Skeletal Radiol (1998) 27:505–510

ARTICLE

Daniel Vanel
Lorraine G. Shapeero
Anne Tardivon
André Western
Jean Marc Guinebretière

Dynamic contrast-enhanced MRI with subtraction of aggressive soft tissue tumors after resection

D. Vanel, M.D. · A. Tardivon, M.D.
Centre Inter-Etablissement
de Résonance Magnétique,
Le Kremlin Bicêtre, France

D. Vanel, M.D. (✉)
L.G. Shapeero, M.D. · A. Tardivon, M.D.
Department of Radiology,
Institut Gustave-Roussy,
39 rue Camille Desmoulins,
F-94805 Villejuif, France

L.G. Shapeero, M.D.
Department of Radiology,
Uniformed Services University
of the Health Sciences,
Bethesda, MD 20814–4799, USA

L.G. Shapeero, M.D.
Department of Radiology,
Walter Reed Army Medical Center,
Washington, DC, 20376–5001, USA

A. Western, MSC
Nycomed Imaging AS, Oslo, Norway

J.M. Guinebretière, M.D.
Department of Pathology,
Institut Gustave-Roussy,
Villejuif, France

Abstract *Objective.* To report the application of dynamic contrast-enhanced subtraction MRI for detecting recurrences in aggressive or malignant soft tissue tumors.
Design. The imaging studies consisted of static (T1- and T2-weighted spin-echo) acquisitions, followed by dynamic conventional spin-echo short TR/TE images (at 45 s, 1 min 30 s and 5 min) after a bolus of intravenous contrast medium. Contrast images were subtracted from the precontrast scan on the console.
Patients. Ninety-eight patients were studied who had had aggressive or malignant soft tissue tumors treated by surgery, and were followed up to assess recurrences.
Results. Subtraction MRI characterized recurrences better than routine sequences in 10 patients (1 lesion was seen only with this technique, 6 were better delineated, and 3 inflammatory pseudotumors were identified), and less well in 4 cases.
Conclusion. As the number of levels studied on dynamic images is limited, and all but one recurrence were detected on T2-weighted images, it remains logical to start the examination with T2-weighted spin-echo images, and to use the dynamic study only if contrast injection is required.

Key words MRI · Soft tissue tumors · Follow-up · Dynamic study (MRI) · Contrast medium (MRI)

Introduction

Local recurrences of malignant or aggressive soft tissue tumors are frequent (50–100% of cases) [1], and multiple surgical procedures, chemotherapy, and radiation therapy make their detection difficult. MRI, using T2-weighted images and standard contrast-enhanced T1-weighted images, has been the most widely used method for distinguishing recurrent tumor from diffuse postradiation changes, nonenhancing postoperative fibrosis, and postoperative fluid collections [2]. These sequences cannot always differentiate the post-treatment inflammatory mass from recurrent tumor. In other tumors such as those of bone [3] or breast [4], dynamic contrast-enhanced MR studies have proven helpful for distinguishing these masses by showing two separate vascular phases: an early tumoral phase and a later inflammatory phase. This study reports the application of dynamic contrast-enhanced MR technique with subtraction for detecting recurrences in aggressive or malignant soft tissue tumors.

Materials and methods

One hundred consecutive adult patients who had previously been treated for malignant or aggressive soft tissue tumors and were routinely sent for MRI (Table 1), were entered into the study within 18

Table 1 Histology of the lesions studied

Liposarcoma	25
Malignant fibrous histiocytoma	18
Synovial sarcoma	11
Aggressive fibromatosis	11
Neurofibrosarcoma	10
Leiomyosarcoma	6
Fibrosarcoma	5
Soft tissue Ewing sarcoma	2
Soft tissue chondrosarcoma	1
Clear cell carcinoma	1
Lymphoma	1
Rhabdomyosarcoma	1
High-grade sarcoma (unclassified)	6
Total	98

months. Aggressive fibromatosis behaves locally as a malignant tumor, and raises the same local problems, and has therefore been included in the study. There were 55 women and 45 men. The mean age was 46 years (range 18–81 years). All patients had had previous surgery, and 62 had had radiation therapy. There were 62 tumors of the lower extremities, 12 of the upper extremities, 15 of the trunk, six of the pelvis, and three of the neck. Ninety-eight examinations, performed on a 1.5 T unit (Signa GE Milwaukee), were analyzed. A surface coil was used where possible, including all examinations of the extremities, the back and the neck, but not the studies of the proximal thighs or pelvis. Pregnant patients, those who were breast-feeding, or participating in another clinical trial, and those who had previously participated in this study were excluded. Written informed consent was obtained. The study had the approval of our ethics committee. Two patients were excluded after having given informed consent: one was too wide for the unit, and one had a benign lesion at final histological examination (fibroelastoma).

