Can MRI diffusion-weighted imaging identify postoperative residual/recurrent soft-tissue sarcomas?

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Abstract

Purpose: The aim of this study was to evaluate contrast-enhanced magnetic resonance imaging (CE-MRI) and quantitative diffusion-weighted imaging (DWI) with apparent diffusion coefficient (ADC) mapping in the detection of recurrent/residual postoperative soft tissue sarcomas. **Materials and Methods:** This study included 36 patients; 27 patients had postoperative recurrent/residual soft tissue sarcomas and 9 patients had postoperative and treatment-related changes (inflammation/fibrosis). The DWI was obtained with 3 b values including 0, 400, and 800 s/mm^2. Calculation of the ADC value of the lesion was done via placing the region of interest (ROI) to include the largest area of the lesion. ADC values were compared to histopathology. **Results:** Our results showed that including CE-MRI improved the diagnostic accuracy and sensitivity in recurrence detection compared to conventional non-enhanced sequences. However, it showed low specificity (55.56%) with a high false-positive rate that may lead to an unnecessary biopsy of a mass such as region of postoperative scar tissue. **Conclusion:** The joint use of gadolinium-enhanced MRI and quantitative DWI with ADC mapping offer added value in the detection of recurrent/residual postoperative soft tissue sarcoma. This combined use increased both the diagnostic sensitivity and specificity with a cut-off average ADC value for detecting nonmyxoid recurrent/residual lesions $\leq 1.3 \times 10^{-3}$ mm^2/s (100% specificity and 90.48% sensitivity). Our results showed limited value of DWI with ADC mapping in assessing myxoid sarcomatous tumor recurrences.

Key words: ADC value; diffusion-weighted imaging; soft tissue sarcoma

Introduction

Soft tissue sarcomas/tumors (STSs) are a variegated group of disorders that have remarkable diagnostic and therapeutic challenges for clinical care. The evaluation of posttreatment response in STS is one of the most important aspects of patient care, as therapeutic options may change depending on the success of response.[1]

Following surgery, the main mantle of magnetic resonance imaging (MRI) is to evaluate the surgical site for recurrent tumors. MRI is the modality of choice for differentiation between a residual or a recurrent tumor and postoperative fibrosis or inflammation.[2]

Differentiating residual or a recurrent tumor from treatment-related tissue changes after surgical resection

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is a common dilemma because of nonspecific signal abnormalities by standard MRI as there is overlap in the imaging features of benign postsurgical reaction and subtle residual or recurrent disease.[3,4]

The aim of the study was to evaluate the efficacy of gadolinium-enhanced MRI and quantitative diffusion-weighted imaging with apparent diffusion coefficient (ADC) mapping in the detection of residual/recurrent postoperative soft-tissue sarcomas and to define the cut-off ADC values of residual/recurrent tumors.

Materials and Methods

This prospective study included 36 patients (16 women and 20 males); their ages ranged from 17 to 73 years with a median age of 38 years. The study was performed in a specialized oncology centre between March 2015 and November 2016.

We included patients of postoperative follow-up who were candidates for MRI after resection of soft-tissue sarcoma in isolation or with radiation and/or chemotherapy.

MRI was performed on a high-field system (1.5 Tesla) closed magnet unit (Phillips Achieva XR). Conventional MRI, diffusion-weighted imaging (DWI), and post-gadolinium DTPA MRI were performed. First blind characterization and detection of lesions were performed, following which diffusion images with ADC values were reviewed.

The morphological features of each lesion were recorded including size, shape, margin, signal characteristics, and pattern of enhancement. The provisional diagnosis was then reported. We reviewed the diffusion images with ADC values measured for each lesion by two different regions of interest. The first region of interest included the average of the whole lesion, whereas the second included the most restricted diffusion area on the ADC map (least ADC value/maximum restricted diffusion; MRDA).

Measurements of the ADC value was made using an electronic cursor applied for each lesion three times when possible, and then the mean ADC value for the lesion was calculated. ADC of the minimum, maximum, and average values was obtained and expressed as mean and standard deviation.

In statistical analysis, features considered positive for recurrent disease included mass-like abnormality of

hypo- or isointense signal at T1-weighted imaging, hyperintense signal at T2-weighted imaging, identification of a mass on conventional imaging, mass-like contrast enhancement, and the presence of a low-signal-intensity mass at ADC mapping.

Results

Preoperative histologic diagnoses in the patients included in our study were:

Synovial sarcoma (n = 12), myxoid liposarcoma (n = 9), pleomorphic sarcoma (n = 7), myxofibrosarcoma (n = 3), malignant peripheral nerve sheath tumor (MPNT) (n = 2), spindle cell sarcoma (n = 1), infantile fibrosarcoma (n = 1), high-grade fibrosarcoma (n = 1).

Out of 36 patients, 27 patients (75%) were proven to have postoperative recurrent/residual soft tissue sarcomas, and 9 patients (25%) had benign postoperative changes (inflammation/fibrosis).

There were 27 proven recurrences and residuals having the following histologic diagnoses: synovial sarcoma (n = 11), myxoid liposarcoma (n = 5), pleomorphic sarcoma (n = 5), myxofibrosarcoma (n = 2), malignant peripheral nerve sheath tumour (MPNT) (n = 2), spindle cell sarcoma (n = 1), infantile fibrosarcoma (n = 1), and 9 cases with postoperative inflammation/fibrosis.

Most tumors were in the lower extremity (30 out of 36) and the remaining 6 were in the upper extremity.

The interval between the surgery and the MRI exam was variable, ranging from 1 month up to 10 years after surgery, with an average of 18 months of follow-up duration.

Detailed analysis of mean ADC (mm^2/s) values and MDRA of recurrent/residual nonmyxoid, myxoid lesions, and benign postoperative changes is shown in the Table 1, including the average ADC±standard deviation.

