Treatment of malignant bone tumours by extracorporeally irradiated autograft-prosthetic composite arthroplasty

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Autogenous bone graft which has been either autoclaved or irradiated is commonly used in oriental countries as an alternative to allograft. We started to use the technique of extracorporeal irradiation of the resected specimen and reimplantation (ECIR) in 1991. There was, however, a high incidence of fracture of the irradiated bone and loss of articular cartilage. In an attempt to reduce these complications, we combined the irradiated autograft with a conventional arthroplasty. Between 1995 and 1998, 14 patients underwent limb salvage by this method. Seven had an osteosarcoma, two bony metastases, three a chondrosarcoma, one a malignant fibrous histiocytoma, and one a leiomyosarcoma. Ten tumours were located in the proximal femur, two in the proximal humerus, and two in the distal femur.

One patient who had a solitary metastasis in the proximal part of the left femur died from lung metastases 13 months after operation. The remaining 13 patients were alive and without evidence of local recurrence or distant metastases at a mean follow-up of 43 months (28 to 72). Postoperative palsy of the sciatic nerve occurred in one patient, but no complications such as wound infection, fracture, or nonunion were seen. All host-irradiated bone junctions healed uneventfully within eight months. Using the Enneking functional evaluation system, the mean postoperative score for all 14 patients was 80% (57 to 93).

The use of irradiated autograft prosthesis composites reduces the complications of ECIR and gives good

functional results. It may be a good alternative in limb-salvage surgery, especially in countries where it is difficult to obtain allografts.

J Bone Joint Surg [Br] 2002; 84-B:1156-61.

Submitted: 1 June 2002; Accepted: 26 July 2002

Wide local excision is an accepted alternative to amputation in the management of malignant bone tumours. If a limb-salvage procedure is indicated oncologically, some consideration must be given to the type of reconstructive procedure to be chosen. The applicability of the technique, the level of surgical complexity, the age and functional demands of the patient, the morbidity, the incidence of complications and the durability of the procedure must be considered.¹ Currently, we are able to choose from a variety of methods of reconstruction, including osteoarticular allografts, intercalary allografts, allograft-prosthetic composites, arthrodesis with autogenous or allogenic bone, custom-made prostheses, and rotationplasty.²⁻¹¹ Prosthetic reconstruction has many advantages, particularly with regard to maintaining mobility and the early restoration of function. In a review of 1001 custom-made cemented prostheses implanted at a single institution, the results varied according to the anatomical site of the implant.² The survival rate of the implant at ten years was 93.8% for a proximal femoral replacement, 67.4% for a distal femoral prosthesis, and 58% for a proximal tibial prosthesis. Survival of the implant in 82 patients treated at another institution was similar, with overall rates of 83% at five years and 67% at ten years.⁷ Although the results have been satisfactory, the long-term survival of the implant is still of some concern, and this limits its acceptance. Allografts are used at many oncological centres, but are not always available. The complication and failure rates are still high using this method, the major problems being infection, fracture, nonunion, and loss of articular cartilage.^{8,10} With advances in patient selection, allograft banking, and surgical technique, the outcome after biological replacement should improve.

Before 1993, modular replacement prostheses were not available in Taiwan and the supply of allografts was limited. Thus, since 1991, we have used an alternative technique, namely resection of the tumour, extracorporeal irradiation and re-implantation of the resected bone

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0301-620X/02/813508 \$2.00

Table I. Details of the 14 patients with malignant bone tumours treated by extracorporeally irradiated autograft-prosthetic composite arthroplasty

