Reconstruction after intercalary resection of malignant bone tumours

COMPARISON BETWEEN SEGMENTAL ALLOGRAFT AND EXTRACORPOREALLY-IRRADIATED AUTOGRAFT

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Received 22 March 2004; Accepted after revision 18 November 2004

We reviewed 29 patients who had undergone intercalary resection for malignant tumours. Of these, 14 had received segmental allograft reconstruction and 15 extracorporeally-irradiated autograft.

At a mean follow-up of 71 months (24 to 132), 20 were free from disease, five had died and four were alive with pulmonary metastases. Two patients, one with an allograft and one with an irradiated autograft, had a local recurrence. Reconstruction with extracorporeally-irradiated autograft has a significantly lower rate of nonunion (7% vs 43%, \( p = 0.031 \)) but an insignificantly higher rate of fracture (20% vs 14%, \( p = 0.535 \)) than that with segmental allograft. Using the Enneking functional evaluation system, the mean postoperative score for the patients without local recurrence was 87% (80% to 96%) and was similar in both groups.

Extracorporeally-irradiated autograft could be an acceptable alternative for reconstruction after intercalary resection, especially in countries where it is difficult to obtain allografts.

Segmental skeletal defects which result from intercalary resection of malignant bone tumours are commonly reconstructed using large segmental allografts with satisfactory long-term results.\(^1\)-\(^4\) Allografts restore bone stock and allow better soft-tissue attachment compared with metal implants. However, there are significant complications associated with the use of large segmental bone allografts, particularly when they are inserted into a systemically-compromised host or when the operative site is depleted of soft tissues, or has been subjected to radiation.\(^2\)-\(^8\) The most commonly encountered complications are fracture, nonunion and infection.\(^2\)-\(^8\) The rate of fracture has been reported to be from 14% to more than 50%.\(^5\) Nonunion of the host-allograft junction is also a common problem. The results of 104 segmental allografts transplanted at a single institution were reviewed,\(^1\) and 31 cases of nonunion of the allograft at one or both junctions were found. These complications usually occurred within the first three to four years of surgery, but after that period, the graft became a relatively competent, stable system.\(^3\),\(^9\)

Because the supply of allografts is limited in our country, we used extracorporeally-irradiated autograft as an alternative to allograft in some cases. This procedure was first reported by Uyttendaele et al in 1988.\(^10\) It has several theoretical advantages, including preservation of bone stock, perfect matching for size and no risk of transmission of infectious diseases.

Our aim was to compare the clinical outcome and complications associated with the use of either segmental allografts or extracorporeally-irradiated autografts for reconstruction of defects after intercalary resection of malignant bone tumours.

Patients and Methods
We studied 29 patients who had undergone intercalary resection for malignant tumours between 1993 and 2001 (Tables I and II). There were 19 men and ten women aged from nine to 74 years. There were 23 cases of high-grade osteosarcoma (22 stage IIB, 1 stage III), two of chondrosarcoma, two of malignant fibrous histiocytoma, one of leiomyosarcoma and one of solitary plasmacytoma. Twenty tumours were located in the femur, six in the tibia and three in the humerus. Wide excision was performed to ensure the removal of an intact cuff of normal tissue surrounding the lesion. Resections of the bone were made at least 2 cm from any signs of involvement, according to the MR scans. The mean length of the resected bone was 16.8 cm (10.3 to 26.1).

If the resected bone had not been extensively destroyed, reconstruction with extracor-
Porely-irradiated autograft was performed. Of the 29 patients, 14 had segmental allografts and 15 extracorporeally-irradiated autografts. There were no significant differences between the two groups with regard to age, primary tumour, site, local or systemic staging, type of tumour, and length of resection. Allografts were obtained from the bone bank at the authors' institution. All were fresh-frozen. Storage and investigation for bacterial infection and other blood-borne transmissible diseases were performed according to the regulations established by the American Association of Tissue Banks.

