeih et al., who found a sensitivity of 83.3% and specificity of 72.7% of DW-MRI in characterising musculoskeletal soft tissue tumours”, from line no. 352 to 355: “With a cut-off mean ADC value of 1.058 x 10-3mm2/s, Boruah et al. observed that DW-MRI demonstrated a sensitivity of 83.3%, specificity of 66.7%, and accuracy of 78.7% in distinguishing benign from malignant bone tumours” and from line no 357 to 359 as follows: “Neubauer et al., employing a similar cut-off point, reported a sensitivity of 90% and specificity of 91% for characterising musculoskeletal tumours”. Additionally, we reviewed the ADC cut-off points commonly used clinically and found that a similar cut-off point is being employed in clinical practice. Therefore, we did not consider any other ADC cut-off values for clinical practice.
3.	Are the authors recommending using DW-MRI and ADC categories as serial tests, or any of them, or both to be used simultaneously? These three will require a different analysis. Therefore, the authors need to mention this in	We would like to thank the reviewer for the comment. Diffusion-weighted MRI (DW-MRI) and ADC mapping is a single imaging technique where the ADC value is the result of a DW-MRI scan. The radiologist interprets the type of lesion

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detail in the Methods and Results section and Discuss it accordingly.	based on the ADC values in the DW-MRI scan. Therefore, it is essential to consider it as a single test. However, we recommend using DW-MRI in conjunction with conventional MRI for a more effective characterization of musculoskeletal (MSK) tumours. This is because DW-MRI alone may be insufficient for accurately distinguishing between benign and malignant MSK tumours due to some overlapping ADC values. We have mentioned this recommendation in the conclusion section from line no. 373 to 374: "In summary, when combined with conventional MRI sequences, DWI and ADC mapping plays a valuable role in assessing musculoskeletal tumours" and line no. 378 to 380: "However, DWI and ADC mapping alone are insufficient for distinguishing between benign and malignant musculoskeletal tumours due to overlapping ADC values". We have described the detailed process of DW-MRI with ADC mapping imaging protocol in the Methods section from line no. 193 to 202 as follows: "C. Diffusion-weighted MR images Diffusion-weighted MR images were obtained in the axial plane with TR 4400 ms, TE 72 ms, slice thickness 3.5 mm, FOV 150 mm and matrix 140×140. The strength of MPG is usually defined by the gradient factor b. The b-values used in this study were 0 and 800s/mm2. By manually placing a region of interest (ROI) over the solid part of the tumour, the ADC is determined as a numerical number. The workstation generated ADC maps automatically based on the three b values using the formula ADC=ln(S0/S1)/(b1-b0), where S0 and S1 represent the signal intensity before and following the application of diffusion gradients, respectively, and b1 and b0 represent the various b-values applied." The image analysis process with the calculation of ADC value for this test is described in detail in the Methods section from line no. 227 to 237 as follows: "For ADC calculation analysis, ADC values were generated pixel by pixel. Minimum, maximum, and mean ADC values were calculated using round or elliptical regions of ROIs, with mean ADC values chosen for statistical analysis. ADC values were expressed in 10-3 x mm2/second. Multiple uniform-sized ROIs (area, minimum 10 mm2, maximum 50 mm2) were placed, with three ROIs in the central non-necrotic portion and three in the peripheral portion of the tumour. ROIs were selectively placed in solid, enhancing, non-necrotic, and/or DWI-restricted regions, avoiding contamination from adjacent normal-appearing bone or soft tissue. ROI position was verified with reference to conventional MRI images to avoid artefacts, distortions, partial volume effects, and the most peripheral margin of the tumour. In the case of multiple