The examinations were conducted as follows. First, an intravenous line was established before the beginning of the examination. Pre-contrast static sequences included axial T1-weighted (TR/TE: 500–700/10–20) and T2- weighted (TR/TE: 2000–2500/100) spin-echo acquisitions. Then seven to nine levels were chosen from the T2-weighted images, where lesions were best visualized. They were studied on rapid acquisition conventional spin echo T1-weighted sequences (matrix 128×256, 1 acquisition, TR/TE: 300/17 for an acquisition time of 45 s). The sequences were performed before injection, then following a bolus injection of gadodiamide, a nonionic gadolinium chelate (Omniscan, Nycomed, Oslo, Norway), at a dosage of 0.1 mmol/kg. The sequences with contrast medium were started at the same time as the 20 s bolus was initiated and acquired in 45 s, then at 1.5 min (early images) and 5 min (late images) [2–4]. The initial T1-weighted sequence was repeated at 10 min (late images). Postcontrast images were subtracted from the precontrast scan by using the subtraction function on the console.

The following MRI criteria were applied for diagnosis: (a) on standard sequences, a mass-like high signal on T2-weighted sequence; (b) enhancement on standard contrast-enhanced T1-weighted sequence; (c) a mass enhancing during the early vascular images on gadolinium-enhanced subtraction images. The criteria for no recurrence were as follows: (a) on standard sequences, no high signal or a non-mass-like high signal on T2-weighted sequences; (b) on standard postcontrast T1-weighted images, no enhancement or enhancement without a definite mass; (c) on gadolinium-enhanced dynamic subtraction images, no or late enhancement. The MR studies were read by two senior radiologists individually with consensus diagnosis if there was disagreement.

Twenty-one patients underwent surgery within 2 weeks, because of a clinically or radiologically suspected recurrence, and no disseminated disease. The others were followed for at least 2 years.

Results

Of the 21 patients who underwent surgery within 2 weeks after the MR examination, 19 had a recurrence and two did not have a tumor (MRI was considered negative, but a mass was palpated by the surgeon). One recurrence was operated on 2 months later. Five patients with positive MR findings but a nonoperable lesion (either nonremovable or associated with metastases) underwent chemotherapy first. No surgery was possible in the follow-up period. There were thus 24 patients with a recurrence.

On T2-weighted images, 29 patients had a high signal intensity mass. Twenty-three of the 24 tumors were detected, with one false negative (Fig. 1) and six false positives, which included one granuloma, three inflammatory masses and two hygromas.

On conventional postcontrast T1-weighted spin-echo images 25 masses took up contrast medium, including the three false positive studies due to inflammatory masses (Fig. 2).

On the dynamic subtracted images 22 masses took up contrast medium early, including one false positive, which was a probable 5 mm large granuloma. As the lesion was small, and the scar thick, surgery was considered difficult. (The mass disappeared spontaneously on MRI examinations at 3 and 6 months.) There were three false negative examinations. A 2 cm large, poorly vascularized recurrent neurofibrosarcoma was easily visible on T2-weighted images but did not take up contrast medium early (Fig. 3). Close follow-up was decided on, and 2 months later, at the control MR examination, the mass had increased in diameter by 10% and early contrast uptake was noted. Surgery confirmed the recurrence. The incorrect level was chosen from the T2-weighted images in a patient with an aggressive fibromatosis, who had had multiple surgery and a 100 cm long scar. A very small focus (3 mm large) of high signal inside the scar was visible but ignored, and the dynamic study was done at another level (Fig. 4). Six months later, an obvious recurrence was detected at that level. Respiratory motion artifact made a large recurrence of a liposarcoma, which was obvious on static images, impossible to detect on the poor-quality subtraction image (Fig. 5).

