Received:
4 April 2016

Revised:
16 July 2016

Accepted:
25 July 2016

<http://dx.doi.org/10.1259/bjr.20160302>

Cite this article as:

Kim JI, Lee IS, Song YS, Park SK, Choi K-U, Song JW. Short-term follow-up MRI after unplanned resection of malignant soft-tissue tumours; quantitative measurements on dynamic contrast enhanced and diffusion-weighted MR images. *Br J Radiol* 2016; **89**: 20160302.

FULL PAPER

Short-term follow-up MRI after unplanned resection of malignant soft-tissue tumours; quantitative measurements on dynamic contrast enhanced and diffusion-weighted MR images

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Objective: To determine the diagnostic availability of dynamic contrast-enhanced (DCE) and diffusion-weighted (DW) MR images for evaluating residual tumours at short-term follow-up after unplanned excision of malignant soft-tissue tumours.

Methods: From January 2013 to September 2014, 38 patients underwent first follow-up MRI, including DCE and DW imaging (DWI), within 3 months of unplanned malignant soft-tissue tumour excision. The presence or absence of definite nodule formation, focal fluid/haematoma collection, oedema and fascial thickening around or at tumour beds were evaluated using conventional MR images. The volume transfer constant between blood plasma and extravascular/extracellular space (EES) (K_{trans}), rate constant between EES and blood plasma (K_{ep}), volume of EES space per unit volume of tissue and initial area under the concentration curve (iAUC) values with time-concentration curve (TCC) plots were obtained on DCE images, and apparent diffusion coefficient (ADC) values were measured on ADC maps. All data were statistically analyzed.

Results: Of the 21 patients who underwent re-excision, 12 patients had a residual tumor and 9 did not. All conventional MRI variables, except definite nodule formation, were insignificantly related to the presence of residual tumour. However, ADC values were found to be significantly associated with the presence of residual tumour, as were the DCE MRI variables, K_{trans} , K_{ep} and iAUC. In particular, TCC pattern and K_{ep} were most significantly associated with residual tumour.

Conclusion: Additional DCE images may be useful for determining the presence of residual tumours in tumour beds during short-term follow-up after inadequate malignant soft-tissue tumour excision.

Advances in knowledge: The addition of DCE MRI and quantitative analysis of the images obtained might be useful for determining the presence of residual tumour in a tumour bed during short-term follow-up after inadequate excision of a malignant soft-tissue tumour, although DWI was also found to be helpful.

INTRODUCTION

The goal of the surgical treatment of malignant soft-tissue tumours is complete tumour removal with an adequate resection margin.¹ However, sometimes, unplanned resections are carried out because surgeons fail to consider sarcoma. Unplanned resection is defined as resection of presumed benign masses without appropriate pre-operative imaging, biopsy or attention to surgical margins.² Marginal excisions frequently result in residual tumour in the tumour bed, with rates ranging from 23 to 59%.²⁻⁴ When there is a considerable load of residual sarcoma in the wound, additional wide

resection has been recommended.² However, it is difficult to determine the amount of tumour remaining, because post-operative changes may share many of the characteristics of tumours on conventional MR images.⁵ Therefore, the determination of the presence of residual tumour is usually difficult using conventional MR images in the short term after inadequate excision of malignant soft-tissue tumours.

Dynamic contrast-enhanced (DCE) MRI enables dynamic sampling at many time points and provides important information about tissue perfusion, tissue vasculature,

capillary permeability and interstitial space volume.⁶ Therefore, it may aid the detection of viable tumours.⁷ Diffusion-weighted imaging (DWI) also provides functional tissue information, which can be combined with anatomical information to improve lesion characterization.⁸ The restriction of water diffusion observed in tumours is attributed to increased cellularity and has been used to examine changes in surgical beds and evaluate the possibility of tumour recurrence.⁹ Although several articles have suggested the use of MRI for the differentiation of post-treatment changes and tumour recurrence, little information is available regarding the imaging findings of residual tumours during the short term after unplanned soft-tissue sarcoma excision.

Accordingly, the purpose of this study was to determine the diagnostic efficacies of DCE MRI and DWI for the evaluation of residual tumours in tumour beds within 3 months of the unplanned excision of malignant soft-tissue tumours.

METHODS AND MATERIALS

This study was approved by our institutional review board and informed consent was obtained from all patients.