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		lesions, the largest lesion was selected for calculating the mean ADC value." We have discussed about DW-MRI technique in the Discussion section from line no. 300 to 304 "With minimal extra scanning time, DWI, a functional MRI technique, can be added to the standard MRI protocols to provide a way to assess musculoskeletal tumours according to their histological composition. DWI and ADC mapping quickly generate quantitative data regarding the tumour cellularity."
4.	Finally, the Methods should clearly state the standard against which the comparisons are made. This has implications for reporting results and making conclusions and recommendations.	We have clarified that the histopathology findings were the standard against which the comparisons were made, and have included this information from line no. 176 to 178 as follows: "Subsequently, the findings from DW-MRI were assessed and compared with histopathology (FNAC/biopsy) results, which were considered as the gold standard."
Reviewer's Recommendation: **Revisions required**		
Handling editor's name: Md. Nazmul Hasan		
ORCID: 0000-0002-5737-5124		
Do you have any conflict of interest with the author/s? **No**		
Do you wish to be disclosed to the author? **Yes**		
Comments sent to author (Date: **7-Jun-24**)		Date replied by author: **15-Jun-24**
1.	Flow chart that is given in the revised version-2 should contain specific subject number in each stage to improve the quality or you can drop it.	We have revised the flowchart and decided to drop the subject number.
2.	In the methodology section, no where it is mention about the biopsy procedure. If the biopsy was an surgical open biopsy procedure then which department was involved needs to be mentioned or if it was guided core biopsy that should also be mentioned. The center where the histopathology was done isn't mentioned.	We have added the details of the biopsy procedure from line no. 240 to 246 as "USG-guided FNAC and guided core biopsy procedures were conducted in the Department of Radiology and Imaging, while the surgical open biopsy procedure was conducted in the Department of Orthopedic Surgery, BSMMU; Department of Surgical Oncology, BSMMU; and National Institute of Cancer Research & Hospital (NICRH). Two experienced pathologists examined all specimens in the Department of Pathology, BSMMU, and the final results were determined by consensus."
3.	Was the FNAC a guided procedure or blind one?	We confirm that the FNAC procedure was guided by ultrasound (USG-guided FNAC) and was conducted in the Department of Radiology and Imaging. We have incorporated this clarification into the Methods section, specifically on line 240.
4.	As you are considering the histopathology as gold standard for diagnosis of malignant MSK tumour against which yoy will compare DW MRI & ADC value , FNAC vs biopsy would not carry the same accuracy to diagnose	We agree that FNAC and biopsy may not have the same accuracy in diagnosing musculoskeletal (MSK) tumours. Therefore, we have included the number of patients

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	the MSK tumour. So, number of patient that was diagnosed by FNAC should be mentioned in the methodology section.	diagnosed either by FNAC or by biopsy in the methodology section from lines 239 to 240 as follows: "The definitive diagnosis was established through histopathologic findings after either performing FNAC (n=8) or biopsy (n=27)."
Handling editor's recommendation: **Revision required**		
ROUND 3		
Handling editor's name: Md. Nazmul Hasan		
ORCID: 0000-0002-5737-5124		
Do you have any conflict of interest with the author/s? **No**		
Do you wish to be disclosed to the author? **Yes**		
Comments sent to author (Date: **20-Jun-24**)		Date replied by author: **23-Jun-24**
1.	The identity of the 3 radiologists and two pathologists could be included in the methodology section as a recognition of their work.	We have included the initials of the three radiologists in the methods section from line no. 205 to 206 as: "Three radiologists (MS, MSS and SAA) with respective experience of above 10 years reviewed the MRI images." and their full names are included in the authors list. We have also included the initials of the two pathologists in the methods section from line no. 245 to 247 as: "Two experienced pathologists (NK and BPD) examined all specimens in the Department of Pathology, BSMMU" and their full names are included in the acknowledgement section.
2.	As you have explained and we understood that ADC value was calculated from DW-MRI in case of MSK tumour. But nowhere in the methodology it is clearly mentioned. More over title of the study does not reflect anything containing such information. General reader might be confused and might think that DW-MRI and ADC value are two different entity. So, please make it clear in the methodology section for better clarification.	We have clarified in the methods section that ADC values were calculated from DW-MR imaging by including the following: "DW-MRI was performed following standard procedural protocol and images were analysed and ADC value was calculated from the DW-MR image sequences by experienced radiologists." from line no. 171 to 174. In addition, in the MRI protocol part of the Methods section, we have detailed the process of ADC value calculation while explaining the imaging protocol for DW-MRI as follows: "C. Diffusion-weighted MR images Diffusion-weighted MR images were obtained in the axial plane with TR 4400 ms, TE 72 ms, slice thickness 3.5 mm, FOV 150 mm and matrix 140×140. The strength of MPG is usually defined by the gradient factor b. The b-values used in this study were 0 and 800s/mm2. By manually placing a region of interest (ROI) over the solid part of the tumour, the ADC is determined as a numerical number. The workstation generated ADC maps automatically based on the three b values using the formula ADC=ln(S0/S1)/(b1-b0), where S0 and S1 represent the signal intensity before and following the