Subtraction MRI provided more information than routine sequences in 10 patients. One lesion was seen only with this technique (Fig. 1). Six lesions were better delineated from the associated inflammatory changes. Three inflammatory pseudotumors were correctly identified, because of their late vascular uptake (Fig. 2). No surgery was performed, and the masses were stable on 2-year follow-up.

During the follow-up of the cases considered negative on MR images, two recurrences appeared 2 months after the MR examination. Even retrospectively no lesion was identified on any sequence. Both recurrences grew very

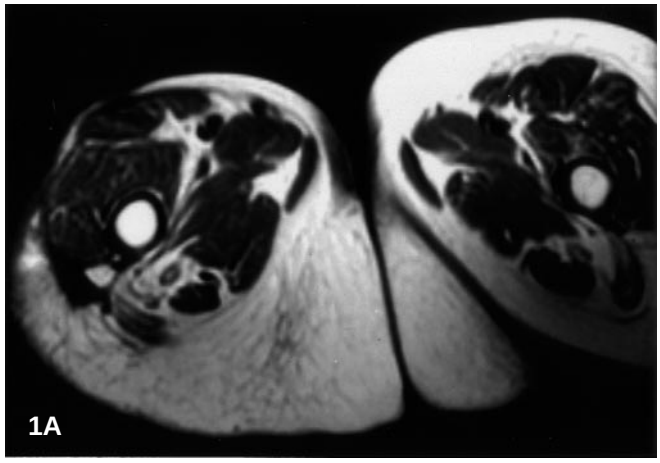
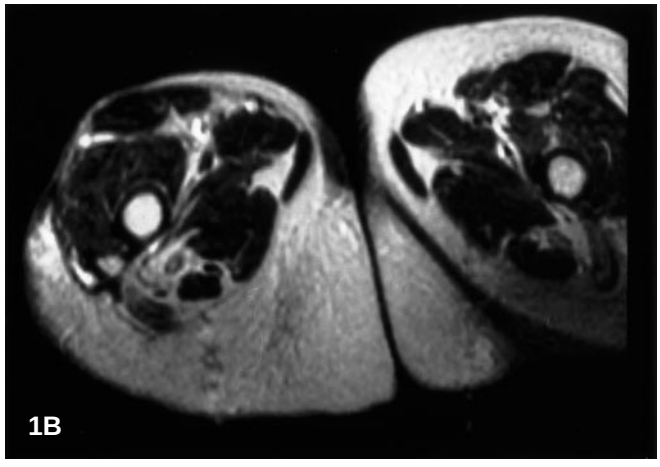
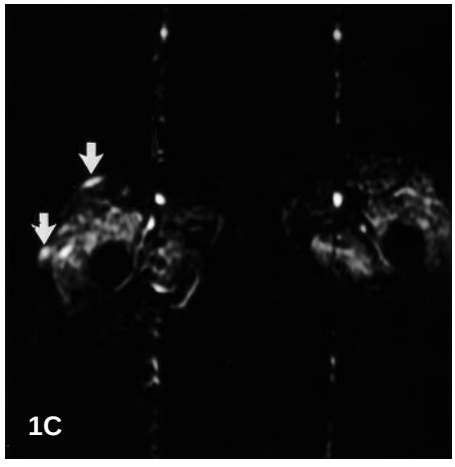
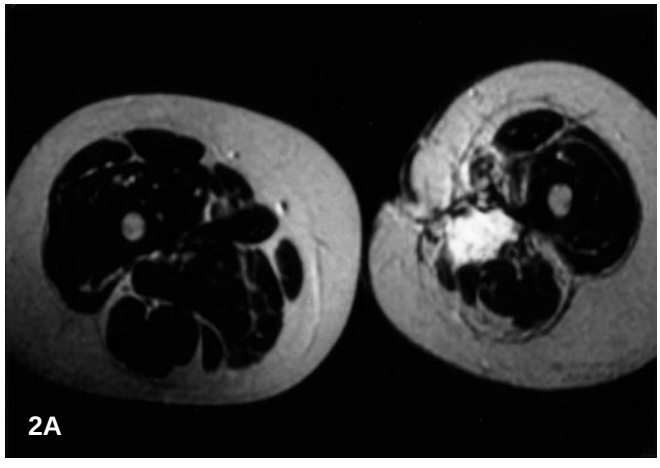