Patients

38 patients [22 females and 16 males; age range, 16–84 years (mean, 50.5 years)] with follow-up MR images, including DCE and DW images, obtained within 3 months after unplanned excision of malignant soft-tissue tumours and taken from January 2013 to September 2014 were enrolled in this study. Patients had undergone initial surgery for an unanticipated malignant soft-tissue tumour at outside local institutions, and wide excision for malignancy was not considered. Times between first operation and first follow-up ranged from 7 to 90 days (mean 42.3 days). Patients who underwent first follow-up MRI at more than 3 months after surgery were excluded. No therapy was used for all patients before undertaking first follow-up MRI after initial surgery. The diagnostic standard used was histologic findings after re-excision for 21 (55%) patients and clinical/imaging follow-up findings obtained at 3, 6 and 12 months in the remaining 17 (45%) patients. Re-excision was performed when MRI findings indicated a probability of remnant malignancy regardless of conventional or functional images or when there was mass effect in the tumour bed on physical examination. In cases diagnosed by clinical/imaging follow-up, no remnant malignancy was concluded when post-operative changes had subsided and there was no evidence of a growing lesion in the tumour beds at 1 year post-operatively. Follow-up imaging work-ups performed at more than 1 year post-operatively were considered evaluations of recurrent tumours and thus, the results of these investigations were not included.

Patient ages and genders, tumour locations, resected tumour sizes, times between initial tumour excision and first follow-up MRI and histopathologic diagnoses were also evaluated.

MRI protocols

MRI studies were performed in a 3-T MR scanner (MAGNETOM Trio, A tim system; Siemens Medical Solutions, Erlangen, Germany) using a body or surface coil depending on lesion location and size.

Conventional MR sequences included T_1 weighted [repetition time (TR)/echo time (TE), 400–765/9.6–12 ms; echo train length 3–5] and T_2 weighted (TR/TE 2600–4500/60–127 ms, ETL 15) fast spin-echo sequences using variable planes, including at least two orthogonal planes with fat suppression on at least one T_2 weighted image plane. Field of view (FOV) and matrix size were chosen based on lesion location and size.

DW images were acquired in the axial plane using the single-shot echoplanar imaging technique with b -values of 0, 50, 500, 800 and 1400 s mm⁻²; TR/TE of 4900–6800/63–86; FOV of 100–400 mm; matrix size 68–142 × 42–140; 1–9 (median 4) number of excitations; slice thickness 1.5–7 mm with variable slice gap; and an acquisition time of about 4 min 30 s. ADC (apparent diffusion coefficient) maps were generated automatically.

DCE images were obtained after completing the above sequences. First, three pre-contrast T_1 weighted three-dimensional volumetric interpolated breath-hold examinations [TR/TE of 5.5/1.8, 1 number of excitations and 2-mm slice thickness with different flip angles (2°, 8°, and 15°)] were obtained to determine the tissue T_1 relaxation times before contrast arrival. FOV and matrix size were adjusted according to anatomy and ranged from 100 to 250 mm and from 192 to 138 pixels, respectively. This imaging was followed by a DCE series with fat suppression in the axial plane at a TR/TE of 5.5/1.8, flip angle of 8° and a slice thickness of 2.0 mm with no interslice gap. This series was repeated 40 times after injecting the contrast agent intravenously by bolus injection (0.1-mmol kg⁻¹ gadolinium at 1.2 ml s⁻¹) followed by a 20-ml saline flush. The time resolution of each dynamic set was 12 s.

Delayed enhanced images were obtained in three planes by fat-suppressed, fast spin-echo T_1 weighted imaging.

Imaging processing

DCE MRI data were transferred to a post-processing workstation and analyzed using Tissue 4D software (Siemens healthineers, Erlangen).

The first step involved converting volumetric interpolated breath-hold examinations signal intensities to contrast agent concentrations. Quantitative parameters [volume transfer constant between blood plasma and extracellular/extravascular space (EES) (K_{trans}), rate constant between EES and blood plasma (K_{ep}), volume of EES space per unit volume of tissue (V_e) and initial area under the concentration curve (iAUC)] were then calculated from time–concentration curves (TCCs) based on the pharmacokinetics model using the presumed arterial input function (AIF). The AIF has three population-averaged options (fast, intermediate and slow) provided by Tissue 4D software (Siemens Healthcare, Erlangen, Germany), and the optimum AIF was chosen based on the volume of interest (VOI) curve of each patient.¹⁰ K_{trans} and V_e maps were then calculated from T_1 maps, gadolinium concentration/time plots and AIFs using Tofts model.¹¹

MRI analysis

The presence or absence of definite nodule formation, focal fluid/haematoma collection, oedema and fascial thickening

around or at tumour beds were evaluated using conventional MR images by consensus between two musculoskeletal radiologists with 12 and 4 years' experience, respectively. Tumour bed depths were classified as deep (deep to compartmental fascia) or superficial (involving skin/subcutaneous fat).