### Table I. Details of 15 patients with malignant bone tumours which were treated by extracorporeally-irradiated autograft

<table>
<thead>
<tr>
<th>Case</th>
<th>Gender</th>
<th>Age (yrs)</th>
<th>Diagnosis</th>
<th>Surgical stage*</th>
<th>Site</th>
<th>Length of resection (cm)</th>
<th>Type of fixation</th>
<th>Vancomycin-impregnated cement in graft</th>
<th>Follow-up (mths)</th>
<th>Complications</th>
<th>Chemo-therapy</th>
<th>Oncological result†</th>
<th>Functional score (%)</th>
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<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>17</td>
<td>Osteosarcoma</td>
<td>IIB</td>
<td>Humerus</td>
<td>14.4</td>
<td>Plate</td>
<td>No</td>
<td>132</td>
<td>Graft fracture (7 mths)</td>
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<td>NED</td>
<td>90</td>
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<tr>
<td>2</td>
<td>F</td>
<td>14</td>
<td>Osteosarcoma</td>
<td>IIB</td>
<td>Femur</td>
<td>19.1</td>
<td>IM‡ nail + plate</td>
<td>No</td>
<td>126</td>
<td>-</td>
<td>Yes</td>
<td>NED</td>
<td>87</td>
</tr>
<tr>
<td>3</td>
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<td>Osteosarcoma</td>
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<td>Femur</td>
<td>20.0</td>
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<td>NED</td>
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<td>IM nail + plate</td>
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<td>-</td>
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<td>NED</td>
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<td>Femur</td>
<td>10.9</td>
<td>IM nail + plate</td>
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<td>Plate</td>
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<td>Plate</td>
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<td>Plate</td>
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<td>16.9</td>
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<td>28</td>
<td>Local recurrence</td>
<td>Yes</td>
<td>DOD Amputation</td>
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* Musculoskeletal Tumor Society system
† AWD, alive with disease; NED, no evidence of disease; DOD, died of disease
‡ IM, intramedullary

### Table II. Details of 14 patients with malignant bone tumours which were treated by segmental allograft

<table>
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<tr>
<th>Case</th>
<th>Gender</th>
<th>Age (yrs)</th>
<th>Diagnosis</th>
<th>Surgical stage*</th>
<th>Site</th>
<th>Length of resection (cm)</th>
<th>Type of fixation</th>
<th>Vancomycin-impregnated cement in graft</th>
<th>Follow-up (mths)</th>
<th>Complications</th>
<th>Chemo-therapy</th>
<th>Oncological result†</th>
<th>Functional score (%)</th>
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<td>M</td>
<td>17</td>
<td>Osteosarcoma</td>
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<td>Femur</td>
<td>10.3</td>
<td>IM‡ nail + plate</td>
<td>No</td>
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<td>Graft fracture (83 mths)</td>
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<td>NED</td>
<td>90</td>
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<td>M</td>
<td>12</td>
<td>Osteosarcoma</td>
<td>IIB</td>
<td>Femur</td>
<td>18.6</td>
<td>IM nail + plate</td>
<td>No</td>
<td>127</td>
<td>Local recurrence</td>
<td>Yes</td>
<td>NED</td>
<td>Amputation</td>
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<td>IIA</td>
<td>Femur</td>
<td>11.5</td>
<td>IM nail + plate</td>
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<td>93</td>
<td>Nonunion (distal)</td>
<td>No</td>
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<td>Femur</td>
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<td>IM nail + plate</td>
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<td>Femur</td>
<td>26.1</td>
<td>IM nail + plate</td>
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<td>77</td>
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<tr>
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<td>M</td>
<td>17</td>
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<td>Humerus</td>
<td>11.9</td>
<td>Plate</td>
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<td>65</td>
<td>-</td>
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<td>NED</td>
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<td>Osteosarcoma</td>
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<td>Femur</td>
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<td>IM nail + plate</td>
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<td>63</td>
<td>Nonunion (both sides)</td>
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<td>DOD</td>
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<td>Femur</td>
<td>18.8</td>
<td>IM nail + plate</td>
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<td>62</td>
<td>Nonunion (proximal)</td>
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<td>NED</td>
<td>83</td>
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<td>9</td>
<td>M</td>
<td>44</td>
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<td>IM nail + plate</td>
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<td>62</td>
<td>Nonunion (distal)</td>
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<td>NED</td>
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<tr>
<td>10</td>
<td>M</td>
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<td>IIB</td>
<td>Tibia</td>
<td>13.8</td>
<td>Plate</td>
<td>Yes</td>
<td>48</td>
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<td>Femur</td>
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<td>Plate</td>
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<td>30</td>
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<td>M</td>
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<td>Tibia</td>
<td>17.0</td>
<td>Plate</td>
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<td>30</td>
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<td>NED</td>
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<td>14.0</td>
<td>IM nail + plate</td>
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<td>26</td>
<td>-</td>
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<td>DOD</td>
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<td>24</td>
<td>-</td>
<td>Yes</td>
<td>AWD</td>
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</table>

* Musculoskeletal Tumor Society system
† AWD, alive with disease; NED, no evidence of disease; DOD, died of disease
‡ IM, intramedullary
With regard to extracorporeally-irradiated autografts, the excised specimen containing the tumour-bearing bone and its surrounding tissues was immediately sent for irradiation with a dose of 30,000 rads using a linear accelerator. Transport and irradiation of the bone took about 50 minutes. After irradiation, the bulk of the tumour and the surrounding soft tissues except the tendons were removed.

