En-bloc resection, extracorporeal irradiation, and re-implantation in limb salvage for bony malignancies

A. W. Davidson,
A. Hong,
S. W. McCarthy,
P. D. Stalley

From The New South
Wales Bone and Soft
Tissue Sarcoma
Service, The Royal
Prince Alfred
Hospital, Sydney,
Australia

We treated 50 patients with bony malignancy by *en-bloc* resection, extracorporeal irradiation with 50 Gy and re-implantation of the bone segment.

The mean survivor follow-up was 38 months (12 to 92) when 42 patients were alive and without disease. There were four recurrences. The functional results were good according to the Mankin score (17 excellent, 13 good, nine fair, three failures), the Musculoskeletal Tumour Society score (mean 77) and the Toronto Extremity Salvage score (mean 81). There was solid union, but bone resorption was seen in some cases. The dose of radiation was lethal to all cells and produced a dead autograft of perfect fit.

Extracorporeal irradiation is a useful technique for limb salvage when there is reasonable residual bone stock. It allows effective re-attachment of tendons and produces a lasting biological reconstruction. There should be no risk of local recurrence or of radiotherapy-induced malignancy in the replanted bone.

Intra-operative extracorporeal irradiation and re-implantation of the bone segment was first reported by Spira and Lubin¹ in two patients as a method of limb salvage for bone sarcoma. The dose of radiation is lethal and produces a dead autogenous bone graft of the correct dimensions for re-implantation and reconstruction. There should be no risk of local recurrence and radiotherapy-induced malignancy.² Extracorporeal irradiation was introduced to Australia at our institution in 1996.² We now report the results and complications in our first 50 patients.

Patients and Methods

Fifty patients with bone malignancy were reviewed, in whom after *en-bloc* resection, reconstruction had been undertaken by re-implanting the extracorporeal irradiation bone segment. There were 21 pelvic, 17 femoral, 11 humeral and one tibial lesion. These included 21 Ewing's sarcomas, 16 osteosarcomas,^{3,4} 11 chondrosarcomas, one metastatic osteosarcoma and one metastatic melanoma.

All the patients with Ewing's sarcoma and osteosarcoma had chemotherapy. In three patients with pelvic lesions post-operative radiotherapy was given because of intralesional resection (case 4) marginal resection (case 43) and contaminated margins (case 48).

There were 23 men and 27 women with a mean age at presentation of 23 years (3 to 66) and at review of 25 years (6 to 68).

Of the 50 patients eight were either dead or dying. One (case 32) was oncologically clear but had undergone an amputation. She refused to attend and was interviewed by telephone. The remaining 41 were reviewed clinically and radiologically, using the Musculoskeletal Tumour Society score (MTSS),⁵ the Toronto extremity salvage score (TESS)^{6,7} and the score of Mankin et al.⁸

Operative technique. After *en-bloc* resection, the segment is wrapped in a wet sterile drape to minimise air gaps, placed in two sealed sterile plastic bags and wrapped in another sterile drape. This is delivered for radiotherapy. Meanwhile, the operative site is prepared for re-implantation and marginal biopsies taken. On return the specimen is removed from the inner plastic bag and soaked in iodine solution. It is cleared of unnecessary soft tissue leaving important muscle insertions for re-attachment and then re-implanted.

Extracorporeal irradiation. Thirty-two segments were irradiated with 4 to 6 MV photons from a linear accelerator.^{2,9} They were surrounded by water-equivalent materials and irradiated isocentrically with parallel opposed fields. All segments had a single midplane dose of 50 Gy at a rate of 1.8 to 2.0 Gy per minute. The mean time between the bone segment and returning it to the operating room was 35 minutes.

■ A. W. Davidson, FRCSEd (Tr & Orth), Orthopaedic Oncology Fellow
■ A. Hong, MMed, PhD, Consultant Radiation Oncologist
■ S. W. McCarthy, FRCPA, Consultant Pathologist
■ P. D. Stalley, FRACS, Consultant Orthopaedic Oncologist
The New South Wales Bone and Soft Tissue Sarcoma Service, The Royal Prince Alfred Hospital, Missenden Road, Camperdown, Sydney, New South Wales 2050, Australia.

