MRI surveillance after resection for primary musculoskeletal sarcoma

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This study reports the experience of one treatment centre with routine surveillance MRI following excision of musculoskeletal sarcoma. The case notes, MRI and histology reports for 57 patients were reviewed. The primary outcome was local tumour recurrence detected on either surveillance MRI in asymptomatic patients, or interval MRI in patients with clinical concern. A total of 47 patients had a diagnosis of soft-tissue sarcoma and ten of a primary bone tumour. A total of 13 patients (22%) had local recurrence. Nine were identified on a surveillance scan, and four by interval scans. The cost of surveillance is estimated to be £4414 per recurrence detected if low-grade tumours with clear resection margins are excluded. Surveillance scanning has a role in the early detection of local recurrence of bone and soft-tissue sarcoma.

The successful treatment of musculoskeletal sarcoma depends on close liaison between specialities, and therefore local sarcoma groups have developed to co-ordinate diagnosis and treatment. The tumour grade,1 resection margin2 and response to adjuvant treatment3 are key factors known to affect local control following resection, but vary according to the histological diagnosis. Whereas MRI is effective in staging musculoskeletal sarcoma,4 its role in surveillance for the early detection of local recurrence is uncertain, although retrospective studies suggest it may aid early diagnosis.5 Many centres rely on clinical screening to identify recurrence6 and reserve MRI for selected patients. There is recent evidence that routine chest radiography may be helpful in detecting metastatic disease following treatment of high-grade soft-tissue sarcoma,7 but to our knowledge there is no published evidence that routine MRI screening will enable early detection of recurrent tumour.

For a screening test to be considered useful, it should identify pathology in the asymptomatic patient, the intervention should be acceptable to the patient, accurate for diagnosis and affordable, and a positive result should lead to an alteration in outcome.8 This study is an audit of a single centre’s experience of routine post-resection surveillance MRI for musculoskeletal sarcoma to assess its value as a screening tool according to this criteria.

Patients and Methods

Between 1997 and 2001 an unselected group of patients undergoing resection of a primary musculoskeletal sarcoma were enrolled in a post-operative MRI surveillance programme. During this period surveillance was more likely to be offered if the patient had a high-grade lesion, but since 2002 all patients undergoing limb salvage musculoskeletal sarcoma resection have undergone surveillance. We reviewed the records of our local sarcoma group and identified 57 patients (35 males, 22 females) with a mean age of 49 years (6 to 78), who were diagnosed with bone or soft-tissue sarcoma between 1997 and 2004 and who had routine post-treatment MRI. The minimum follow-up from resection was two years (mean 59 months, 24 to 107). Ten patients had a primary bone tumour and 47 a primary soft-tissue sarcoma. Information on the site of the tumour, histological grade, Enneking stage9 and resection margin was also collected.

All patients underwent MRI at six months, one year, and then annually for five years following resection. The MRI protocol10 required all patients who had soft-tissue tumours to undergo water-weighted sequences (short $T_1$ inversion recovery (STIR) and fat-suppressed fast spin echo (FSE) $T_2$) in at least two planes, although $T_1$-weighted images were also obtained in at least one plane for liposarcomas. If a hyperintense mass was identified on the initial sequences, $T_1$-weighted sequences were performed in at least two planes before and
after intravenous administration of gadolinium chelates. An enhancing mass was assumed to represent recurrent tumour. Chondroid tumours were considered to have recurrent disease if a hyperintense mass was present on STIR or T2-weighted images, irrespective of the post-contrast images. Dynamic post-contrast scans were not used. Similar sequences were used for bone sarcomas. For the purposes of this study, a surveillance recurrence was defined as local tumour recurrence on routine MRI, and an interval recurrence as local recurrence on MRI performed outside the surveillance programme because of clinical concern. If local recurrence was identified by interval scan following a negative surveillance scan, the MR films were reviewed by an independent observer to determine whether the local recurrence could be seen on the preceding surveillance scan. The cost of the surveillance programme was estimated.