Case	Gender	Age (yrs)	Diagnosis	Surgical stage*	Site	Autograft at junction	Follow-up (mths)	Mean time to union (wks)	Mean Enneking ¹³ function score (%)
1	F	21	Leiomyosarcoma	II B	Proximal femur	No	72	18	90
2	F	63	Chondrosarcoma	I A	Proximal femur	No	63	18	77
3	M	70	Malignant fibrous histiocytoma	II B	Proximal femur	Yes	59	24	70
4	M	67	Chondrosarcoma	II B	Proximal femur	No	53	24	77
5	F	18	Osteosarcoma	II B	Proximal humerus	No	47	12	80
6	M	71	Solitary metastatic adenocarcinoma of unknown origin	-	Proximal femur	No	43	24	90
7	M	61	Chondrosarcoma	II B	Proximal femur	No	40	18	80
8	F	25	Osteosarcoma	II B	Proximal femur and acetabulum	No	35	24	67
9	M	17	Osteosarcoma	II B	Proximal femur	No	31	18	73
10	M	17	Osteosarcoma	II B	Proximal humerus	No	30	18	90
11	F	17	Osteosarcoma	II B	Proximal femur	No	29	18	90
12	M	18	Osteosarcoma	II B	Distal femur	Yes	29	18	90
13	M	16	Osteosarcoma	II B	Distal femur	Yes	28	12	93
14	M	51	Solitary metastasis from adrenal cortex carcinoma	-	Proximal femur	No	13	32	57

*Musculoskeletal Tumor Society system

(ECIR). This procedure was first described by Uyttendaele et al¹² in 1988. It has several theoretical advantages, including the preservation of the range of movement of a joint, restoration of the normal mass of bone, and avoidance of early and late loosening and breakage of a massive prosthesis. In our initial series, however, there were five fractures of the irradiated bones (26.3%), four cases of loss of articular cartilage (21.1%), two of nonunion at the site of the osteotomy (10.5%), and two wound infections (10.5%) in a total of 19 osteoarticular ECIRs at a mean follow-up of 25 months (12 to 49). In an attempt to reduce these complications, we have combined the irradiated autograft with a conventional arthroplasty.

We now assess the clinical results of extracorporeally-irradiated autograft-prosthetic composite arthroplasty.

Patients and Methods

Malignant bone tumours, including primary sarcomas or solitary bony metastases, without extensive associated destruction of bone, pathological fracture, or major neurovascular involvement may be treated by this technique. In order to avoid future leg-length discrepancy we excluded patients younger than 15 years. Between April 1995 and December 1998, 14 patients underwent limb salvage by this method (Table I). There were nine men and five women with a mean age of 37.9 years (16 to 71). There were seven cases of osteosarcoma, two of bony metastases, three of chondrosarcoma, one of malignant fibrous histiocytoma, and one of leiomyosarcoma. Ten lesions involved the proximal femur, two the proximal humerus, and two the distal femur. One osteosarcoma involved the acetabulum and the proximal femur (case 8).

Seven patients with osteosarcoma had neoadjuvant chemotherapy consisting of cisplatin, doxorubicin, and ifosfamide. All patients, except the three with chondrosarcoma, received postoperative chemotherapy. Wide local excision was carefully undertaken in order to ensure removal of an intact cuff of normal tissue surrounding the lesion. The bone containing the lesion was divided at least 2 cm above the furthest evidence of involvement, as seen on MRI. The excised specimen, including the tumour-bearing bone and its surrounding tissues, was irradiated with a dose of 300 Gy using a linear accelerator.⁶ 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 and ligaments, were removed. Preparation of the irradiated autograft was carried out away from the operating table, and the prostheses were inserted in the usual manner. The prosthetic stem was secured within the medullary canal of the irradiated bone with vancomycin-impregnated polymethylmethacrylate. The assembled autograft and prosthesis were then fixed to the host bone by dynamic compression plates or cable plates. The canal of the host bone was left without cement. In six of the ten patients who underwent proximal femoral resection, a 25.4 cm extensively porous-coated prosthesis (DePuy, Warsaw, Indiana) was used. The distal host bone was fixed securely to the porous-coated stem by a 0.5 mm under-reaming technique without using supplementary plates. In the two patients who underwent distal femoral reconstruction, stripped autogenous bone grafts prepared from the removed tibial articular surface were placed at the irradiated autograft-host bone junction and secured by mersilene tapes. In the remaining 12 patients, additional autogenous bone graft was not routinely used. The patient who had involvement of both the acetabu-

Fig. 1a

Fig. 1b

Case 8. Radiograph and MR scan (a) of a 25-year-old woman with an osteosarcoma involving both the proximal femur and acetabulum and a radiograph 35 months after surgery showing healing of the site of the osteotomy and no evidence of loosening of the prosthesis (b).

lum and proximal femur (case 8) had a wide excision of the acetabulum through the superior and inferior pubic rami. It was irradiated along with the proximal femur, reconstructed by plates and screws, and replaced with a cemented cup (Fig. 1).