Correspondence should be sent to Mr A. W. Davidson at 94 Barons Court Road, Fulham, London W14 9DX, UK; e-mail: alastair_davidson@hotmail.com

©2005 British Editorial Society of Bone and Joint Surgery
doi:10.1302/0301-620X.87B6.15950 \$2.00

J Bone Joint Surg [Br]
2005;87-B:851-7.

Received 27 August 2004;
Accepted after revision
14 December 2004

Fig. 1

Radiograph showing pelvic reconstruction with the extracorporeal irradiation-THR composite.

Fig. 2

Radiograph showing pelvic extracorporeal irradiation reconstruction with preservation of the immature femoral head.

Eighteen bone segments measuring less than 19 cm in length and 12 cm in thickness were inserted into a cylindrical canister and irradiated in a blood product irradiator (Gammacell 3000 Elan, Nordion, Ontario, Canada).¹⁰ Each segment was placed in the centre of the canister and water-equivalent material used to fill the remaining space. The dose rate was 4.5 Gy per minute and the mean time from collection to return 20 minutes.

Pelvic reconstruction (21 cases). Total hip replacement (THR) was indicated in 13 skeletally mature patients in whom resection included the acetabulum (Fig. 1).¹¹ A support ring with a cemented polyethylene acetabular cup and an S-

Fig. 3

Radiograph showing femoral extracorporeal irradiation reconstruction.

ROM femoral stem (DePuy, Warsaw, Indiana) with a 28 mm metal head were used after re-implantation and fixation of the pelvis. In four skeletally immature patients, the femoral head was returned to the acetabulum to preserve the natural joint and proximal femoral growth plate (Fig. 2).

Femoral reconstruction (17 cases). Intercalary resection was performed when possible with stabilisation of the extracorporeal irradiation graft by a nail or plate. Eleven of 14 such patients had a vascularised fibular graft. This was added to the extracorporeal irradiation graft either in parallel (Fig. 3) or into a trench (Figs 4 and 5). In two patients in whom the proximal femur had been resected and the abductors preserved, the limb was reconstructed by an extracorporeal irradiation graft and S-ROM THR composite, attaching the abductors to their tendon stumps and stabilising the distal osteotomy by a plate (Fig. 6).

Tibial reconstruction (One case). In one patient (case 2) a diaphyseal chondrosarcoma was treated by intercalary

Fig. 4

Photograph showing femoral extracorporeal irradiation graft with a trench cut for a vascularised fibular graft.

Fig. 6

Radiograph showing proximal femoral reconstruction with the extracorporeal irradiation-THR composite.

Fig. 5

Radiograph showing femoral extracorporeal irradiation reconstruction with a vascularised fibular graft.

Fig. 7

Radiograph showing tibial extracorporeal irradiation reconstruction with a vascularised fibular graft.

Fig. 8

Photograph showing a humeral extracorporeal irradiation graft.

Fig. 9

Radiograph showing a humeral reconstruction with an extracorporeal irradiation-Bigliani shoulder composite.

Fig. 10

Radiograph showing dissolution of the humeral extracorporeal irradiation graft.

humeral head was replaced by a cemented long-stem Bigliani prosthesis (Fig. 9) before re-implantation of the graft-prosthesis composite. This was because in the first two cases (8 and 10) there was dissolution of the humeral head (Fig. 10). The eight proximal humeral cases thereafter had reconstruction by an extracorporeal irradiation graft-prosthesis composite. In one further case an intercalary resection/reconstruction with an extracorporeal irradiation-vascularised fibular graft composite was performed.

Results

The mean survivor follow-up was 38 months (12 to 92), measured from the date of surgery. The results are summarised in Table I which includes the significant incidence

resection, ECI and re-implantation, combined with a vascularised fibular graft and stabilised by a plate (Fig. 7).