DCE and DW images were evaluated with no prior knowledge of pathologic diagnoses, clinical decisions, histories or other imaging results.

Analysis of diffusion-weighted imaging and apparent diffusion coefficient maps

First, we investigated whether signal drop areas were present in tumour beds on ADC maps by comparing them with bright signal intensity areas on DW images (qualitative analysis). If signal loss was observed on an ADC map in an area corresponding to high signal intensity on a DW image, a small (0.09–0.35 cm²) round region of interest (ROI) was drawn in that region. When no signal loss was observed on an ADC map, an ROI was drawn within the tumour bed in a random location, while avoiding artefacts, haematoma and necrosis. All ADC values, including the minima, maxima and mean values, were measured within ROIs (quantitative analysis). The two radiologists measured ADC values independently and one of the radiologists remeasured values 1 month later.

Analysis of dynamic contrast-enhanced MR images

Two experienced radiologists and one technician selected optimal slices and drew ROIs by consensus for the post-processing of DCE images.

To investigate DCE images, an optimal slice showing diffusion restriction or a highly enhanced solid portion was selected. A VOI was then applied to contain the entire lesion. Based on the colour pattern within the VOI containing the lesion, one or more than two ROIs were applied to areas expected to represent hyperperfusion (red coloured). Total pixel areas of VOIs and ROIs depended on tumour bed sizes and the sizes of red-coloured regions. After applying ROIs, voxelwise perfusion maps including K_{trans} , K_{ep} , V_e and iAUC were calculated using Tissue 4D software by applying Tofts model.^{11,12} Signal intensities were then converted into gadolinium concentrations and TCC plots were calculated.

By DCE MRI, seven types of TCCs were obtained and defined as follows: Type I (continuous rapid increase in concentration with time); Type II (gradual increase in concentration with time); Type III (initial rapid increase in concentration followed by a slow increase); Type IV (initial rapid increase in concentration followed by a plateau); Type V (initial rapid increase in concentration followed by a slight decrease); Type VI (initial rapid increase in concentration followed by slow washout); and Type VII (initial rapid increase in concentration followed by rapid washout). Types I, II and III TCCs were assigned to Pattern I, because they all exhibited increasing concentration. Type IV was assigned to Pattern II (plateau pattern) and Types V, VI and VII were assigned to Pattern III owing to their decreasing patterns.

Statistical analysis

Fisher's exact test with the χ^2 test was used to determine whether gender, depth of tumour bed, conventional MRI findings (the presence or absence of a definite nodule formation, focal fluid/haematoma collection, oedema and fascial thickening around or at the tumour bed) and the presence or absence of signal drop areas on ADC maps in areas corresponding to high signal intensity on DW images affected the ability to discriminate the presence or absence of residual tumour. The two-sample *t*-test was used to determine whether age, DCE MR parameters, TCC types and ADC values were useful for determining the presence or absence of residual tumour. For ADC values, intraobserver and interobserver agreements were assessed using intraclass correlation coefficients. The analyses were performed using IBM SPSS® statistics v. 21 (IBM Corp., New York, NY; formerly SPSS Inc., Chicago, IL).

Receiver-operating characteristic curve analysis was used to determine optimal thresholds for ADC values and DCE MR parameters using Medcalc software by version 14.12.0 (Microsoft Partner, Ostend, Belgium). Statistical significance was accepted for *p*-values of <0.05.

RESULTS

Of the 21 patients who underwent re-excision, 12 patients [5 females, 7 males; age range 16–73 years (mean age 49.7 years)] had a residual tumour and 9 patients did not. The other 17 patients were deemed to have no residual tumour by clinical and imaging follow-ups at 1 year after initial surgery. The 12 patients with residual tumour underwent first follow-up MRI at a mean duration of 40.8 days (range 7–89 days) after initial surgery, and the 26 patients without a residual tumour underwent follow-up at a mean duration of 43 days (range 7–90 days) after initial surgery.