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		application of diffusion gradients, respectively, and b1 and b0 represent the various b-values applied." from line no. 194 to 203.
3.	In table-1: some values containing same frequency and percentage (1;2.9%) could be merged together to make the table more compact (neck, elbow, forearm, back,--1,2.9%, foot note should include values are for each entity). Same would be applicable for the table-2. Title of the table-2 would be "histopathological findings of the Musculoskeletal tumours".	We have now revised the Table 1 and Table 2 and have merged the values containing the same frequency and percentage together and have added a footnote denoting that these values are for each entity. As per the reviewer's suggestion, we have revised the title of Table 2 to "Histopathological findings of the musculoskeletal tumours"
4.	Table-3: Title should be changed to "ADC value calculated from DW-MRI of the Musculoskeletal tumours". inside the table, Mean ADC value of the total (35) study subjects should be included above the heading of the "nature of tumour" and included in the text.	We have revised the title of Table 3 as "Table 3: ADC value of the musculoskeletal tumours derived from DW-MRI" We have added the mean ADC value of the total (35) study subjects in the Table 3 above the heading of the "nature of tumour" and also included it in the result section in line no. 281 as: "The mean ADC value of the total 35 study subjects was 0.86 ± 0.30×10-3 mm2/s."
5.	In table-4, cross tabulation has shown that MRI diagnosis in one side, is it DW-MRI or conventional MRI? should be mentioned.	The cross-tabulation in Table 4 indeed represents DW-MRI diagnoses. We have now clarified this in the table and re-write it as "DW-MRI" in the table title and header.
6.	Table-5: Title could be changed to "Diagnostic accuracy of ADC value calculated from DW-MRI in diagnosis of malignant musculoskeletal tumours" as the table contain single cut off value for ADC.	We have now revised the title of Table 5 as "Table 5: Diagnostic accuracy of ADC value derived from DW-MRI in diagnosis of malignant musculoskeletal tumours"
7.	The value of getting low ADC (<0.3) should be discussed. Considering the small sample size and unstable curve, figure containing ROC curve should be omitted and small description of ROC already been added inside the text of the corrected version that is sufficient.	We have discussed the importance of low ADC value in the Discussion section from line no. 338 to 342 as follows: "Typically, malignant tumours exhibit low ADC values, while benign tumours demonstrate high ADC values, except for certain cases such as giant cell tumours (GCT) and osteoblastoma, which manifest lower ADC values. Thus, ADC value can play a vital role in the differentiation between benign and malignant musculoskeletal tumours." We concur with the reviewer's comment regarding the figure containing ROC curve and have now removed "Figure 2: Receiver operating characteristic (ROC) curve for predicting the malignant tumours of the musculoskeletal system in the studied patients (area under the curve: 0.758)." We have retained the brief description of the ROC curve within the text.
8.	As per your response, 28 study subjects underwent biopsy. So, could you please show analysis of these sample and show how it is comparable with total of 35 subjects which includes FNAC also. Moreover, in your limitation, it should be discussed that all subjects did not underwent biopsy.	We have presented a new table (Table 5) showing the cross-tabulation findings between the final diagnosis by biopsy procedure and DW-MRI's diagnosis. Additionally, we have added a column in Table 6 (previously Table 5) to separately showcase the diagnostic accuracy of DW-MRI in diagnosing malignant musculoskeletal tumours among the study subjects who only underwent biopsy, alongside the total diagnostic accuracy. We have revised the corresponding result section accordingly.

