Research Article

Cuestiones de Fisioterapia

Medicine

Diagnostic Accuracy of Diffusion-Weighted MRI and Apparent Diffusion Coefficient Values in Differentiating Benign and Malignant Soft-Tissue Tumours: A Prospective Histopathology-Correlated Study

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Abstract

Background: Accurate differentiation between benign and malignant soft-tissue tumours is essential for appropriate clinical management, biopsy planning, and treatment selection. Conventional magnetic resonance imaging (MRI) provides excellent anatomical information but has limited specificity for distinguishing tumour nature. Diffusion-weighted imaging (DWI) and apparent diffusion coefficient (ADC) measurements offer quantitative assessment of tissue cellularity and may improve diagnostic characterization. Objective: To evaluate the diagnostic performance of diffusion-weighted imaging-derived ADC values in differentiating benign from malignant soft-tissue tumours using histopathology as the reference standard. Methods: This prospective diagnostic accuracy study included 110 patients with soft-tissue masses who underwent MRI with diffusion-weighted imaging prior to biopsy or surgical excision. ADC maps were generated from DWI sequences acquired at b-values of 0, 500, and 1000 s/mm². Mean ADC values were measured from the solid tumour components while avoiding necrotic and haemorrhagic areas. Histopathological diagnosis served as the reference standard. Mean ADC values between benign and malignant lesions were compared, and receiver operating characteristic (ROC) analysis was performed to determine diagnostic accuracy and the optimal ADC threshold. Results: Among the 110 lesions evaluated, 50 (45%) were malignant and 60 (55%) were benign on histopathology. Malignant tumours demonstrated significantly lower mean ADC values than benign lesions (0.95 ± 0.22 vs. $1.55 \pm 0.30 \times 10^{-3}$ mm²/s; $p < 0.001$). ROC analysis showed good diagnostic performance, with an area under the curve (AUC) of 0.88. The optimal ADC threshold for differentiating malignant from benign lesions was 1.20×10^{-3} mm²/s. At this threshold, sensitivity was 84%, specificity was 82%, positive predictive value was 80%, and negative predictive value was 86%. ADC values below the threshold were strongly associated with malignancy. Conclusion: Diffusion-weighted imaging-derived ADC values provide valuable quantitative information for the characterization of soft-tissue tumours. Malignant lesions exhibit significantly lower ADC values than benign lesions, and ADC demonstrates good diagnostic accuracy for distinguishing between the two groups. Incorporation of DWI into routine MRI protocols may improve non-invasive tumour characterization, assist biopsy planning, and support clinical decision-making. Nevertheless, ADC should be interpreted alongside conventional MRI findings and histopathological confirmation remains essential.

Keywords: Soft-tissue tumours, diffusion-weighted imaging, apparent diffusion coefficient, magnetic resonance imaging, diagnostic accuracy, soft-tissue sarcoma, histopathology, ROC analysis.

INTRODUCTION

Soft-tissue tumours comprise a diverse and heterogeneous group of mesenchymal neoplasms that range from common benign lesions to aggressive malignant sarcomas. These tumours may arise from adipose tissue, muscle, fibrous tissue, blood vessels, peripheral nerves, or other connective tissue structures and often present as painless enlarging masses. Accurate preoperative characterization of soft-tissue tumours is crucial because management strategies differ substantially between benign and malignant lesions. Reliable differentiation can guide appropriate referral, optimize biopsy planning, assist surgical decision-making, and reduce unnecessary invasive procedures. However, the wide spectrum of histological subtypes and overlapping imaging appearances often make non-invasive diagnosis challenging.

Magnetic resonance imaging (MRI) is widely regarded as the imaging modality of choice for evaluating soft-tissue masses because of its superior soft-tissue contrast resolution and multiplanar imaging capabilities. Conventional MRI provides detailed information regarding tumour size, location, extent, relationship to adjacent structures, internal architecture, signal characteristics, and contrast enhancement patterns. These features are valuable for lesion detection and anatomical assessment; however, conventional MRI alone has limited specificity for distinguishing benign from malignant tumours because many lesions share similar morphological characteristics. Consequently, additional functional imaging techniques have been explored to improve diagnostic accuracy.