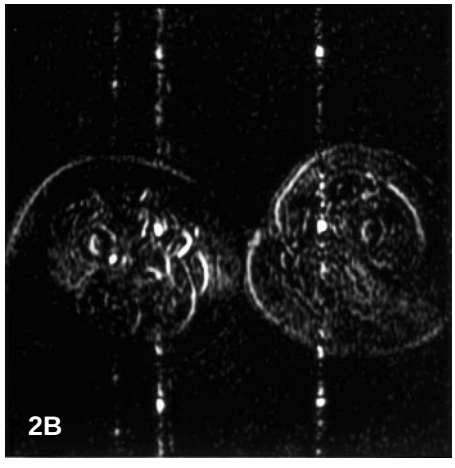
Fig. 1 **A** Clinically obvious multiple cutaneous recurrences of a liposarcoma in an 81-year-old woman 2 years after surgery and radiation therapy. MRI was performed to rule out deep lesions. The tumors are not visible on **A** T1-weighted (TR/TE: 700/12) or **B** T2-weighted (TR/TE: 2500/100) axial images. On subtraction gadolinium-enhanced images (**C**, TR/TE: 300/17), two lesions are visible (*arrows*)

Fig. 2A, B Inflammatory pseudotumor in a 59-year-old woman studied 4 years after surgery and radiation therapy. **A** A poorly defined high signal mass is visible on T2-weighted images (TR/TE: 2500/100). **B** The mass is not visible on subtraction 45 s after injection. It took up contrast medium late. There was no recurrence 2 years later





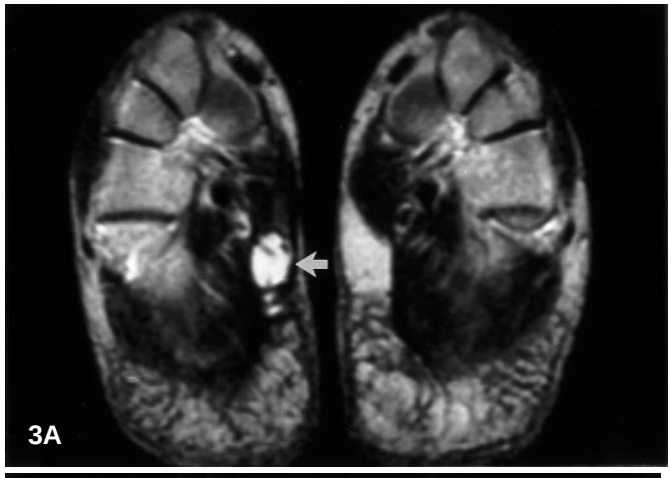


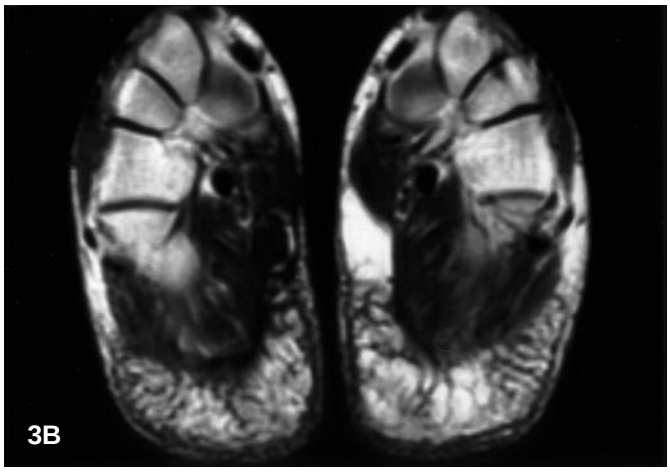


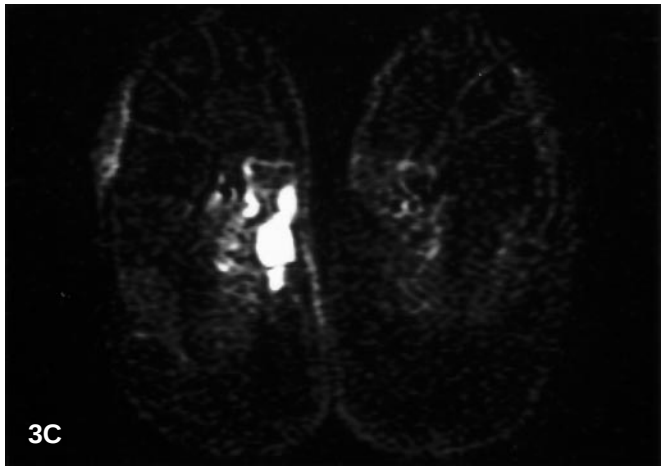
rapidly, with clinical changes visible daily, and surgery confirmed the recurrences.