Static postcontrast T1-weighted MRI achieved 87.5% sensitivity and specificity of only 55.6% because mass-like enhancement was observed in many cases without recurrence (5 of 9 patients with benign postoperative changes).

Decreased signal intensity mass at ADC mapping raised specificity to 100% in the detection of recurrence/residual

Table 1: Detailed analysis of mean ADC (mm²/s) values and MDRA of recurrent/residual nonmyxoid, myxoid lesions, and benign postoperative changes

Pathology	Recurrent/Residual (Nonmyxoid)	Recurrent/Residual myxoid lesions	Benign postoperative changes
No. of cases	21	6	9
Mean ADC (±standard deviation)	1.1±0.2	1.71±0.69	1.9±0.3
MRDA (±standard deviation)	0.81±0.25	1.39±0.67	1.4±0.26

(absent in all 9 patients with postoperative changes), yet this feature does not always exist in all cases (70.37% sensitivity; 19 of 27 patients).

The diagnostic performance of each imaging feature in the detection of recurrent/residual disease is illustrated in Table 2; sensitivity and specificity calculated according to positivity for malignancy.

Regarding the lesion size, the ADC map performance was comparable to contrast-enhanced sequences in detecting small recurrent/residual lesions. Lesions as small as 0.6 cm were depicted as low signal intensity within the surgical bed at the ADC map [Table 3].

Similar to the findings of the qualitative assessment of the ADC maps, the quantitative ADC measures of recurrent/residual disease (mean, 1.23×10^{-3} mm^2/s $\pm$ 0.46) were different than those of postoperative changes (mean, 1.9×10^{-3} mm^2/s $\pm$ 0.3) ($P < 0.0001$).

Receiver operator curve analysis was conducted to establish a cut-off ADC value for detecting recurrent/residual lesions with high specificity [given the relatively high observed sensitivity (87.5%) yet low specificity (55.6%) of the post-contrast sequences].

The cut-off average ADC value for detecting recurrent/residual lesions was found to be $\leq 1.4 \times 10^{-3}$ mm^2/s

Table 2: The diagnostic performance of each imaging feature

Parameter	Sensitivity	Specificity	Accuracy	P
Hypo- or isointensity at T1-weighted imaging	81.48%	11.11%	63.88%	1.0 (insignificant)
Hyperintensity at T2-weighted imaging	81.48	11.11	63.88%	1.0 (insignificant)
Mass at conventional imaging	59.26	88.89	66.66	0.0198 (significant)
Mass at T1-weighted postcontrast imaging	87.5	55.56	78.78	0.0962 (not quite significant)
Low-signal-intensity mass at ADC mapping (including myxoid tumors)	70.37	100	77.77	0.0003 (significant)
Low-signal-intensity mass at ADC mapping (excluding myxoid tumours)	85.71	100	90	0.0001 (significant)
Minimum ADC ≤1.2	88.89	88.89	88.88	<0.0001 (significant)
Average ADC ≤1.4	85.19	100	88.88	<0.0001 (significant)
Minimum ADC ≤1.2 (in nonmyxoid tumors)	95.24	88.89	93.33	<0.0001 (significant)
Average ADC ≤1.3 (in nonmyxoid tumors)	90.48	100	93.33	<0.0001 (significant)
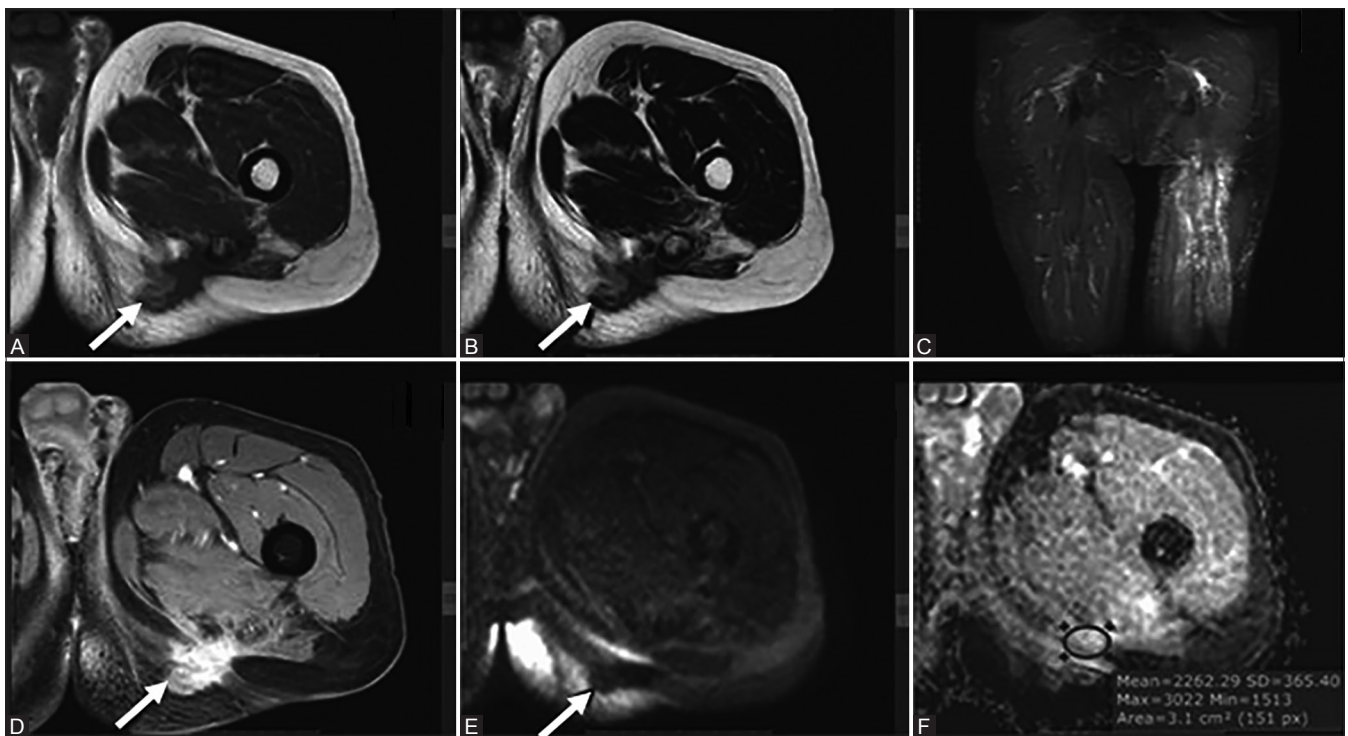
Figure 1 (A-F): MRI images 10 months postsurgical excision of left thigh liposarcoma: (A-C) T1, T2, and STIR weighted images showing an operative bed ill-defined irregular lesion, eliciting a low signal in T1 and T2 with a bright signal in STIR. (D) Homogeneous post-contrast enhancement (arrows) (E and F) DWI and ADC show facilitated diffusion and high ADC measurements (Mean 2.2×10^{-3} mm^2/s, Minimum 1.5×10^{-3} mm^2/s) in keeping with benign postoperative changes (circle). Wide excision revealed granulation tissue negative for residual malignancy