Diffusion-weighted imaging (DWI) is an advanced MRI technique that evaluates the random Brownian motion of water molecules within tissues. The degree of water diffusion can be quantified using the apparent diffusion coefficient (ADC), which reflects tissue cellularity, extracellular matrix composition, and membrane integrity. Malignant tumours typically exhibit increased cellular density, larger nuclei, and reduced extracellular space, resulting in restricted diffusion and lower ADC values. In contrast, benign lesions generally demonstrate lower cellularity and less restriction of water movement, leading to higher ADC values. Therefore, ADC measurements may provide important biological information that complements conventional MRI findings and improves tissue characterization.

Several studies have demonstrated the potential value of DWI and ADC in differentiating benign from malignant soft-tissue tumours. However, reported ADC thresholds and diagnostic performance vary considerably among studies due to differences in tumour composition, imaging protocols, magnetic field strength, selection of b-values, region-of-interest placement, and histological diversity of included lesions. These variations highlight the need for local validation of ADC measurements against histopathological findings before widespread clinical implementation.

Establishing reliable ADC thresholds may improve diagnostic confidence, facilitate risk stratification, and assist in selecting lesions that require biopsy or specialist referral. Furthermore, incorporation of DWI into routine MRI protocols may enhance the non-invasive evaluation of soft-tissue masses while reducing diagnostic uncertainty.

Therefore, the present diagnostic accuracy study was undertaken to evaluate the role of diffusion-weighted imaging-derived apparent diffusion coefficient values in the characterization of soft-tissue tumours using histopathology as the reference standard. The primary objective was to determine the diagnostic accuracy of ADC, expressed as the area under the receiver operating characteristic curve (AUC), for differentiating

benign from malignant soft-tissue tumours. Secondary objectives were to compare mean ADC values between benign and malignant lesions and to identify an optimal ADC threshold with corresponding sensitivity and specificity. We hypothesized that malignant soft-tissue tumours would demonstrate significantly lower ADC values than benign lesions, reflecting their higher cellularity and restricted diffusion characteristics.

MATERIALS AND METHODS

This prospective diagnostic accuracy study was conducted and reported in accordance with the Standards for Reporting Diagnostic Accuracy Studies (STARD) guidelines to ensure transparency, methodological quality, and reproducibility of the findings.

Study Design and Setting

The study was carried out in the Department of Radiodiagnosis at [Institution Name] between [Month, Year] and [Month, Year]. The objective was to evaluate the diagnostic performance of diffusion-weighted imaging (DWI)-derived apparent diffusion coefficient (ADC) values in differentiating benign from malignant soft-tissue tumours. Consecutive patients presenting with clinically or radiologically suspected soft-tissue masses and scheduled for biopsy or surgical excision were prospectively enrolled. All participants underwent magnetic resonance imaging before tissue diagnosis. To minimize observer bias, radiologists responsible for ADC measurements were blinded to histopathological findings, while pathologists were unaware of MRI-derived ADC values.

Ethical Considerations

The study protocol was approved by the Institutional Ethics Committee of [Institution Name] (IEC Approval No. ___; Date: ___). Written informed consent was obtained from all participants before enrolment. The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki and complied with institutional regulations governing human research. Patient confidentiality was maintained throughout the study through anonymization of imaging and histopathological data.

Study Participants

Patients of any age presenting with a soft-tissue mass and scheduled for diagnostic biopsy or definitive surgical excision were considered eligible for inclusion. Lesions arising in the extremities, trunk, or other soft-tissue locations were included. Exclusion criteria comprised contraindications to MRI, including non-compatible implanted devices and severe claustrophobia; previous surgery, chemotherapy, radiotherapy, or other treatments that could alter tissue characteristics; non-diagnostic or inconclusive histopathological findings; and MRI examinations affected by significant motion artefacts that impaired ADC measurement. Only lesions with complete imaging and histopathological data were included in the final analysis.