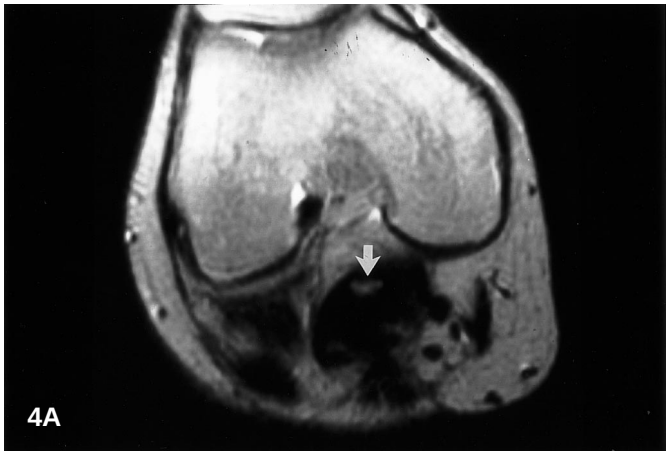
Discussion

Our MR protocol used very simple spin-echo sequences, which are available on all units. More sophistication can of course be used. Fat suppression, combined with T2-weighted or fast T2-weighted spin-echo sequences improves the conspicuity of the lesions. It was not used in our study as it was not initially available and we did not want to change the protocol. It has some limitations: a limited number of levels can be studied and a very homogeneous field is required [5–8]. Fat presaturation can be used after contrast injection, instead of subtraction.









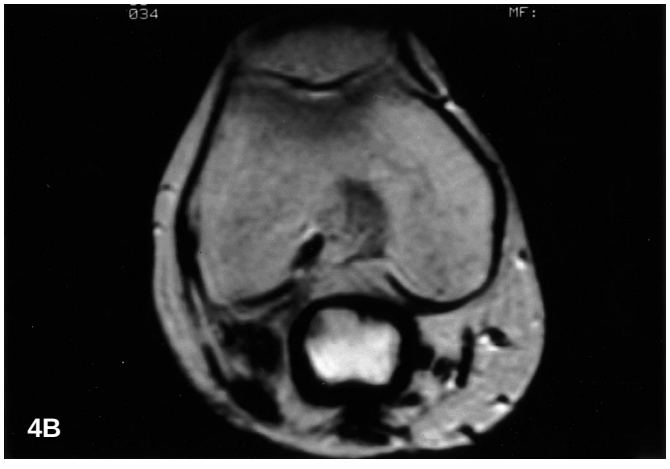


Fig. 3A–C Systematic follow-up of a neurofibrosarcoma of the foot in a 58-year-old woman studied 10 months after surgery. **A** A mass is visible on T2-weighted images (*arrow*) (2000/100). **B** The mass has a low signal on T1-weighted images (500/11) and did not enhance early. **C** The mass takes up contrast medium late (TR/TE: 300/17, 5 min delay). Surgery was not performed immediately. Two months later the tumor had increased a little in size, and early enhancement had appeared. Surgery revealed a poorly vascularized tumor.

Fig. 4A, B A 24-year-old woman who had aggressive fibromatosis and had undergone multiple operations. **A** On axial T2-weighted (TR/TE: 2000/100) images there is a very limited high signal (*arrow*) in a low signal intensity scar. Dynamic images were made at another level. **B** Six months later the recurrence is obvious, as a high-intensity mass inside a low-intensity scar (TR/TE: 2000/100)

The results are the same, as only the locations with an uptake of contrast medium have a high signal. A spoiled gradient-echo fast sequence could improve the results, allowing faster acquisitions at more levels.