The locations of resected tumours were as follows: thigh (*n* = 12), shoulder (*n* = 6), chest wall (*n* = 4), lower leg (*n* = 3), knee (*n* = 3), forearm (*n* = 2), inguinal area (*n* = 2), elbow (*n* = 2), hand (*n* = 1), axilla (*n* = 1), buttock (*n* = 1) and back (*n* = 1). 17 [in 27/38 (71%) patients] tumour beds were located in the superficial layer and 11 (29%) tumour beds in the deep layer. Resected tumour sizes ranged from 2 to 20 cm (mean 5.57 cm) in cases with residual tumours and from 1 to 12.3 cm (mean 4.52 cm) in cases without residual tumours. Histologic diagnoses are summarized in Table 1. Based on pathological reports or slides from referring institutions, 8 patients had grade 2, 6 patients had grade 3 and 5 patients had grade 1 soft-tissue sarcoma. The remaining 19 patients could not be graded.

Age, gender, the time between excision and first follow-up MRI, tumour bed depth, tumour size and histologic grade at initial surgery were not significantly associated with the presence of residual tumour (*p* > 0.05).

Of the conventional MRI factors, only nodule formation was found to be associated with the presence of residual tumour (*p* < 0.05) (Table 2). However, only nine patients showed definite nodule formation and three of these nine patients were confirmed to have no residual tumour (Figure 1). Also, 6 of the 12 patients with residual tumour showed no nodule formation at the tumour bed (Figure 2).

Table 1. Histologic diagnoses of resected tumours

Diagnosis	Number (total = 38)
Liposarcoma	8
Leiomyosarcoma	5
Dermatofibrosarcoma protuberans	4
Malignant peripheral nerve sheath tumour	3
Myxofibrosarcoma	2
Extraskelatal osteosarcoma	2
Undifferentiated pleomorphic sarcoma	3
Rhabdomyosarcoma	2
Soft-tissue metastasis	2
Squamous cell carcinoma	2
Melanoma	1
Synovial sarcoma	1
Sarcomatoid carcinoma	1
Lymphoma	1
Merkel cell carcinoma	1

Nine [superficial ($n = 8$) and deep ($n = 1$)] DW images were non-diagnostic owing to inappropriate image quality caused by poor signal-to-noise ratio, ghosting or artefact. On ADC maps, average values of minimum, maximum and mean ADC values in patients with a residual tumour were $1.16 (0.58\text{--}1.59) \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$, $1.61 (1.08\text{--}2.69) \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$ and $1.38 (0.86\text{--}2) \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$, respectively, and in patients without a residual tumour, these values were $1.47 (0.79\text{--}2.96) \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$, $2.10 (1.22\text{--}3.89) \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$ and $1.81 (1.05\text{--}3.26) \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$, respectively. Maximum and mean ADC and the presence of signal drop area on ADC maps were found to be significantly associated with the presence of residual tumour ($p < 0.05$) (Figure 3)

(Table 3). Intraobserver and interobserver agreements regarding ADC measurement were almost perfect; the minimum, maximum and mean ADC values for intraobserver and interobserver agreements were 0.928 and 0.867, 0.916 and 0.888, and 0.932 and 0.897, respectively.

Regarding DCE MR parameters, the mean values of K_{trans} , K_{ep} , V_e and iAUC in patients with a residual tumour were 0.145 min^{-1} ($0.03\text{--}0.303 \text{ min}^{-1}$), 0.562 min^{-1} ($0.254\text{--}1.134 \text{ min}^{-1}$), 0.282 min^{-1} ($0.05\text{--}0.65 \text{ min}^{-1}$) and 10.68 min^{-1} ($2.37\text{--}26.23 \text{ min}^{-1}$), respectively, and corresponding values in cases without a residual tumour were 0.051 min^{-1} ($0.01\text{--}0.21 \text{ min}^{-1}$), 0.249 min^{-1} ($0.05\text{--}2.42 \text{ min}^{-1}$), 0.307 min^{-1} ($0.01\text{--}0.43 \text{ min}^{-1}$) and 3.043 min^{-1} ($0.11\text{--}7.7 \text{ min}^{-1}$), respectively. K_{trans} , K_{ep} and iAUC were found to be significantly associated with the presence of residual tumour ($p < 0.05$). Regarding TCC types, mean patterns of VOI and ROI graphs were 1.9 and 3, respectively, for patients with a residual tumour, and 1 and 1.04, respectively, for those without a residual tumour, and the pattern of graphs was significantly different between two groups (Table 3). According to receiver-operating characteristic curve analysis, TCC type regarding ROI most significantly predicted the presence of residual tumour (Figure 4) and of the quantitative values, K_{ep} was the most significant (Table 4).