with 100% specificity and 85.19% sensitivity, and the cut-off minimum ADC value were found to be $\leq 1.2 \times 10^{-3}$ mm^2/s with 88.89% specificity and 88.89% sensitivity.

All nine patients with postoperative changes showed high average ADC values $>1.4 \times 10^{-3}$ mm^2/s (the estimated cut-off for recurrence/residual), whereas 23 out of 27 patients with recurrent/residual tumors showed ADC values $\leq 1.4 \times 10^{-3}$ mm^2/s. Only 4 out of 27 patients with recurrent/residual tumors representing 14.8% showed high ADC values $>1.4 \times 10^{-3}$ mm^2/s, imitating recorded values for benign changes; all these 4 cases were of myxoid pathologies. Table 4 shows how excluding the recurrent myxoid lesions affected the minimum and average ADC values statistical parameters.

Discussion

Early detection of postoperative soft tissue sarcoma residual/recurrence allows a larger variegation of treatment choices and results in better prognosis than late identification of recurrence.[5] Therefore, early detection of recurrence is crucial to treat sarcomas, making it the main goal of postoperative MRI.

The differentiation of postoperative changes from a recurrent tumor with conventional MR sequences is challenging.[3]

Table 3: Lesion sizes detected at postcontrast images and ADC map

Recurrent/Residual lesion size	Postcontrast images (area of mass-like enhancement)	ADC map low signal intensity lesion)
Minimum	0.6 cm	0.6 cm
Maximum	9 cm	7 cm
Mean	2.8 cm	2.3 cm

Table 4: Minimum and mean ADC cut-off values with inclusion and after exclusion of recurrent myxoid lesions

Parameter	Cut-off	Sensitivity	Specificity	Accuracy	P
Minimum ADC (MRDA)					
In all recurrent cases	1.2	88.89	88.89	88.88	<0.0001
In non-myxoid recurrences	1.2	95.24	88.89	93.33	<0.0001
Mean ADC					
In all recurrent cases	1.4	85.19	100	88.88	<0.0001
In non-myxoid recurrences	1.3	90.48	100	93.33	<0.0001