Humeral reconstruction (11 cases). When *en-bloc* resection of the proximal humerus was performed (Fig. 8) the

Table I. Details and results in the 50 patients

Case	Age at onset (yrs)	Bone	Resection + reconstruction	Diagnosis	Survival (mths)	Mankin score	MTSS* score	TESS† score	Complications‡	Re-operations
1	6	Pelvic	P1, 2	Ewing's sarcoma	92	Excellent	97	90		
2	37	Tibia	Intercalary	Chondrosarcoma	87	Excellent	93	98	DVT	
3	13	Femur	Intercalary	Ewing's sarcoma	84	Excellent	93	100	Femoral nail breakage	Revision femoral nail
4	34	Pelvis	S, P1	Ewing's sarcoma	Dead					
5	16	Femur	Intercalary	Ewing's sarcoma	69	Good	80	71	FHL contracture Tibial shaft fracture	Tibial nail
6	14	Femur	Intercalary	Osteosarcoma	67	Excellent	100	96		
7	17	Femur	THR	Ewing's sarcoma	65	Fair	50	67	Nonunion	Graft + plating of nonunion
8	3	Humerus	Proximal	Osteosarcoma	64	Failure	67	89	Complete graft resorption	
9	12	Femur	Intercalary	Ewing's sarcoma	59	Excellent	90	93	Nonunion	Removal of distal locking screws Graft + plating of nonunion
10	14	Humerus	Proximal	Osteosarcoma	60	Fair	67	83	AVN humeral head	
11	29	Femur	Intercalary	Osteosarcoma	58	Excellent	97	92	Nonunion	Removal of distal locking screws
12	21	Pelvis	S, P1	Ewing's sarcoma	53	Good	67	88	Wound infection Minor osteolysis at iliac crest under plate	
13	13	Pelvis	P2, 3	Ewing's sarcoma	52	Excellent	97	95	Osteolysis at pubic symphysis	
14	10	Pelvis	P1, 2	Ewing's sarcoma	50	Fair	60	69	4 cm leg-length discrepancy	
15	15	Pelvis	P1, 2	Ewing's sarcoma	Dead					
16	46	Pelvis	P2, 3	Chondrosarcoma	Dead					
17	39	Pelvis	P2	Chondrosarcoma	46	Fair	50	76	Sciatic nerve palsy	
18	11	pelvis	P1, 2	Ewing's sarcoma	47	Excellent	90	97	Wound infection Peri-acetabular osteolysis	
19	9	Femur	Intercalary	Osteosarcoma	44	Excellent	97	98		
20	15	Humerus	Proximal	Osteosarcoma	Dead					
21	12	Femur	Intercalary	Osteosarcoma	42	Excellent	93	93		Epiphysiodesis
22	56	Femur	Intercalary	Chondrosarcoma	36	Excellent	93	91		
23	16	Femur	Intercalary	Osteosarcoma	37	Excellent	100	96		
24	55	Pelvis	P2	Chondrosarcoma	Dead					
25	17	Femur	Intercalary	Ewing's sarcoma	33	Excellent	100	100	Nonunion	Graft + plating of nonunion
26	66	Pelvis	P1, 2	Chondrosarcoma	33	Good	73	82	IPR stress fracture	
27	14	Femur	Lateral femoral condyle	Osteosarcoma	33	Excellent	87	92	2 cm short + valgus deformity	Varus osteotomy
28	59	Pelvis	P1, 2, 3	Chondrosarcoma	32	Good	90	72		
29	21	Pelvis	P2, 3	Ewing's sarcoma	30	Fair	67	81	Acetabular osteolysis, nonunion and displacement	Revision of acetabular component planned
30	13	Pelvis	S, P1	Ewing's sarcoma	29	Excellent	86	87		
31	38	Humerus	Proximal	Osteosarcoma	27	Fair	63	48	Nonunion	Graft + plate
32	15	Humerus	Proximal	Osteosarcoma	26	Failure	Disarticulation		SRN paraesthesiae	
33	10	Femur	Intercalary	Osteosarcoma	27	Good	77	86	Nonunion Stress fracture	Graft + plate
34	18	Femur	Intercalary	Ewing's sarcoma	26	Excellent	93	94	Nonunion Failure of metalwork	Removal of distal locking screws Revision and fixation
35	17	Humerus	Intercalary	Chondrosarcoma	26	Good	97	99	Wound infection Asymptomatic nonunion	Wound debridement Graft planned
36	53	Pelvis	P2	Metastatic melanoma	24	Good	80	80	-	
37	37	Humerus	Proximal	Osteosarcoma	25	Fair	50	50		
38	17	Humerus	Proximal	Osteosarcoma	22	Good	73	85		
39	58	Pelvis	P1, 2, 3	Chondrosarcoma	21	Fair	20	40	Femoral A+V peri-operative thrombosis	Bypass grafting
40	28	Pelvis	S, P1, 2	Ewing's sarcoma	19	Good	93	74		
41	7	Humerus	Proximal	Ewing's sarcoma	20	Good	73	76	Shoulder instability	Shoulder stabilisation