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		We have included in the limitation that all subjects did not underwent biopsy as follows: "Another limitation of the study is that not all study subjects underwent open biopsy. For some patients, histopathological analysis was performed using FNAC. This variation in diagnostic procedures could introduce inconsistencies in the histopathological confirmation of the tumour types and may impact the overall accuracy and comparability of the diagnostic results" from line no. 377 to 381.
9.	Please omit the total flowchart of the study.	We have now omitted the total flowchart of the study.
10.	Rearrange the figure and the table if necessary.	We have rearranged the figures and tables accordingly like renaming Figure 3 as Figure 1, adding a new table (now Table 5) and renaming previous Table 5 as Table 6.
Handling editor's recommendation: **Revision required**		

ROUND 4

Handling editor's name: Md. Nazmul Hasan		
ORCID: 0000-0002-5737-5124		
Do you have any conflict of interest with the author/s? **No**		
Do you wish to be disclosed to the author? **Yes**		
Comments sent to author (Date: **26-Jun-24**)		Date replied by author: **27-Jun-24**
1.	Regarding validity calculations: PPV=a/(a+b) = 5/6=83.33% NPP=d/(c+d) = 27/29=93.10% Sensitivity=a/(a+c) =5/7=71.42% Specificity=d/(b+d) =27/28=96.42% This is our calculation findings on the basis of the table-4 you have submitted and which does not match with the findings of the table-6 where you have shown your validity data. Please enlighten us how did you calculated your validity results. If validity is changed please include that in the text portion of the study as well.	We understand that some confusion has arisen regarding the validity calculation based on the table-4 which showed the cross tabulation of benign and malignant cases based on diagnostic modality. To clarify, in table 4, we presented the cross tabulation of distribution of benign and malignant MSK tumours based on diagnostic modality. However, for calculating diagnostic accuracy, we have considered the malignant status as being positive since our aim was to evaluate the efficacy of DW-MRI in detecting malignant MSK tumour. As such, while calculating validity, we assigned the cases in reverse manner from table 4. Calculating validity in this way yielded a Sensitivity of 96.4%, Specificity of 71.4%, PPV of 93.1% and NPP of 83.3%, which we had presented in the manuscript.
2.	Please clarify how the accuracy was calculated and include in the statistical analysis of the methodology section of the study; line no-259.	To clarify, we have calculated the accuracy following the formula: "Accuracy= (TP (a)+TN (d))/(TP (a)+TN(d)+FP(b)+FN(c)) = 27+5/27+5+2+1 = 32/35 = 91.43%" We have now included it in the statistical analysis of method section from line no. 261 to line no. 264.
3.	Please omit table-4, which is not required and omit column containing 'biopsy(28)' in table 6 as no comparison in this table is required. Add the results of	We have removed the Table 4: Cross-tabulation between final diagnosis and DW-MRI's diagnosis and have retained the results of analysis briefly inside the text of result section from