*Cut-off ADC value (positive malignancy if less than or equal to)
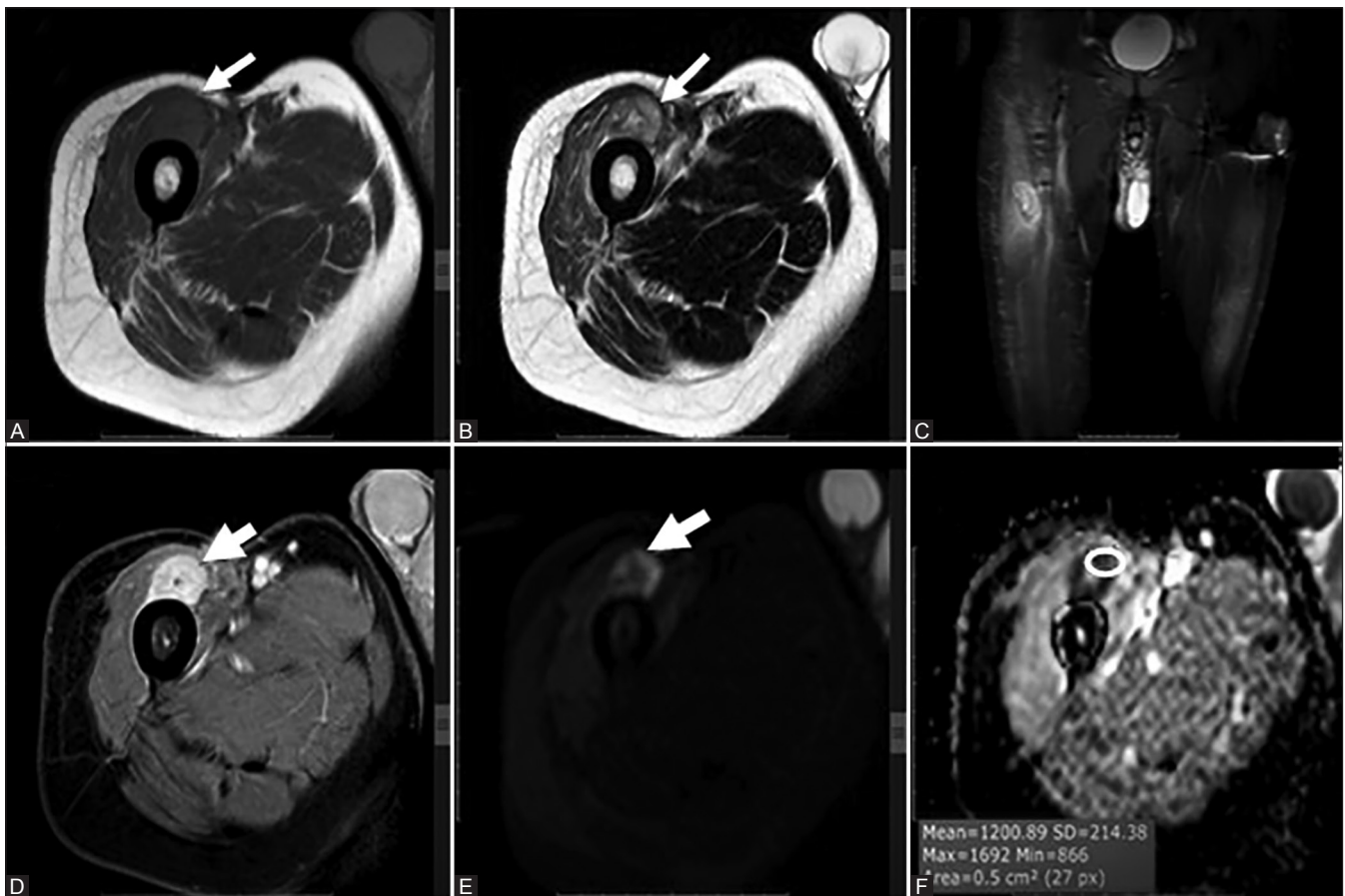
Figure 2 (A-F): MRI images 8 months postsurgical excision of right vastus intermedius synovial sarcoma: (A-C) Axial T1, axial T2, and coronal STIR weighted images showed hardly detectable mass-like area of signal abnormality (arrow) within the right vastus intermedius muscle bed eliciting an isointense signal in T1, high signal in T2 and STIR. (D) Homogeneous enhancement (arrow). (E and F) DWI and ADC restricted diffusion (Mean, 1.2×10^{-3} mm^2/s; Minimum, 0.86×10^{-3} mm^2/s). Wide excision of the operative bed mass revealed recurrent monophasic synovial sarcoma

In our study, most recurrences were hypo or isointense to muscle on T1-weighted sequences and hyperintense to muscle on T2-weighted and STIR sequences with a sensitivity of 81.48% and specificity 11.11%. This was a nonspecific feature for recurrence as 8 out of 9 cases (89%) with benign operative bed changes presented with areas of isointense T1 and high T2 and STIR signal intensities.

Approximately 59.3% of recurrent masses in our series (16 of 27 cases) were identified as suspicious masses on T1- or T2-weighted images. However, subtle recurrences were disregarded in approximately 40.47% (11 of 27 patients) of cases with unenhanced conventional sequences. This matches the findings in other studies by Fayad *et al.* and Grande *et al.*, and points out that intravenous contrast material should be administered for evaluating tumor recurrence.[2,3]

In the study by Afonso *et al.*, incorporating gadolinium MRI resulted in significant improvement in reader's overall accuracy and sensitivity. It also better distinguished solid from cystic masses and improved lesion conspicuity.

Enhancement in the surgical bed is nonspecific as it also occurs in areas of postsurgical and/or post radiation inflammation and fibrosis.[2]

The sensitivity of the static post contrast T1-weighted sequence in the detection of a recurrent/residual tumor is high (87.5%, 21 of 24 patients). However, a mass-like region of enhancement was observed in almost half of the patients without recurrence [44.4% (4 of 9 patients)], resulting in only 55.56% specificity for detecting recurrence. Such a high false-positive rate may lead to an unnecessary biopsy of a mass-like region of postoperative scar tissue.

Unlike T1-weighted and fluid-sensitive imaging which depends on the signal intensity and morphologic features, DWI is a technique of functional imaging.[3]