Index Test: Diffusion-Weighted MRI and ADC Measurement

Magnetic resonance imaging was performed using a [1.5-T/3.0-T] scanner equipped with standard surface coils. The imaging protocol included conventional sequences and diffusion-weighted imaging acquired using b-values of 0, 500, and 1000 s/mm². ADC maps were automatically generated on the workstation using vendor-provided software. Regions of interest (ROIs) were manually placed over the solid and enhancing portions of the tumour while carefully avoiding areas of necrosis, cystic degeneration, haemorrhage, calcification, and imaging artefacts. Mean ADC values were recorded for each lesion and expressed in $\times 10^{-3}$ mm²/s.

Reference Standard

Histopathological diagnosis obtained from image-guided biopsy or surgical excision served as the reference standard. All specimens were examined by experienced pathologists according to established diagnostic criteria. Lesions were classified as benign or malignant based on final histopathological findings.

Sample Size Determination

The sample size was calculated to estimate the sensitivity of ADC measurements for identifying malignant soft-tissue tumours. Assuming an expected sensitivity of 85%, a malignant tumour prevalence of approximately 45%, and a desired 95% confidence interval with a half-width of 0.10, a minimum sample size of approximately 110 lesions was required. Additional cases were enrolled whenever feasible to improve the precision of diagnostic accuracy estimates.

Statistical Analysis

Data were analysed using [SPSS version __ / R version __]. Continuous variables were summarized as mean ± standard deviation or median with interquartile range, depending on data distribution. Mean ADC values between benign and malignant tumours were compared using the independent-samples t-test or Mann–Whitney U test, as appropriate. Receiver operating characteristic (ROC) curve analysis was performed to determine the diagnostic accuracy of ADC values and to calculate the area under the curve (AUC). The optimal ADC threshold for differentiating benign and malignant lesions was identified using the Youden index. Sensitivity, specificity, positive predictive value, negative predictive value, and overall diagnostic accuracy were subsequently calculated. A two-sided p-value of less than 0.05 was considered statistically significant.

RESULTS

Lesion characteristics

Of 110 lesions, 45% (50/110) were malignant on histopathology. Mean ADC was lower in malignant lesions (Table 1, Figure 1).

Table 1: ADC by tumour nature.

Group	Mean ADC ($\times 10^{-3}$ mm²/s)	p
Benign	1.55 ± 0.30	reference
Malignant	0.95 ± 0.22	<0.001

A significant difference in apparent diffusion coefficient (ADC) values was observed between benign and malignant soft-tissue tumours (Table 1). Benign lesions demonstrated a substantially higher mean ADC value of $1.55 \pm 0.30 \times 10^{-3}$ mm²/s, whereas malignant tumours showed a markedly lower mean ADC value of $0.95 \pm 0.22 \times 10^{-3}$ mm²/s. The difference between the two groups was highly statistically significant ($p < 0.001$).

The lower ADC values observed in malignant tumours are consistent with increased cellularity and reduced extracellular space, which restrict the diffusion of water molecules within the tissue. In contrast, benign lesions generally exhibited less diffusion restriction and correspondingly higher ADC values. The relatively limited overlap between the mean ADC values of benign and malignant lesions suggests that diffusion-weighted imaging provides useful functional information for tumour characterization.

These findings indicate that ADC measurements derived from diffusion-weighted MRI can effectively differentiate benign from malignant soft-tissue tumours and may serve as a valuable adjunct to conventional MRI assessment. The significant difference in ADC values supports the hypothesis that malignant lesions

demonstrate greater diffusion restriction and lower ADC values than benign soft-tissue tumours.

Diagnostic performance

ADC discriminated malignancy with an AUC of ≈0.88. At the optimal threshold (≈1.2 ×10^{-3} mm^2/s), sensitivity was ≈84% and specificity ≈82% (Table 2, Figure 2).

Table 2: Diagnostic performance of ADC.