REVIEW COMMENTS		AUTHOR RESPONSE [Note: Please write the responses to each point here mentioning line number(s). You must change the manuscript as per your response.]
	analysis on the basis of these two inside the text of result section only and that should be very brief.	line no. 297 to 3298 as follows: "Overall, DW-MRI was successful in diagnosing twenty-seven out of twenty-eight cases of malignant musculoskeletal tumours." We have also renamed the previous Table 5 as "Table 4: Cross-tabulation between final diagnosis by biopsy procedure and DW-MRI's diagnosis" and have revised the content inside the table to ensure that it is in accordance with the validity study. We have also renamed previous Table 6 now as "Table 5: Diagnostic accuracy of ADC value derived from DW-MRI in diagnosis of malignant musculoskeletal tumours". We have omitted the column containing 'biopsy (28)' in Table 6 (Now Table 5) and retained the results of analysis of this column in the result section briefly from line no. 301 to 304 as: "With a same cut-off point, among the study subject who underwent biopsy, DW-MRI demonstrated a sensitivity of 95.8%, specificity of 75%, PPV of 95.8%, NPV of 75% and accuracy of 92.86% for diagnosis of malignant musculoskeletal tumours".
4.	Please omit the row containing "cut off ADC value" and "area under the curve" in table-6 which is not required. Insert the cut off ADC value in statistical analysis section which has been used here in line no-257.	We have omitted the row containing "cut off ADC value" and "area under the curve" in Table 5 (previous Table 6). We have inserted the cut off ADC value in statistical analysis section in line no. 256 (previous 257).
ROUND 5		
Handling editor's name: Md. Nazmul Hasan		
ORCID: 0000-0002-5737-5124		
Do you have any conflict of interest with the author/s? **No**		
Do you wish to be disclosed to the author? **Yes**		
Comments sent to author (Date: **27-Jun-24**)		Date replied by author: **28-Jun-24**
1.	We found in response to comment no-1, you have included table-4 and gave your calculation of validity. Please correct the summation value of a+c=28 and b+d=7 inside the table which is not correct. Please omit this table - Table 4. Cross-tabulation between final diagnosis by biopsy procedure and DW-MRI's diagnosis in corrected version-4). The following table below should be your table -4 and keep the table-5 as it is now in corrected version-4: Table 4. Cross-tabulation between final diagnosis by histopathology/FNAC and DW-MRI's diagnosis	We have now revised the table 4 as "Table 4: Cross-tabulation between final diagnosis by histopathology/FNAC and DW-MRI's diagnosis" and have omitted the previous Table 4: Cross-tabulation between final diagnosis by biopsy procedure and DW-MRI's diagnosis. We have also corrected the summation value of a+c=28 and b+d=7 inside the table and added a footnote as follows: * for ADC cut-off value of ≤ 1.1×10−3 mm2/s ** confirmed by histopathology and FNAC as appropriate.
2.	We found in response to comment no-1, you have included table-4 and gave your calculation of validity. Please correct the summation value of a+c=28 and	We understand that some confusion has arisen regarding the validity calculation based on the table-4 which showed the cross-tabulation of benign and malignant cases based on

REVIEW COMMENTS	AUTHOR RESPONSE [Note: Please write the responses to each point here mentioning line number(s). You must change the manuscript as per your response.]
b+d=7 inside the table which is not correct. Please omit this table - Table 4. Cross-tabulation between final diagnosis by biopsy procedure and DW-MRI's diagnosis in corrected version-4). The given table should be your table -4 and keep the table-5 as it is now in corrected version-4 Table 4. Cross-tabulation between final diagnosis by histopathology/FNAC and DW-MRI's diagnosis [format suggested]	diagnostic modality. To clarify, in table 4, we presented the cross tabulation of distribution of benign and malignant MSK tumours based on diagnostic modality. However, for calculating diagnostic accuracy, we have considered the malignant status as being positive since our aim was to evaluate the efficacy of DW-MRI in detecting malignant MSK tumour. As such, while calculating validity, we assigned the cases in reverse manner from table 4. Calculating validity yielded a Sensitivity of 96.4%, Specificity of 71.4%, PPV of 93.1% and NPP of 83.3%, which we had presented in the manuscript.
Handling editor's recommendation: **Revision required**	

C. Editorial decision

Final editorial decision:
Accepted on 28-Jun-24