Quantitative DWI with ADC mapping is an established technique that has been used throughout the body to distinguish lesions according to their cellularity, with advantages being rapid acquisition and good reproducibility.[6,7]
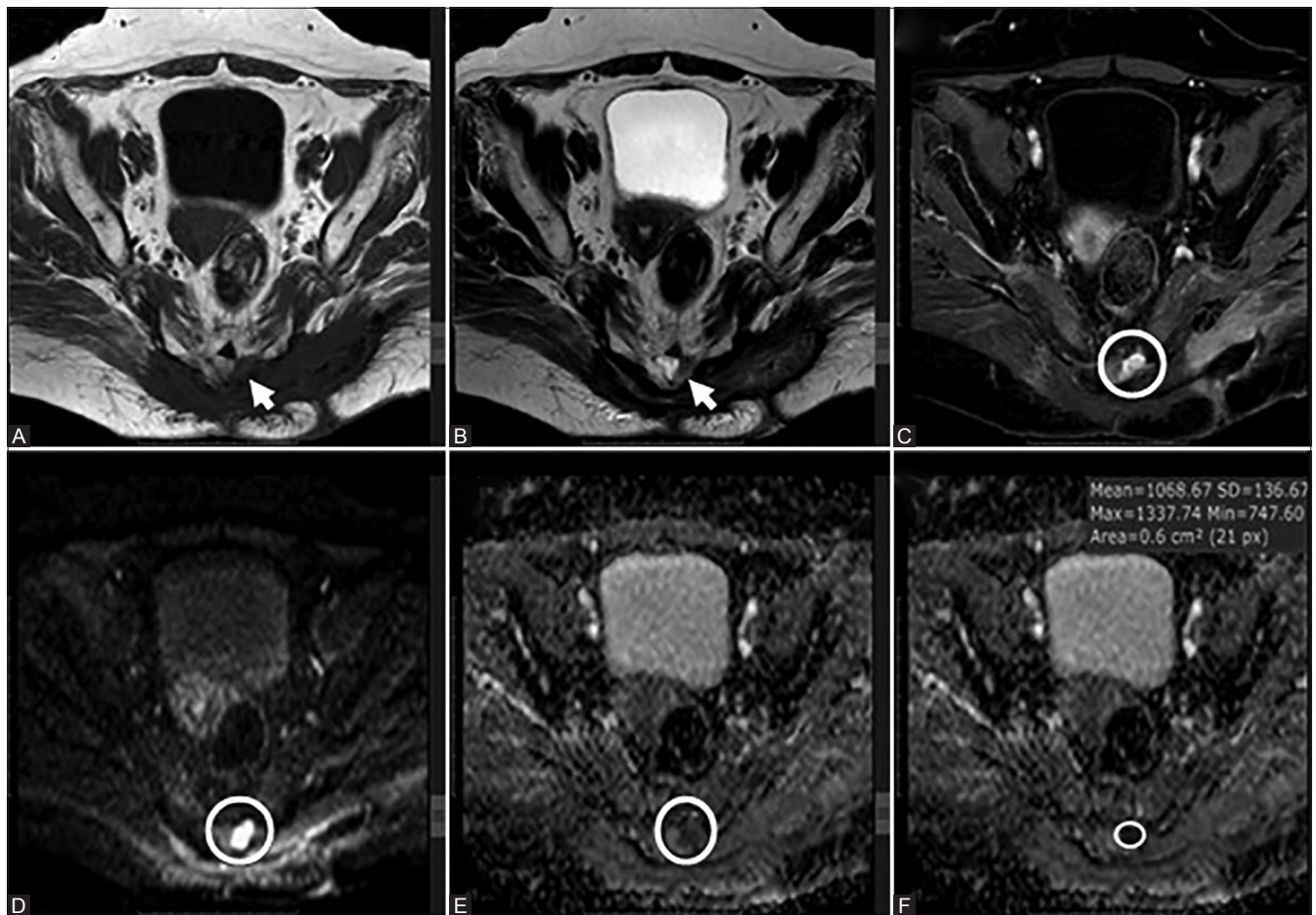
Figure 3 (A-F): MRI images 8 months postsurgical excision of a left gluteal myxoid liposarcoma: Axial T1 (A) and axial T2 (B) images showed dense surgical bed scarring of isointense signal intensity in T1 and low signal intensity in T2. (C) Fat-suppressed contrast-enhanced T1 weighted image showed avidly enhancing deep left pre-sacral nodule (circle). (D-F) Restricted diffusion (Mean, 1×10^{-3} mm^2/s; minimum 0.75×10^{-3} mm^2/s). Wide excision confirmed the presence of microscopic recurrent myxoid lipo-sarcoma within the scar tissue

The part played by quantitative ADC mapping in the discrimination of benign from malignant soft-tissue lesions has been debatable. Einarsdóttir *et al.* reported notable overlap in their ADC values, whereas Razek *et al.* and Pekcevik *et al.* reported that ADCs can discriminate malignant from benign soft-tissue masses.[8-10]

In our study, ADCs of recurrent nonmyxoid sarcomas (mean, 1.2×10^{-3} mm²/s ± 0.46) were significantly dissimilar from those of postoperative changes (mean, 1.9×10^{-3} mm²/s ± 0.3) ($P < 0.0001$), and the addition of qualitative and quantitative assessment of the ADC maps gave 100% specificity in recurrence detection.

This is comparable to the study by Grande *et al.* were the mean ADC values of recurrent disease and postoperative fibrosis were 1.08×10^{-3} mm²/s ± 0.19 and 0.9×10^{-3} mm²/s ± 0.0; $P = 0.03$, respectively [Figure 1].

However, our study showed limited diagnostic value of the use of DWI with ADC mapping in the assessment of myxoid sarcomatous tumor recurrences as they showed relatively high ADC map signals and high-recorded ADC values mimicking postoperative changes.

Our study included 6 cases of recurrent malignant myxoid tumors showing areas of high ADC values in the recurrent lesions, 5 of which showed homogeneously high mean ADC values, with an average of about 1.71×10^{-3} mm²/s compared to a mean ADC of approximately 1.1×10^{-3} mm²/s in nonmyxoid tumors ($P < 0.0003$).

This matches the results of Nagata *et al.* who showed that the ADC (mean + SD) in myxoid-containing tumors was $1.92 \pm 0.41 \times 10^{-3}$ mm²/s, whereas that in nonmyxoid tumors was $0.97 \pm 0.33 \times 10^{-3}$ mm²/s ($P < 0.01$) [Figure 2].[11]

This reflects overlap in the ADC values within benign and malignant soft-tissue tumors particularly, myxoid lesions, and rendering use of DWI for soft tissue lesion characterization or recurrence detection [Figure 3].[12]

In nonmyxoid tumors, if the mean ADC value exceeds 1.3×10^{-3} mm²/s, the possibility of malignancy (residual/recurrence) is low. The specificity of ADC values is dependent on the cut-off value that determines the differentiation between benign and malignant lesions. In our study, we obtained cut-off mean ADC value of 1.3×10^{-3} mm²/s (in nonmyxoid lesions) with 90.48% sensitivity and 100% specificity ($P < 0.0001$).