In the follow-up of malignant and aggressive soft tissue tumors, the configuration of the lesion and, more importantly, its signal intensity are helpful for defining its character. The T2-weighted sequence was the most useful first step for evaluating a recurrent tumor [2, 9]. The absence of high signal intensity and the presence of low signal intensity implies an absence of recurrent tumor and the presence of a post-operative scar [10–12]. There are, however, two potential pitfalls. Firstly, isolated tumor cells may be too small to be detected on MRI [9]. Secondly, some soft tissue tumors may be mistaken for benign fibrous tissue because they contain a large quantity of col-

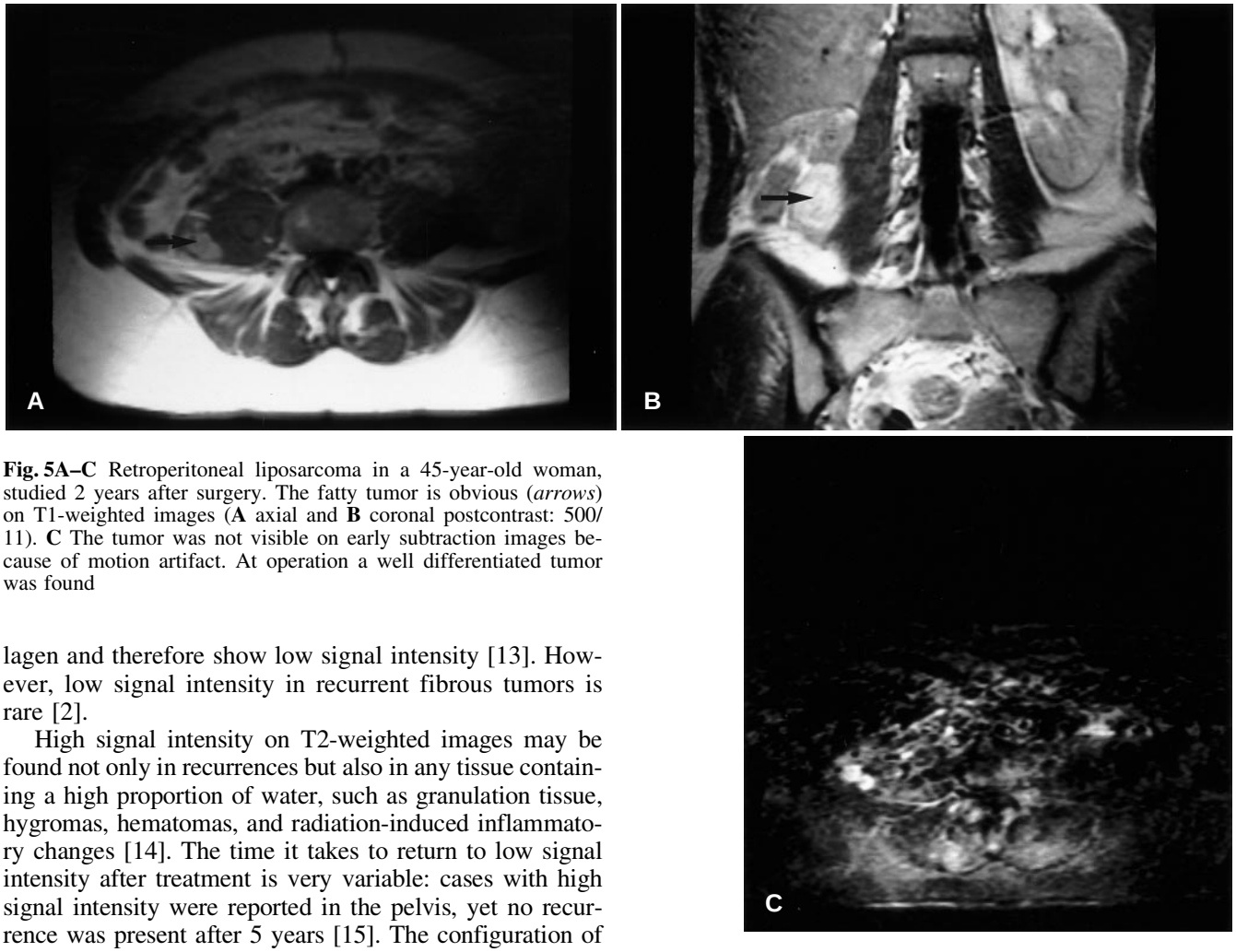


Fig. 5A–C Retroperitoneal liposarcoma in a 45-year-old woman, studied 2 years after surgery. The fatty tumor is obvious (*arrows*) on T1-weighted images (**A** axial and **B** coronal postcontrast: 500/11). **C** The tumor was not visible on early subtraction images because of motion artifact. At operation a well differentiated tumor was found

lagen and therefore show low signal intensity [13]. However, low signal intensity in recurrent fibrous tumors is rare [2].