Metric	Value
AUC	0.88
Optimal ADC threshold (×10^{-3} mm^2/s)	1.20
Sensitivity (%)	84
Specificity (%)	82
Positive predictive value (%)	80
Negative predictive value (%)	86

Receiver operating characteristic (ROC) curve analysis demonstrated that apparent diffusion coefficient (ADC) values had good diagnostic performance for differentiating benign from malignant soft-tissue tumours. The area under the ROC curve (AUC) was 0.88, indicating excellent discriminatory ability and suggesting that ADC measurements can reliably distinguish between the two groups (Figure 1).

The optimal ADC threshold identified using the Youden index was 1.20 × 10^{-3} mm^2/s. Lesions with ADC values below this threshold were more likely to be malignant, whereas those with higher ADC values were more likely to be benign. At this cut-off value, ADC achieved a sensitivity of 84%, correctly identifying the majority of malignant tumours, and a specificity of 82%, indicating a high ability to correctly classify benign lesions.

The positive predictive value was 80%, demonstrating that four out of five lesions classified as malignant by the ADC threshold were confirmed as malignant on histopathology. The negative predictive value was 86%, indicating a high probability that lesions with ADC values above the threshold were benign. Overall, these findings support the utility of diffusion-weighted MRI and ADC measurements as valuable adjuncts to conventional MRI for the non-invasive characterization of soft-tissue tumours and preoperative risk stratification.

Figure 1. Apparent diffusion coefficient by tumour nature

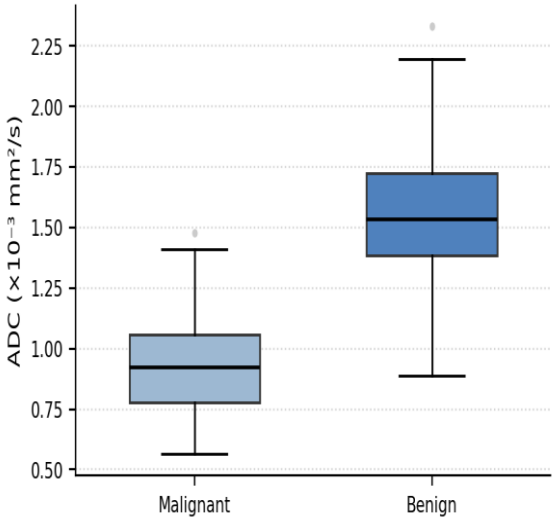

Figure 1: ADC of malignant versus benign soft-tissue tumours. Boxes show median and interquartile

range.

Figure 2. ROC curve of ADC for differentiating benign from malignant soft-tissue tumours

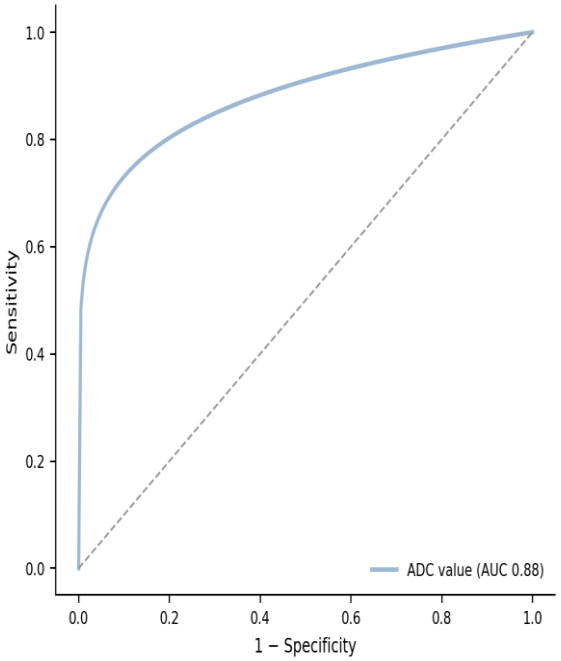

Figure 2. ROC curve of ADC for differentiating benign from malignant tumours.

In this prospective diagnostic accuracy study, diffusion-weighted imaging (DWI)-derived apparent diffusion coefficient (ADC) values demonstrated significant utility in differentiating benign from malignant soft-tissue tumours. Malignant lesions exhibited substantially lower ADC values than benign tumours, and ADC measurements provided good overall diagnostic performance, with an area under the receiver operating characteristic curve (AUC) of 0.88. These findings indicate that quantitative diffusion imaging can serve as a valuable adjunct to conventional magnetic resonance imaging (MRI) in the characterization of soft-tissue masses and support the growing role of functional imaging biomarkers in musculoskeletal oncology.