This is higher than the results of Nagata *et al.* who found that there was a difference in mean ADC between malignant ($1.08 \pm 0.30 \times 10^{-3}$ mm²/s) and
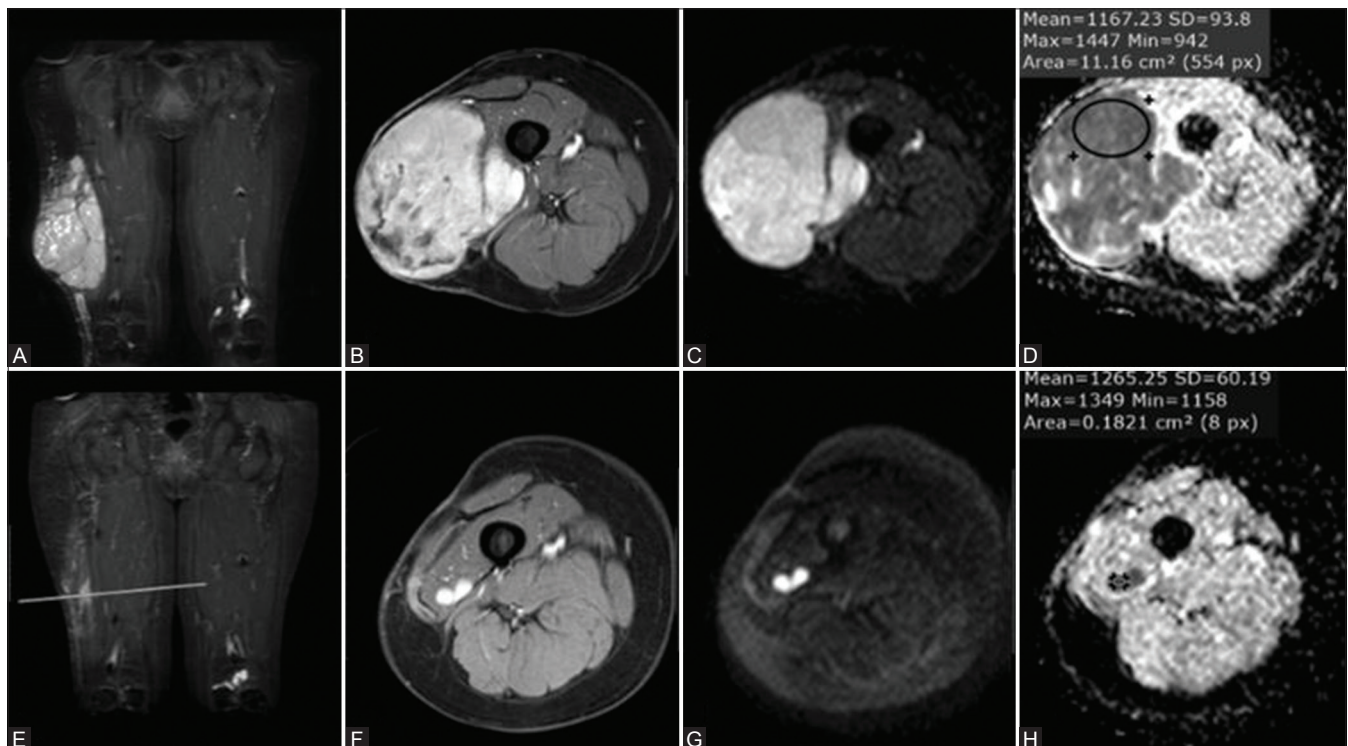
Figure 4 (A-H): Coronal STIR, axial THRIVE, DWI (b = 800) and ADC MR images of a case of right mid-thigh synovial sarcoma pre (A-D) and 3 months postsurgical excision (E-H). Showing operative bed nodular signal abnormality eliciting high STIR signal (E) avid homogenous post-contrast enhancement (F), and restricted diffusion pattern (G and H) with Mean ADC value of 1.26×10^{-3} mm²/s; minimum 1.15×10^{-3} mm²/s) compared to initial preoperative ADC values of (Mean 1.2×10^{-3} mm²/s; minimum 0.94×10^{-3} mm²/s) (F). Wide excision of the operative bed lesion was positive for residual malignancy
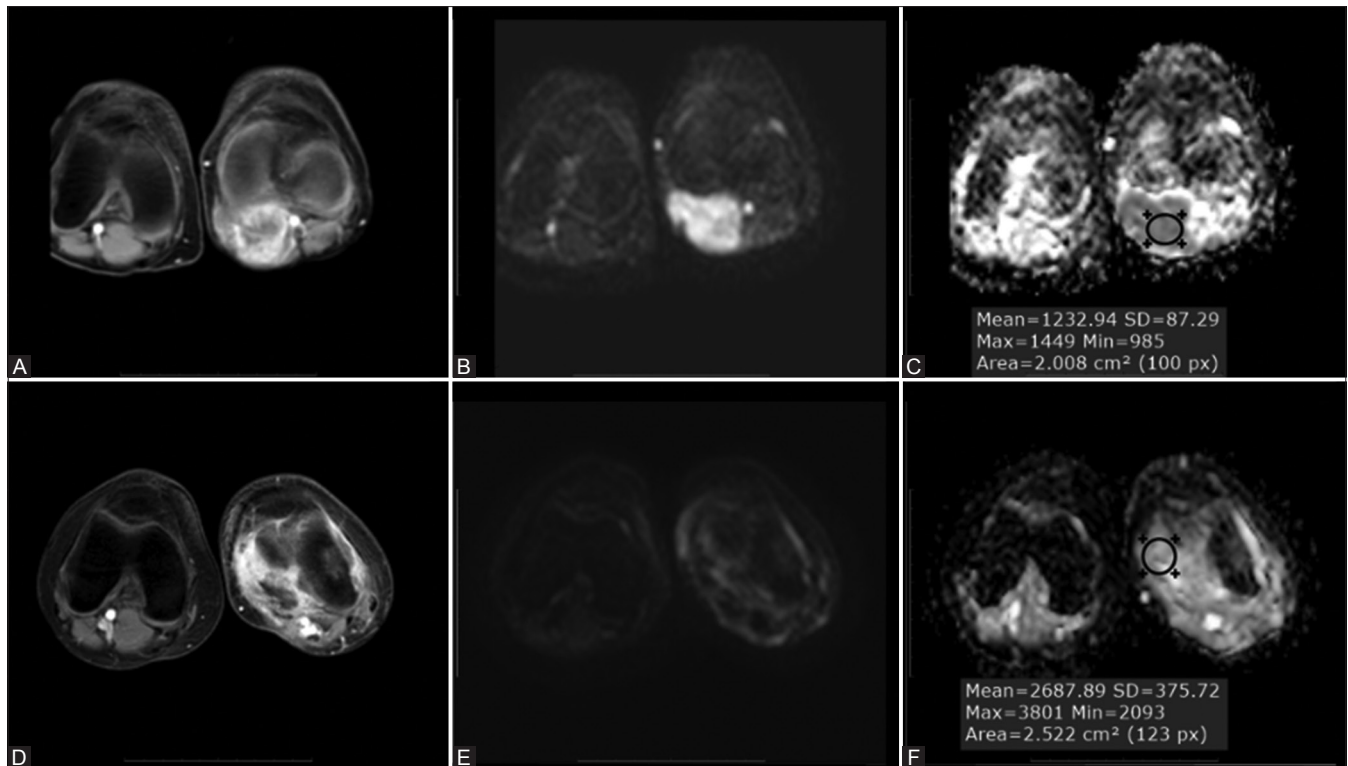
Figure 5 (A-F): Axial THRIVE, DWI (b = 800) and ADC MR images of a case of left popliteal fossa synovial sarcoma pre (A-C) and 2 months post-surgical excision (D-F). Operative bed diffuse post-contrast enhancement (D), facilitated pattern of diffusion (E) and diffuse high signal at the ADC map (F), and recording high ADC measurements (Mean 2.6×10^{-3} mm^2/s; minimum 2×10^{-3} mm^2/s) compared to the initial preoperative ADC values of (Mean 1.2×10^{-3} mm^2/s; minimum 0.98×10^{-3} mm^2/s) (C). Wide excision revealed granulation tissue negative for residual malignancy