When we applied TCC-type type threshold regarding ROI obtained with DCE image, the sensitivity, specificity, positive-predictive value and negative-predictive value were 100, 96, 92 and 100%. For DCE parameters threshold, corresponding values were 100, 92, 86 and 100% and for ADC value thresholds, corresponding values were 40, 95, 80 and 75%. The number of discordant cases between ADC values and DCE parameters regarding the presence of residual tumour was eight.

DISCUSSION

In the present study, 12 (32%) cases were confirmed to have residual tumour. It has been suggested that the most important factors of local disease control are operative margin, grade and post-operative radiotherapy.^{13,14} However, in this study,

Table 2. The abilities of conventional MR parameters to evaluate the presence of residual tumour in tumour beds after unplanned excision of malignant or aggressive soft tissue tumours

	Definite nodule or mass formation		Haematoma formation or fluid collection		Oedema around or at the tumour bed		Fascial thickening around or at the tumour bed	
	Yes	No	Yes	No	Yes	No	Yes	No
Positive residual tumour	6	6	2	10	7	5	12	0
No residual tumour	3	23	7	19	9	17	21	5
Sensitivity (%)	66.7		22.2		43.8		36.4	
Specificity (%)	79.3		65.5		77.3		100	
PPV (%)	50		16.7		58.3		100	
NPV (%)	88.5		73		65.4		19.2	
Accuracy (%)	76		55.2		63.2		44.7	
p-value	0.036		0.685		0.282		0.278	

NPV, negative-predictive value; PPV, positive-predictive value.

Figure 1. A 69-year-old female patient with follow-up MR images obtained at 8 days after the excision of melanoma in the subcutaneous fat layer of the left anterior thigh: (a) the axial delayed enhanced MR image is showing definite nodule formation (arrow), haematoma (arrowhead), oedema and fascial thickening at the tumour bed. (b) The apparent diffusion coefficient (ADC) map is not showing evidence of gross diffusion restriction (signal drop) (arrowheads), compared with the corresponding high signal area (arrow) on DW image. The mean ADC value of the tumour bed was $1.74 \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$. (c) By dynamic contrast-enhanced MRI, the volume transfer constant between blood plasma and extracellular/extravascular space was 0.032 and the time-concentration curve of the region of interest was Pattern I (Type III, continuously increasing concentration). Functional MR images raised no suspicion of residual tumour and pathologic examination of the specimen obtained during re-excision revealed only fat necrosis.

operative margin and histologic grade, resected tumour size, time between excision and follow-up MRI, age and gender were not found to be significantly associated with the presence of residual tumour.

A residual lesion may initially be too small or may be overlooked because of the absence of a definite mass effect.¹⁵ Tumour recurrence is characterized by a discrete nodule or mass,¹⁶ but this characteristic feature is unusual for residual tumours in tumour

Figure 2. A 68-year-old male patient with follow-up MR images obtained 14 days after excision of pleomorphic liposarcoma from the subcutaneous layer of the right shoulder: (a) the axial delayed contrast-enhanced T_1 weighted image with fat suppression is showing diffuse fascial thickening and oedema (arrows) around the tumour bed. The apparent diffusion coefficient (ADC) map (not shown) did not show evidence of diffusion restriction; the mean ADC value was $1.93 \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$. (b) By dynamic contrast-enhanced MRI, the volume transfer constant between blood plasma and extracellular/extravascular space was 0.106 and the time-concentration curve was of Pattern III (Type V, a washout curve shape).