Once the joint had been reconstructed, the soft tissues were attached to the irradiated bone in order to enhance stability and allow early functional recovery. In reconstruction of the hip, the tendons of gluteus medius and minimus were sutured to the corresponding tendons on the greater trochanter. The repair was secured by non-absorbable mersilene tapes through drill holes in the trochanter. The origin of the tendon of vastus lateralis was also repaired, creating a strong lateral buttress. Postoperatively, patients used crutches for six weeks, initially with partial weight-bearing, but without active abductor exercises. Weight-bearing was thereafter increased and active abductor exercises were undertaken. When there was radiological healing at the site of the osteotomy, unassisted full weight-bearing was allowed.

In two patients (cases 12 and 13) an all-cemented constrained condylar knee prosthesis (Zimmer, Warsaw, Indiana) was used for reconstruction of the knee (Fig. 2). Range of movement and muscle-strengthening exercises were encouraged immediately after surgery. Partial weight-bearing was started on the fifth to seventh postoperative day. Unrestricted full weight-bearing was not allowed until the site of the femoral osteotomy had healed.

In reconstruction of the shoulder (cases 5 and 10), the rotator cuff and capsule were sutured to the remaining tendons on the proximal humerus using non-absorbable sutures (Fig. 3). The long head of the biceps was sutured to coracobrachialis and the short head of the biceps, which were then secured to the coracoid process with a non-absorbable suture passed through a drill hole. The muscles, including the del-

toid and pectoralis major, were then repaired to cover the composite. Postoperatively, the upper limb was supported by a sling. Passive range of movement was started immediately after surgery. Isometric exercises and active movement were begun at four weeks. Normal daily activities were encouraged, but objects weighing more than 4.5 kg were not lifted until there was radiological union of the site of the osteotomy.

The patients were followed up every six weeks to evaluate the healing of the site of the osteotomy, functional recovery, and potential complications until union of the osteotomy and every three months thereafter. The osteotomy was considered to be healed radiologically when callus bridged the site in both the anteroposterior and lateral planes.

Results

One patient (case 14), who had a solitary deposit in the proximal femur, died from lung metastases 13 months after operation. The remaining 13 patients were alive without evidence of local recurrence or distant metastases at a mean follow-up of 43 months (28 to 72). Damage to the sciatic nerve occurred in the patient who had an osteosarcoma involving both the femur and acetabulum (case 8). She was treated by physiotherapy and was able to walk without a splint one year later, but evidence of nerve palsy was still evident at follow-up at 35 months. There were no other complications such as wound infection, fracture, dislocation, nonunion, or prosthetic loosening in the remaining patients. To date, no patient has required further surgery. All host-irradiated bone junctions healed uneventfully within eight months. The mean time to union of the site of the osteotomy was 20 weeks (12 to 32). Using the functional evaluation system of Enneking et al,¹³ the mean postoperative score was 80% (57 to 93).

Fig. 2a

Fig. 2b

Case 13. Radiographs and MR scan (a) of a 16-year-old male with an osteosarcoma involving the distal femur and radiographs five months after surgery showing good healing of the site of the osteotomy (b).

Discussion

Since the concept of bone donation is not widely accepted in Asian countries, autogenous bone graft which has been autoclaved or irradiated is commonly used as an alternative to allograft.¹⁴ In our previous series, there was only one local recurrence in 13 stage-IIB osteosarcomas treated by ECIR at a mean follow-up of 42 months, but the rate of complications was high at 62%.³ The results were similar to those in another of our studies of 19 malignant bone tumours treated by osteoarticular ECIR. Based on this experience, we consider that irradiation with 300 Gy will achieve local control of malignant bone tumours. The rate of complications, however, is high. Since April 1995, in order to reduce this, we began to use extracorporeally-irradiated autograft-prosthetic composite arthroplasty. The results and incidence of complications in this series are satisfactory and encouraging.