benign ($1.76 \pm 0.53 \times 10^{-3}$ mm^2/s) tumors with sensitivity and specificity of 76.3% and 76.7%, respectively, achieved when an ADC value threshold of 1.35×10^{-3} mm^2/s was used.

Our results showed high specificity of mean ADC (100%) yet lower sensitivity (85.19% and 90.48% in nonmyxoid tumors) compared to the minimum ADC sensitivity measurements (88.89% and 95.24% in nonmyxoid tumors), indicating that mean ADC measurements alone are highly specific but not sensitive in the detection of residual tumors. Thus, average ADC should be accompanied with measuring peripheral maximum restricted areas as well.

Excluding the category of recurrent/residual myxoid tumors from the analysis of the recorded ADC values increased the sensitivity and accuracy of qualitative and quantitative ADC observations (both mean and minimum ADC measurements), showing a cut-off average ADC value for detecting recurrent/residual lesions of $\leq 1.3 \times 10^{-3}$ mm^2/s with 90.48% sensitivity and a cut-off minimum ADC value of $\leq 1.2 \times 10^{-3}$ mm^2/s with 95.24% sensitivity. This denotes the poor diagnostic performance of ADC maps in the detection of recurrent/residual myxoid soft tissue sarcomas compared to other pathological subtypes.

Among the 37 cases included in our study, preoperative MRI was available for 12 cases; 10 were diagnosed with postoperative recurrent/residual masses and 2 with postoperative benign changes. The recurrent/residual masses showed no obvious difference in the recorded ADC values in the pre-and postoperative examinations [Figures 4-6].

Restrictions in our study were the absence of some pathological types of soft tissue sarcomas and the limited number of cases, making it difficult to know if our results can be applied to all soft tissue sarcomas in addition to the lack of all preoperative MRI examinations for all patients.