Figure 3. A 44-year-old male patient with follow-up MR images obtained 83 days after excision of rhabdomyosarcoma within the vastus muscle: (a) axial delayed contrast-enhanced T_1 weighted image with fat suppression is showing focal nodular enhancement through fascia around the tumour bed (arrow). (b) The apparent diffusion coefficient (ADC) map is showing gross diffusion restriction (signal drop) (arrow) in the lesion; the mean ADC value was $1.62 \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$. (c) The volume transfer constant between blood plasma and extracellular/extravascular space by dynamic contrast-enhanced MRI was 0.109 and the time-concentration curve was of Pattern III (Type VII, washout curve shape). Functional MR images raised suspicion of residual tumour, which was later demonstrated by pathology after re-excision.

beds during short-term post-operative follow-up. In the present study, three of the nine cases with definite nodule formation had non-residual tumour. Furthermore, 9 patients of 21 patients who underwent re-excision did not have a residual tumour. Re-excision surgery was necessary in these nine patients because their conventional MR images showed definite mass or nodule formations, prominent fascial thickening or large amount of fluid collection in the tumour bed, and there were mass effects on physical examinations. Therefore, conventional MR findings

including definite nodule formation and physical examinations might not be useful for short-term follow-up.

Contrast enhancement helps differentiate post-treatment haematoma and recurrent tumour,¹⁷ but conventional contrast-enhanced MRI cannot separate residual tumour from inflammation or infection shortly after surgery.¹⁸ Employing dynamic imaging will typically show a steep enhancement slope on a time-intensity plot for a recurrent or residual tumour as compared with surrounding

Table 3. The diagnostic performances of functional MR parameters for residual tumour

Functional MR parameters	<i>p</i> -value
K_{trans}	0.001
K_{ep}	0.016
V_e	0.683
iAUC	0.005
VOI graph	0.005
ROI graph	<0.001
Minima ADC	0.088
Maxima ADC	0.03
Mean ADC	0.027
The presence of low-signal area on ADC mapping	<0.001

ADC, apparent diffusion coefficient; iAUC, initial area under the concentration curve; K_{ep} , rate constant between extracellular/extravascular space (EES) and blood plasma; K_{trans} , volume transfer constant between blood plasma and EES; ROI, region of interest; V_e , volume of EES space per unit volume of tissue; VOI, volume of interest.

soft tissues.¹⁶ For DCE MRI, contrast accumulates in areas of high perfusion, and in disordered leaking vasculature, as would be expected for tumours.¹⁹ DCE MRI has been used to evaluate bone and soft-tissue tumours, but qualitative analyses have been performed in most studies and therefore, we added quantitative analyses.

Obtaining quantitative estimates of tissue kinetic parameters using DCE MRI requires knowledge of the concentration of contrast agent in blood plasma.¹⁰ ROI and pixel signals can provide information about blood flow, capillary leakage and related physiological parameters.¹² Changes in enhancement patterns using TCC provide information on the vascular

pharmacokinetics of tumours, which can be assessed qualitatively by characterizing enhancement patterns or quantitatively by calculating various pharmacokinetic parameters.²⁰ K_{ep} is defined as the ratio of transfer constant to EES ($K_{ep} = K_{trans}/V_e$). K_{trans} has several physiologic interpretations that depend on the balance between capillary permeability and blood flow in the tissue of interest. In high-permeability situations, K_{trans} is equal to blood plasma flow per unit volume of tissue.¹² K_{trans} determines the amplitude of the initial response (the amount of tracer that enters the EES) and K_{ep} determines the washout rate from the EES back into the blood plasma; that is it controls the time required for the impulse to subside.²¹ In the present study, K_{trans} , K_{ep} , iAUC and TCC patterns of ROIs in tumour beds were found to be significantly associated with the presence of residual tumour.

DWI reflects the cellular status of tissues and is sensitive to changes in the microdiffusion rates of water within intracellular and extracellular spaces.^{22,23} Aggressive tumour tissues are highly cellular and intact cell membranes restrict water diffusion.¹⁹ Furthermore, DW images can be assessed qualitatively, by visually assessing signal intensities, and quantitatively, by measuring ADCs.⁸ It is essential to correlate qualitative DWI findings with ADC maps, which provide quantitative assessments of lesion diffusivity. ADC is an established marker of tumour cellularity (highly cellular regions have low ADC values),²⁴ and ADC mapping has been used to investigate the benignity and malignancy of lesions.²⁵ In the present study, the maximum and mean ADC values were found to be significantly associated with the presence of residual tumour ($p < 0.05$), although the presence or absence of a low signal region on ADC maps was also found to be significant. Many authors who have studied the ADC values of various benign and malignant tumours have concluded that the mean ADC values of benign soft-tissue tumours and malignant soft-tissue tumours overlap.^{18,26} Also, the relatively low spatial resolution of DWI, the inability of ADC maps to detect small or superficially located lesions and the