High signal intensity on T2-weighted images may be found not only in recurrences but also in any tissue containing a high proportion of water, such as granulation tissue, hygromas, hematomas, and radiation-induced inflammatory changes [14]. The time it takes to return to low signal intensity after treatment is very variable: cases with high signal intensity were reported in the pelvis, yet no recurrence was present after 5 years [15]. The configuration of the area of high signal intensity should also be considered to obtain the correct diagnosis. In the radiation therapy portals, a feather-like pattern of high signal intensity without a mass in muscles dissecting along fascia planes usually indicates inflammatory changes rather than recurrence.

Only a few patients exhibiting areas of high signal intensity but without a mass subsequently develop a recurrence. Either the lesion may initially be too small or may be overlooked because no definite mass effect is seen and the lesion is isointense with inflammation.

When masses have a high signal intensity on T2-weighted images, the addition of contrast medium to routine sequences allows differentiation of a nonenhancing hematoma or hygroma from enhancing tumor or inflammation. The extensively necrotic tumor that does not enhance because the few minute foci of residual tumor are below the resolution of MRI is an exception [2]. Another exception is the uncommon mucoid tumor that may enhance only in areas of active tumor with the mucoid tissue remaining of low signal intensity. Although not yet reported, a completely mucoid tumor could theoretically be mistaken for a hygroma [16].

Standard contrast-enhanced MRI cannot, however, separate a recurrent tumor from a rare inflammatory mass. Different dynamic gadolinium-enhanced MR techniques for studying musculoskeletal tumors have addressed this issue. The region of interest (ROI) technique [17, 18] uses a preselected part of the image and obtains curves to evaluate the uptake of contrast in the region after injection. The limitations are that only the selected region is studied, an average of the whole ROI is obtained and results seem not to be reproducible [19]. Factor analysis of medical image sequences allows a pixel-by-pixel evaluation of contrast uptake by the entire image but sophisticated software is required and is not currently available on standard consoles [20]. First-pass images [21] demonstrate the whole image on the slope of uptake of contrast media after the injection. The technique is simple to use but requires software that is not currently available. Gadolinium-enhanced subtraction MRI, which we used in this study, also allows differentiation between inflammation and residual tumor. It is easy, fast, and available on every unit. Active tumor increases its signal rapidly whereas in-

flammatory changes enhance only after 3–9 min. Whichever dynamic sequence is chosen, tumor takes up contrast medium within the 2 first min, probably because of abnormal tumor vessels whereas in inflammatory changes the uptake is after 2 min, mainly because of uptake by the capillaries [22].

The main limitations of all dynamic sequences are patient motion and technical factors. With patient motion, subtraction cannot be performed accurately, because of misregistration. Slow injection of contrast medium could potentially be a limiting technical factor because the time parameters for the early and late vascular phases would not be consistent. This was not a problem in our study. Variable injection rates could be avoided by using automatic machine injection of contrast medium.

Conclusion

The MR evaluation of malignant or aggressive soft tissue tumors in the post-treatment follow-up should begin with a T2-weighted sequence. If there is no high signal intensity, or widespread high signal intensity with no mass, the examination is considered negative and is finished. If there is a high signal intensity mass, dynamic subtracted T1-weighted images should be obtained and are accurate in differentiating tumor from inflammatory changes.