No local recurrence was noted radiologically or clinically in any patient. We are optimistic about the antitumour effect of extracorporeal irradiation of 300 Gy. Ueda et al¹⁵ also reported no local recurrence in ten patients who received 50 Gy ECIR for malignant tumours in the upper limb. The optimal dose of irradiation will need to be determined by further studies.

Oncological assessment is difficult because of the variety and small number of our tumours. The high rate of survival for the seven patients with osteosarcoma is encouraging. The relatively older age of the patients and aggressive chemotherapy may be responsible for the good short-term results.

Nonunion of the junction between the allograft and the host bone was reported in 17% of 718 allograft reconstructions.⁸ Springfield¹⁰ reported that healing at this junction took between six and 12 months. In another study, the mean time required for radiological union at the allograft host bone junction was 14 months.¹⁶ As for autoclaved autogenous grafts, Harrington et al¹⁷ found that 37 of 42 patients had evidence of union within two years of the reconstruction. They observed that the revascularisation of these grafts occurred much more slowly when compared with conventional autogenous grafts or allografts. This may be because autoclaved bone is more resistant to capillary invasion.^{17,18} All patients in our series showed evidence of union within eight months of the reconstruction. The rate of union and the time to union compared favourably with those reported for allografts or autoclaved autogenous grafts used for reconstruction after the resection of tumours. Perfect anatomical reduction and the rigid fixation afforded by the long stem of the prosthesis and plates may be the most important factors in promoting healing of the junction. In addition, all of the six in whom a 25.4 cm extensively porous-coated femoral stem had been used, achieved satisfactory union at the junction without supplementary plate fixation. The under-reaming technique gives reliable fixation at the junction. With these excellent results, we plan to continue using this type of prosthesis.

Fatigue fractures, which are common in the allograft and irradiated osteoarticular autograft groups,^{3,8,19,20} did not occur. Good intramedullary fixation which is afforded by the stem of the prosthesis and bone cement may protect the graft from the repeated stresses which contribute to fatigue fracture.

Fig. 3a

Fig. 3b

Case 10. Radiograph and MR scan (a) of a 17-year-old male with an osteosarcoma involving the proximal humerus and radiographs three months after surgery showing good healing of the site of the osteotomy (b).

The most serious complication is infection. Great care must be taken to avoid contaminating the operative field and the resected bone during the whole procedure. We believe that the absence of infection in this series was due primarily to routinely impregnating the cement with vancomycin and providing adequate cover of the irradiated bone and prosthesis with muscle.

The implants combined with irradiated autograft provide additional stability which is not present in an osteoarticular irradiated autograft or an osteoarticular allograft arthroplasty, in which stability of the reconstructed joint is of great concern.²¹ In addition, by replacing the joint with an implant, degeneration of cartilage is not a problem. The technique restores bone stock, which may allow for further surgery such as revision arthroplasty. Even if the reconstruction fails, we can still use a custom prosthesis or an allograft-prosthetic composite to replace it. Furthermore, although it is reported that irradiation reduced the mechanical strength of bone,^{22,23} adequate strength should be provided by using cement and a prosthesis.

Irradiated autograft prosthesis composites have therefore been shown to achieve predictable healing at the site of the osteotomy, reduce the complications of ECIR, and give good functional results. The results compare favourably with other more conventional reconstructive procedures and the technique has several potential long-term advantages. It could be an acceptable alternative in limb-salvage surgery, 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