**Results**

Of the lesions 46 (81%) were appendicular and 11 (19%) were in a limb girdle. There were 21 low-grade (37%) and 36 high-grade (63%) lesions, shown with their Enneking stage in Table I. Recurrence was identified in 13 patients (22%) within five years of surgical resection. Nine (69%) were identified on routine surveillance in asymptomatic patients, and four (31%) on scans requested because of
clinical concern (Table II). Recurrence was detected in four of the ten patients (40%) with a primary bone tumour, and in nine of the 47 (19%) with a soft-tissue sarcoma. There were no significant differences in the rate of recurrence between limb girdle or appendicular sites, high- or low-grade lesions, intra- and extra-compartmental spread, and the presence or absence of contaminated resection margins (Table III). There were no recurrences in low-grade lesions excised with clear margins. The median volume of the recurrent lesion based on the histology at the time of resection was 125.0 cm³ (2.1 to 2126.3). There was no statistical difference in the mean volume of the lesions detected on interval or surveillance MRI. In nine of the 13 recurrences a biopsy was performed before excision to confirm the diagnosis.

On surveillance scanning, the recurrences were detected at six months in three patients, one year in two, two years in three and three years in one. Recurrences were detected on interval scan at less than six months in one, six to 12 months in one, one to two years in one and between four and five years in one. Retrospective review by an independent observer of earlier surveillance scans for the three patients with recurrences detected on interval scan after six months confirmed that all had been reported correctly as showing no evidence of recurrent disease.

In our institution MRI costs £175 per scan. A total of 250 surveillance scans were performed and detected nine recurrences at a total cost of £43 750 or £4861 per recurrence. If all patients in the study were followed for five years and no further recurrences detected, the cost per detected recurrence would rise by an estimated £1000 ((50 scans x £175) ÷ 9 recurrences). If surveillance was targeted at those most at risk of recurrence, namely those with high-grade tumours or low-grade tumours with contaminated resection margins, the estimated cost would be £2606 per recurrence ((134 scans x £175) ÷ 9 recurrences) or £4414 ((227 scans x £175) ÷ 9 recurrences) if no further recurrences were detected up to five years (Table III).

Discussion

In this study 69% of the tumour recurrences detected using surveillance MRI were in asymptomatic patients. The screening method used must be acceptable to the patient and repeatable. MRI is non-invasive and fulfils these criteria well, although some patients find the experience unpleasant or impossible to tolerate, but we have not found this to be common in tumour patients.

MRI is shown to be effective in detecting musculoskeletal sarcoma recurrence, especially with the addition of paramagnetic contrast agents. Tumour recurrence can thereby be distinguished from post-operative seroma and radiation and surgical changes. Vanel et al. described MRI findings associated with tumour recurrence, and Reuther and Mutschler showed that MRI is highly accurate in detecting recurrence following resection of sarcomas. These authors reported a sensitivity of 82.5%, a specificity of 96.3%, a positive predictive value of 75% and a negative predictive value of 91.3%. In our study there were no false positive or false negative results.

Is MRI surveillance affordable? Based on the most costly scenario from this study, whereby if all patients had surveillance scans for five years and no further recurrences were detected, we estimate the cost of this surveillance programme to be just under £6000 per recurrence, which is comparable to the costs of breast18 or liver19 cancer screening. Selecting those with high-grade lesions or contaminated resection margins, and hence at the greatest risk of recurrence, would further reduce the cost of the programme. An intervention is deemed to be cost-effective if estimated as less than £50 000 (£25 500) per life-year saved.

Although an attractive proposition, this study does not show whether early detection alters outcome. Ueda, Yoshikawa and Mori stated that local recurrence does not affect prognosis but is rather an indicator of a poor outcome, because the lesion is more likely to be high grade or the excision incomplete. The determination of whether surveillance scans can affect long-term survival would require follow-up over decades to provide adequate survival data and multi-centre involvement to accumulate adequate numbers of patients to counteract confounding factors such as multiple histological diagnoses, grade and stage of lesion, resection margin and treatment.

The estimate of cost-effectiveness is highly dependent on the proportion of patients developing a recurrence. Confounding factors include potential selection bias, as not all patients who were diagnosed during the study period had surveillance scans. Moreover, our cohort was small and potentially unrepresentative,22 as it included bone and soft-tissue sarcomas and a large proportion of high-grade tumours and contaminated resection margins. However, we believe this study demonstrates that MRI surveillance enables early detection of local tumour recurrence in asymptomatic patients, which has not, to our knowledge, been reported previously.

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References


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