Figure 4. A 59-year-old female patient with follow-up MR images obtained at 13 days after excision of pleomorphic sarcoma in the subcutaneous fat layer of the left anterior thigh: (a) axial T_2 weighted image is showing only fascial thickening (arrows) at the tumour bed. The apparent diffusion coefficient (ADC) map (not shown) showed no gross diffusion restriction and the mean ADC was $1.51 \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$. (b) Although the volume transfer constant between blood plasma and extracellular/extravascular space was 0.03, dynamic contrast-enhanced MRI indicated a time-concentration curve (TCC) of Pattern III (Type VII, washout curve shape). The presence of residual tumour was suspected based on TCC type only and this was later confirmed by pathology after re-excision.

Table 4. Receiver-operating characteristic (ROC) curve analysis of dynamic contrast-enhanced MRI parameters and apparent diffusion coefficient (ADC) values

	K_{trans}	K_{ep}	V_e	iAUC	VOI graph	ROI graph	Minima ADC	Maxima ADC	Mean ADC
AUC	0.890	0.951	0.508	0.909	0.792	1	0.617	0.756	0.728
SE	0.0608	0.0456	0.105	0.0541	0.0743	0	0.116	0.102	0.105
95% confidence interval	0.735–0.971	0.817–0.996	0.331–0.683	0.760–0.980	0.624–0.909	0.903–1	0.415–0.793	0.557–0.897	0.528–0.877
z statistic	6.416	9.887	0.0723	7.556	3.924		1.006	2.508	2.176
p-value	<0.0001	<0.0001	0.942	<0.0001	0.0001	<0.0001	0.314	0.012	0.029
Cut-off value	≤ 0.1 ^a (90.9, 83.3)	≤ 0.245 (90.9, 100)	> 0.183 (59.1, 8.3)	≤ 6.105 (90.9, 83.3)	≤ 1 (100, 58.3)	≤ 2 (100, 100)	> 1.59 (27.8, 100)	> 1.75 (72.2, 70)	> 1 (100, 40)

AUC, area under the ROC curve; iAUC, initial area under the concentration curve; K_{ep} , rate constant between extracellular/extravascular space (EES) and blood plasma; K_{trans} , volume transfer constant between blood plasma and EES; ROI, region of interest; SE, standard error; V_e , volume of EES space per unit volume of tissue; VOI, volume of interest.

^a(sensitivity; specificity).

sensitivity of DWI to partial volume averaging are definite shortcomings. Furthermore, lesions with a degree of diffusivity equal to surrounding normal tissue are not easily distinguished on DW images or ADC maps.⁸ In 9 of 38 cases, the DW images and their ADC maps were non-diagnostic owing to inappropriate image quality caused by poor signal-to-noise ratio, ghosting or artefact, which suggests not all lesions are amenable to ADC measurement. Of the 9 cases, tumor-bed was located superficially in 8 and deep in 1. Also, as compared with DCE images, DW images showed relatively low sensitivity for the detection of residual tumours; in fact, DCE and DWI results were discordant in nine patients.

The present study has several limitations that warrant mention. First, the number of patients evaluated was relatively small, because only cases which underwent follow-up MR examinations within 3 months of excision were included. Second, 17 of the 38 patients did not undergo confirmatory re-excision.

However, these cases demonstrated tumour bed improvements during clinical and radiologic 1-year follow-ups. Third, medical records regarding operative margin and histologic grade of resected tumour were inadequate because all first operations were performed at outside institutions.

In summary, DCE MRI parameters, particularly K_{trans} , K_{ep} and iAUC values, TCC type and maximum and mean ADC values on ADC maps were found to be more effective than conventional MRI parameters for determining the presence of residual tumour in a tumour bed after the unplanned excision of malignant soft-tissue tumours. However, DW images including ADC maps were inadequate in some cases, especially when lesions were small, superficially located or affected by motion artefact. Therefore, we conclude that the addition of DCE MRI and its quantitative analysis might be useful for determining the presence of residual tumour in a tumour bed in the short term after inadequate excision of a malignant soft-tissue tumour.

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