Ten grafts were fixed with plates, four with intramedullary nails, and the remaining 15 with intramedullary nails combined with one or two plates. There was no significant difference in the type of fixation between the two groups. Of the ten grafts fixed with plates, all the medullary canals except one were filled with vancomycin-impregnated polymethylmethacrylate (Fig. 1). Autologous iliac bone grafting was performed at bone junctions in all patients. Every patient, except the two with chondrosarcoma, received neoadjuvant and adjuvant chemotherapy.

Patients received antibiotics intravenously peri- and postoperatively, usually for five days. After operation those patients who had undergone a femoral reconstruction used crutches with partial weight-bearing initially until the graft had united and the limb was considered to be stable. In tibial reconstruction, the lower limb was immobilised in a cast, usually for eight weeks. When radiological healing was present at the site of the osteotomy, unassisted walking with full weight-bearing was allowed. In the humeral reconstruction, the upper limb was supported by a sling post-operatively. Passive movements were started after the operation. Objects more than 2 kg were not lifted until there was radiological union at the osteotomy site.

The patients were followed up every six weeks to evaluate the healing of the osteotomy, functional recovery, and potential complications until union, and then every three months thereafter. The site of the osteotomy was considered to be healed radiologically if callus was seen bridging the site in both the anteroposterior and lateral planes. Non-union was defined as failure of union one year after operation.

Statistical analysis. This was performed using the chi-squared test with p < 0.05 considered to be statistically significant.

Results
At a mean follow-up of 71 months (24 to 132), 20 (69%) of the patients were free from disease, five (17%) had died and four (14%) were alive with pulmonary metastases. Two, one with an allograft and one with an irradiated autograft, had local recurrence, and underwent subsequent amputation. Three (20%) of the 15 extracorporeally-irradiated autografts fractured at seven, 16, and 22 months, respectively, after implantation. All of these patients were successfully treated by immobilisation in a cast (Fig. 2). There were two fractures (14%) in the 14 segmental allografts which occurred at 36 and 83 months after implantation, respectively. Both were successfully treated by fixation using a plate and an autogenous graft from the iliac crest. Compared with the segmental allografts, extracorporeally-irra-

Figures 1a and 1b – Radiograph and MR scan of a 38-year-old man with a chondrosarcoma involving the proximal humerus. Figure 1c – Radiograph 49 months after reconstruction with extracorporeally-irradiated autograft showing healing of the sites of the osteotomy. The irradiated bone was filled with vancomycin-impregnated polymethylmethacrylate.
Dilated autografts had a higher fracture rate which was not statistically significant (20% vs 14%; p = 0.535).

Overall, there were seven cases of nonunion of the host-graft junction with a rate of nonunion of 24%. In six of the seven patients, there was associated breakage of an implant. The sites of nonunion were classified as proximal in four cases, distal in two, or both proximal and distal in one. The rate of nonunion was significantly higher (p = 0.031) in patients who had received a segmental allograft (6 of 14, 43%) compared with those who had an extracorporeally-irradiated autograft (1 of 15, 7%). Six (32%) of the 19 grafts which had been fixed with intramedullary nails...
went on to nonunion, but only one of the ten grafts (10%) fixed with plates had this complication (p = 0.206). An assessment as to whether nonunion occurred with greater frequency when the junction was diaphyseal-diaphyseal, metaphyseal-diaphyseal, or metaphyseal-metaphyseal did not show a significant difference. After additional plating or replacement of the broken nails and autogenous bone grafting, all nonunions healed uneventfully. None of the segmental allografts or irradiated autografts was removed. Furthermore, no patient had a wound infection. Using the Enneking functional evaluation system,14 the mean post-operative score for the patients without a local recurrence was 87% (80% to 96%) and was similar in both groups.