1. Sim FH, Beauchamp CP, Chao EYS. Reconstruction of musculoskeletal defects about the knee for tumour. *Clin Orthop* 1987;221:188-201.
2. Cannon SR. Massive prostheses for malignant bone tumours of the limbs: Instructional Course Lecture. *J Bone Joint Surg [Br]* 1997;79-B:497-506.
3. Chen WM, Chen TH, Huang CK, Lin CF, Shih LY, Lo WH. Treatment of high-grade primary osteosarcoma in extremities: 15-year clinical experience in VGH – Taipei. *J Orthop Surg ROC* 2000;17:11-6.
4. Gitelis S, Piasecki P. Allograft prosthetic composite arthroplasty for osteosarcoma and other aggressive bone tumours. *Clin Orthop* 1991;270:197-201.
5. Hejna MJ, Gitelis S. Allograft prosthetic composite replacement for bone tumors. *Semin Surg Oncol* 1997;13:18-24.
6. Kneisl JS, Finn HA, Simon MA. Mobile knee reconstructions after resection of malignant tumours of the distal femur. *Orthop Clin North Am* 1991;22:105-19.
7. Malawer MM, Chou LB. Prosthetic survival and clinical results with use of large-segment replacements in the treatment of high-grade bone sarcomas. *J Bone Joint Surg [Am]* 1995;77-A:1154-65.
8. Mankin HJ, Gebhardt MC, Jennings LC, Springfield DS, Tomford WW. Long-term results of allograft replacement in the management of bone tumours. *Clin Orthop* 1996;324:86-97.
9. Scarborough MT, Helmstedter CS. Arthrodesis after resection of bone tumors. *Semin Surg Oncol* 1997;13:25-33.
10. Springfield DS. Allograft reconstructions. *Semin Surg Oncol* 1997;13:11-7.
11. Tillman RM, Grimer RJ, Carter SR, Cool WP, Sneath RS. Growing endoprosthesis for primary malignant bone tumors. *Semin Surg Oncol* 1997;13:41-8.
12. Uyttendaele D, De Schryver A, Claessens H, et al. Limb conservation in primary bone tumours by resection, extracorporeal irradiation and re-implantation. *J Bone Joint Surg [Br]* 1988;70-B:348-53.

13. **Enneking WF, Dunham W, Gebhardt MC, Malawar M, Pritchard DJ.** A system for the functional evaluation of reconstructive procedures after surgical treatment of tumours of the musculoskeletal system. *Clin Orthop* 1993;286:241-6.
14. **Kang YK, Kim JM Rhee SK, et al.** Allograft versus autoclaved autograft in the treatment of malignant bone tumors. Presented at the 10th International Symposium of International Society of Limb Salvage, Cairns, Australia, April 1999.
15. **Ueda T, Araki N, Uchida A, et al.** Intra-operative extracorporeal radiated bone grafts for reconstruction of bone defect after tumor resection in upper extremities. Presented at the 9th International Symposium of International Society of Limb Salvage, New York, September 1997.
16. **Makely JT.** The use of allografts to reconstruct intercalary defects of long bones. *Clin Orthop* 1985;197:58-75.
17. **Harrington KD, Johnston JO, Kaufer HN, Luck JV Jr, Moore TM.** Limb salvage and prosthetic joint reconstruction for low-grade and selected high-grade sarcomas of bone after wide resection and replacement by autoclaved autogeneic grafts. *Clin Orthop* 1986;211:180-214.
18. **Johnston JO, Harries TJ, Alexander CE, Alexander AH.** Limb salvage procedure for neoplasms about the knee by spherocentric total knee arthroplasty and autogenous autoclaved bone grafting. *Clin Orthop* 1983;181:137-45.
19. **Alman BA, De Bari A, Krajchich JL.** Massive allografts in the treatment of osteosarcoma and Ewing sarcoma in children and adolescents. *J Bone Joint Surg [Am]* 1995;77-A:54-64.
20. **Weiner SD, Scarborough M, Vander Griend RA.** Resection arthrodesis of the knee with an intercalary allograft. *J Bone Joint Surg [Am]* 1996;78-A:185-92.
21. **Araki N, Myoui A, Kuratsu S, et al.** Intraoperative extracorporeal autogenous irradiated bone grafts in tumor surgery. *Clin Orthop* 1999;368:196-206.
22. **Hamer AJ, Strachan JR, Black MM, et al.** Biomechanical properties of cortical allograft bone using a new method of bone strength measurement: a comparison of fresh, fresh-frozen and irradiated bone. *J Bone Joint Surg [Br]* 1996;78-B:363-8.
23. **Currey JD, Foreman J, Laketic I, et al.** Effects of ionizing radiation on the mechanical properties of human bone. *J Orthop Res* 1997;15:111-7.