References

1. Enzinger FM, Weiss SW. Soft tissue tumors, 3rd edn. Washington, DC: CV Mosby, 1995.
2. Vanel D, Shapeero LG, De Baere T, et al. MR imaging in the follow up of malignant and aggressive soft tissue tumors: results of 511 examinations. Radiology 1994; 190: 263–268.
3. De Baere T, Vanel D, Shapeero LG, Charpentier A, Terrier P, Di Paola M. Osteosarcoma after chemotherapy: evaluation with contrast material-enhanced subtraction MR imaging. Radiology 1992; 185: 587–592.
4. Heywang-Köbrunner SH, Viehweg P, Heinig A, Küchler C. Contrast-enhanced MRI of the breast: accuracy, value, controversies, solutions. Eur J Radiol 1997; 24 : 94–108.
5. Mirowitz SA. Fast scanning and fat-suppression MR imaging of musculoskeletal disorders. AJR 1993; 161:1147.
6. Mirowitz SA, Apicella P, Reinus WR, et al. MR imaging of bone marrow lesions: relative conspicuousness on T1-weighted, fat-suppressed T2-weighted, and STIR images. AJR 1993; 162: 215.
7. Pui MH, Chang SK. Comparison of inversion recovery fast spin-echo (FSE) with T2-weighted fat-saturated FSE and T1-weighted MR imaging in bone marrow lesion detection. Skeletal Radiol 1996; 25: 149.
8. Weinberger E, Shaw DW, White KS, et al. Nontraumatic pediatric musculoskeletal MR imaging: comparison of conventional and fast-spin-echo short inversion time inversion-recovery technique. Radiology 1995; 194: 721.
9. Vanel D, Lacombe MJ, Couanet D, Kalifa C, Spielmann M, Genin J. Musculoskeletal tumors: follow-up with MR imaging after treatment with surgery and radiation therapy. Radiology 1987; 164: 243–245.
10. Glazer HS, Lee JK, Levitt RJ. Radiation fibrosis: differentiation from recurrent tumor by MR imaging. Radiology 1985; 756: 721–726.
11. Ebner F, Kressel HY, Mintz MC, et al. Tumor recurrence versus fibrosis in the female pelvis: differentiation with MR imaging at 1.5 T. Radiology 1988; 166: 333.
12. McVicar AD, Oliff JFC, Pringle J, Pinkerton CR, Husband JES. Ewing sarcoma: MR imaging of chemotherapy-induced changes with histologic correlation. Radiology 1992; 184: 859.
13. Sundaram M, McGuire MH, Schajowicz F. Soft-tissue masses: histologic basis for decreased signal (short T2) on T2-weighted MR images. AJR 1987; 148: 1247–1250.
14. Panicek DM, Schwartz LH, Heelan RT, et al. Non-neoplastic causes of high signal intensity at T2-weighted MR imaging after treatment for musculoskeletal neoplasm. Skeletal Radiol 1995; 24: 185.
15. Hawnaur JM, Johnson RJ, Isherwood I, Jenkins JPR. Gd-DTPA in MRI of bladder carcinoma. In: Katayama H, Brasch RC, eds. New dimensions of contrast media. New York: Elsevier, 1991: 357–363.
16. Sundaram M, Baran G, Merenda G, McDonald DJ. Myxoid liposarcoma: MRI appearances with clinical and histological correlation. Skeletal Radiol 1990; 19: 359–362.
17. Erlemann R, Reiser MF, Peters PE, et al. Musculoskeletal neoplasms: static and dynamic Gd-DTPA-enhanced MR imaging. Radiology 1989; 171: 767–773.
18. Fletcher BD, Hanna SL, Fairclough DL, Gronemeyer SA. Pediatric musculoskeletal tumors: use of dynamic, contrast-enhanced MR imaging to monitor response to chemotherapy. Radiology 1992; 184: 243.
19. Erlemann R. Dynamic gadolinium-enhanced MR imaging to monitor tumor response to chemotherapy (letter). Radiology 1993; 186: 904.
20. Bonnerot V, Charpentier A, Frouin F, Kalifa C, Vanel D, Di Paola R. Factor analysis of dynamic MR imaging in predicting the response of osteosarcoma to chemotherapy. Invest Radiol 1992; 27: 847–855.
21. Verstraete KL, Dierick A, De Deene Y, et al. First-pass images of musculoskeletal lesions: a new and useful diagnostic application of dynamic contrast-enhanced MRI. Magn Reson Imaging 1994; 12: 687–702.
22. Vanel D, Verstraete KL, Shapeero LG. Primary tumors of the musculo-skeletal system. Radiol Clin North Am 1997; 35: 213–237.