Discussion

When deciding which reconstructive procedure is the best after intercalary resection of a tumour, the surgeon must consider the applicability of the procedure, the level of difficulty, the patient’s age and functional demands, and the morbidity and incidence of complications.3 Durability of the reconstructive procedure is another important consideration. At present, we are able to choose from a variety of methods of reconstruction, including segmental allografts, metal implants, vascularised fibular grafts, autoclaved autograft, and distraction osteogenesis.3,4,15-19 Segmental allografts have a generally good reputation because they are easy to insert and are able to survive for a long period,3,8,9,20,21 whereas metal implants, vascularised fibular grafts, and distraction osteogenesis are associated with some problems. Implantation of a metal device is relatively easy but its long-term survival is still of great concern, and this limits its acceptance.18 Vascularised fibular grafts are associated with considerable donor-site morbidity and they may fail if the vascular anastomosis is unsuccessful. Distraction osteogenesis could provide bone which will develop sufficient biomechanical strength and durability, but the procedure is relatively time-consuming and demanding.19

Massive bone allografting has become a common reconstructive procedure in recent years. One of the supposed advantages of allografts over synthetic bone substitutes is that they are progressively incorporated by the host. However, it is apparent that patients undergoing massive allograft reconstruction face a high rate of complications.4,8,20,22 In most series the best results were from intercalary allografts because of the absence of joint problems such as laxity, degenerative changes, and pain.20,21,23 However, unless a large stock of bank allograft is available, it may be difficult to find a donor specimen which adequately matches the size and shape of the resected bone. Because the concept of bone donation is not widely accepted, physically treated (autoclaved or irradiated) autogenous bone graft is commonly used in Asian countries as an alternative to allograft.24 The advantages of autoclaved or irradiated autograft for large defects are ease of procurement, absence of the problems which are associated with storage and obtaining grafts of suitable dimensions, ensured sterility, and probable avoidance of an immunological response.10,16,24 To the best of our knowledge, no reports have specifically addressed a comparison of the complications and functional outcome associated with the use of segmental allografts and extracorporeally-irradiated autografts after intercalary resection of malignant bone tumours.

Based on our past experience13,25 and the original report of Uyttendaele et al,10 the resected specimen was irradiated with a dosage of 30,000 rads. In our series, there was only one local recurrence in each group. We are optimistic about the anti-tumour effect of the extracorporeal irradiation with 30,000 rads. Ueda et al26 also reported no local recurrence in ten patients who received extracorporeal irradiation with 5000 rads for malignant tumours in the upper limbs. The optimal dose of irradiation will need to be determined by further research.

Oncological assessment is difficult because of the variety and limited number of our cases. However, the rate of survival for the 23 cases of high-grade osteosarcoma is comparable with that of any other reconstructive technique.4,13-19 In addition, there was no significant difference between allograft and irradiated autograft reconstruction.

Nonunion was the most frequent complication, occurring at eight sites in seven patients. Reconstruction with extracorporeally-irradiated autograft has a lower rate of nonunion (7% vs 43%). Perfect anatomical reduction of the irradiated autograft may be the most important factor in promoting healing of the junction. It is relatively difficult to obtain perfect cortical apposition between the allograft and host cortices at the junctions because of their difference in size. In addition, six of the seven cases of nonunion occurred in the grafts which were fixed with intramedullary rods and only one in the grafts fixed with plates. This may be because of biological variation in the size of the medullary canal and curvature which create offsets with intramedullary fixation that are more easily treated by a plate and screws. However, this number is clearly too small for comment.

Overall, there were only five (17%) fractures of the grafts in our series, three of which occurred in the extracorporeally-irradiated autografts and two in the segmental allografts. The irradiated autograft which had cortical destruction by the tumour may have carried a higher risk of fracture. Surprisingly, all three fractured and irradiated autografts healed well after immobilisation in a cast. The irradiated autograft may have regained the ability to heal and to remodel after conservative treatment. Furthermore, all of the five fractures occurred in the grafts without intramedullary polymethylmethacrylate augmentation. The use of cement seemed to reduce the rate of fracture. However, no conclusions can be reached on the basis of this small clinical series and short-term follow-up.

In our series, a rate of nonunion of 24%, of fracture of 17%, and of infection of 0% compared favourably with
those of previous reports of intercalary reconstruction with an allograft. 2,3,27 The use of extracorporeally-irradiated autografts has a lower rate of nonunion. On the basis of our data, we conclude that intercalary allograft transplantation or extracorporeally-irradiated autograft can provide a satisfactory solution to large skeletal defects created by wide intercalary excisions. With careful selection of the patients and proper augmentation of the irradiated autograft, the use of extracorporeally-irradiated autograft could be an acceptable method of reconstruction after intercalary resection, especially in countries where it is difficult to obtain allografts.

No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article.

References