In conclusion, the inclusion of contrast-enhanced and DWI showed a notable role in postoperative recurrence detection. They increased both the diagnostic sensitivity and specificity for discriminating tumoral recurrence from postoperative nodular scar tissue.
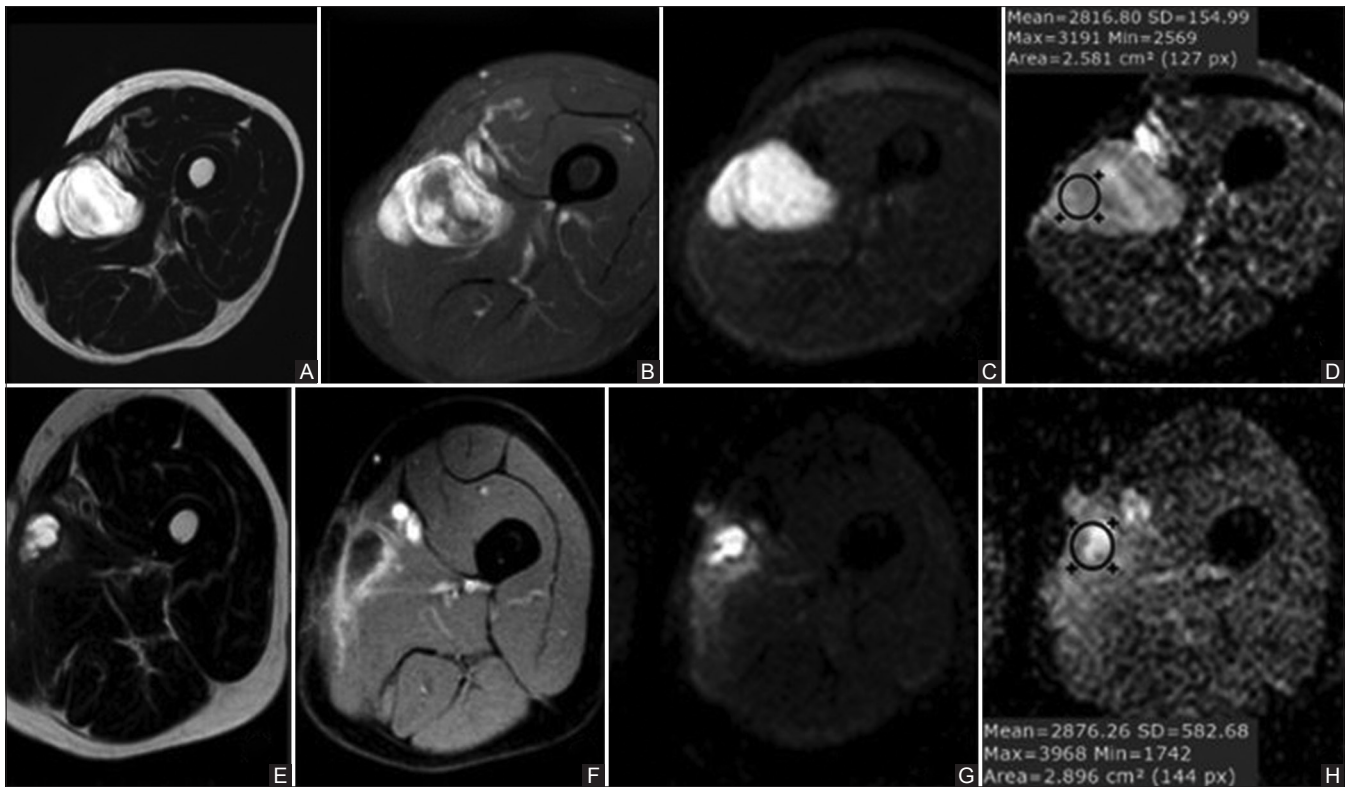
Conflicts of interest
There are no conflicts of interest.

Figure 6 (A-H): Axial T2WI, THRIVE, DWI (b = 800), and ADC MR images of a case of right upper thigh myxoliposarcoma, pre (A-D), and 4 months post-surgical excision (E-H). Operative bed abnormal mass-like area eliciting high T2 WI signal (E) heterogeneous peripheral post-contrast enhancement (F), and high DWI and ADC signal (G and H) with mean ADC value of 2.8×10^{-3} mm^2/s; minimum 1.7×10^{-3} mm^2/s) compared to initial preoperative ADC values of (mean 2.8×10^{-3} mm^2/s; minimum 2.5×10^{-3} mm^2/s) (D). Wide excision of the operative bed lesion revealed residual myxoliposarcoma

References

1. Afonso PD, Kosinski AS, Spritzer CE. Following unenhanced MRI assessment for local recurrence after surgical resection of mesenchymal soft tissue tumors, do additional gadolinium-enhanced images change reader confidence or diagnosis?. Eur J Radiol 2013;82:806-13.

2. Del Grande F, Subhawong T, Weber K, Aro M, Mugera C, Fayad LM. Detection of soft-tissue sarcoma recurrence: Added value of functional MR imaging techniques at 3.0 T. Radiology 2014;271:499-511.

3. Fayad LM, Jacobs MA, Wang X, Carrino JA, Bluemke DA. Musculoskeletal tumors: How to use anatomic, functional, and metabolic MR techniques. Radiology 2012;265:340-56.

4. Khoo MM, Tyler PA, Saifuddin A, Padhani AR. Diffusion-weighted imaging (DWI) in musculoskeletal MRI: A critical review. Skelet Radiol 2011;40:665-818.

5. Hickeson MP. Soft tissue sarcomas. In: Pediatric PET Imaging. Springer: New York; 2006. pp. 302-11.

6. Subhawong TK, Durand DJ, Thawait GK, Jacobs MA, Fayad LM. Characterization of soft tissue masses: Can quantitative diffusion weighted imaging reliably distinguish cysts from solid masses?. Skelet Radiol 2013;42:1583-92.

7. Messiou C, Bonvalot S, Gronchi A, Vanel D, Meyer M, Robinson P, *et al*. Evaluation of response after pre-operative radiotherapy in soft tissue sarcomas; the European Organisation for Research and Treatment of Cancer–Soft Tissue and Bone Sarcoma Group (EORTC–STBSG) and Imaging Group recommendations for radiological examination and reporting with an emphasis on magnetic resonance imaging. Eur J Cancer 2016;56:37-44.

8. Einarsdóttir H, Karlsson M, Wejde J, Bauer HC. Diffusion-weighted MRI of soft tissue tumours. Eur Radiol 2004;14:959-63.

9. Razek A, Nada N, Ghaniem M, Elkhamary S. Assessment of soft tissue tumours of the extremities with diffusion echoplanar MR imaging. La Radiol Med 2012;117:96-101.

10. Pekcevik Y, Kahya MO, Kaya A. Characterization of soft tissue tumors by diffusion-weighted imaging. Iran J Radiol 2015;12.

11. Nagata S, Nishimura H, Uchida M, Sakoda J, Tonan T, Hiraoka K, *et al*. Diffusion-weighted imaging of soft tissue tumors: Usefulness of the apparent diffusion coefficient for differential diagnosis. Radiat Med 2008;26:287-95.

12. Subhawong TK, Jacobs MA, Fayad LM. Diffusion-weighted MR imaging for characterizing musculoskeletal lesions. Radiographics 2014;34:1163-77.