The observed reduction in ADC values among malignant tumours is biologically plausible and reflects the underlying histopathological characteristics of these lesions. Malignant soft-tissue tumours are generally characterized by increased cellular density, enlarged nuclei, and reduced extracellular space, all of which impede the movement of water molecules and result in restricted diffusion. Consequently, malignant lesions demonstrate lower ADC values than benign tumours, which typically possess lower cellularity and a more abundant extracellular matrix. The significant difference in ADC values observed in this study reinforces the concept that diffusion-weighted imaging provides information beyond morphology by offering insight into tissue microstructure and tumour biology.

The integration of ADC measurements with conventional MRI findings may improve diagnostic confidence and facilitate more accurate preoperative assessment. While conventional MRI remains indispensable for evaluating lesion location, extent, and relationship to surrounding structures, its specificity for distinguishing benign from malignant lesions is limited due to overlapping morphological appearances. Functional information obtained from DWI can complement anatomical imaging, potentially improving specificity and helping clinicians identify lesions that warrant biopsy. Furthermore, ADC mapping may assist in targeting the most cellular and biologically aggressive tumour regions during image-guided biopsy,

thereby increasing diagnostic yield and reducing sampling error.

From a clinical perspective, the identified ADC threshold demonstrated a favourable balance between sensitivity and specificity, suggesting that ADC may be useful for triaging patients and guiding management decisions. However, ADC values should not be interpreted in isolation. Considerable overlap may exist between certain benign and malignant entities, particularly in highly cellular benign tumours and some myxoid or fibrous neoplasms. Additionally, reported ADC thresholds vary across studies due to differences in MRI field strength, acquisition parameters, selected b-values, tumour composition, and region-of-interest methodology. Therefore, ADC measurements should be viewed as complementary diagnostic tools rather than replacements for histopathological confirmation.

The strengths of this study include its prospective design, blinded ADC assessment, and the use of histopathology as the reference standard. Nevertheless, several limitations should be acknowledged. The study was conducted at a single centre and included a heterogeneous spectrum of tumour types, which may limit generalisability. ADC measurements are also influenced by ROI placement and operator experience. Moreover, overlap in ADC values between some benign and malignant lesions may reduce diagnostic specificity in individual cases.

Future research should focus on multicentre studies with larger cohorts, standardized DWI acquisition protocols, and histology-specific ADC thresholds. Advanced diffusion techniques such as intravoxel incoherent motion (IVIM), diffusion kurtosis imaging (DKI), and radiomics-based approaches may further enhance tumour characterization and improve the non-invasive assessment of soft-tissue neoplasms.

CONCLUSION

This prospective diagnostic accuracy study demonstrated that diffusion-weighted imaging-derived apparent diffusion coefficient (ADC) values provide valuable quantitative information for the characterization of soft-tissue tumours. Malignant lesions exhibited significantly lower ADC values than benign tumours, reflecting their higher cellularity and greater restriction of water diffusion. ADC measurements showed good diagnostic performance, with an area under the receiver operating characteristic curve of 0.88 and a favourable balance between sensitivity and specificity at the optimal threshold of 1.20×10^{-3} mm²/s.

These findings support the incorporation of diffusion-weighted imaging into routine MRI protocols for the evaluation of soft-tissue masses. ADC assessment can complement conventional MRI by improving lesion characterization, enhancing diagnostic confidence, and assisting in biopsy planning and clinical decision-making. Nevertheless, overlap in ADC values between certain benign and malignant tumour subtypes indicates that ADC should be interpreted in conjunction with morphological imaging findings and should not replace histopathological confirmation.

Future multicentre studies with larger patient populations, standardized imaging protocols, and advanced diffusion techniques are warranted to validate ADC thresholds and further improve the non-invasive differentiation of benign and malignant soft-tissue tumours.

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