* MTSS, Musculoskeletal Tumour Society score

† TESS, Toronto Extremity Salvage score

‡ DVT, deep-venous thrombosis; AVN, avascular necrosis; FHL, flexor hallucis longus; IPR, inferior pubic reamus; SRN, sensory radial nerve; A, artery; V, vein

Table I (cont). Details and results in the 50 patients

Case	Age at onset (yrs)	Bone	Resection + reconstruction	Diagnosis	Survival (mths)	Mankin score	MTSS* score	TESS† score	Complications‡	Re-operations
42	51	Humerus	Proximal	Ewing's sarcoma	18	Fair	67	62	Minor proximal osteolysis and erosion of glenoid	
43	13	Pelvis	S	Chondrosarcoma	Dying	Failure	Paraplegic		Post-operative drop foot	
44	21	Pelvis	P1, 2	Ewing's sarcoma	Dead					
45	8	Femur	Intercalary	Ewing's sarcoma	15	Failure	Unable to walk		Failure of fixation	Revision fixation + graft planned
46	28	Pelvis	P1, 2, 3	Metastatic osteosarcoma	Dying	Failure	Acetabulum		Failure of acetabular component	
47	15	Femur	THR	Chondrosarcoma	12	Excellent	93	98		
48	13	Femur	Intercalary	Osteosarcoma	12	Good	73	80		Epiphysiodesis
49	16	Pelvis	P2, 3	Ewing's sarcoma	12	Good	80	71		
50	5	Humerus	Proximal	Osteosarcoma	12	Good	70	81	Minor osteolysis of proximal humerus beneath prosthesis	

* MTSS, Musculoskeletal Tumour Society score

† TESS, Toronto Extremity Salvage score

‡ DVT, deep-venous thrombosis; AVN, avascular necrosis; FHL, flexor hallucis longus; IPR, inferior pubic reamus; SRN, sensory radial nerve; A, artery; V, vein

of problems and complications which are predictable in such a group of patients.

Of the 50 patients, 42 (84%) are free from disease and eight have died or are dying, of whom seven had high-grade pelvic malignancies. Local recurrence occurred in four patients. Two had differentiated acetabular chondrosarcoma and one a sacral mesenchymal chondrosarcoma (cases 16, 24 and 43). There was one soft-tissue recurrence in a proximal humeral osteosarcoma (case 32), which required disarticulation of the shoulder.

In the 41 disease-free survivors the outcome was generally good. There were 17 excellent, 13 good and nine fair results with two failures according to the Mankin score. The mean values of the MTSS and TESS were 77 (20 to 100) and 81 (40 to 100), respectively.

Most patients had solid bony union, but there was considerable osteolysis in several cases, especially humeral cases 8 and 10. Other examples of osteolysis are described in Table I.

Discussion

Extracorporeal irradiation and re-implantation is a useful, convenient and inexpensive technique. It should act as a bridge for creeping substitution and incorporation thereby providing the chance of a lifelong biological solution.^{1,12,13} ECI allows re-attachment of muscle tendons and preserves natural joints, thus eliminating the problems of prosthetic wear. In our patients, reliable bony union of osteotomies was observed, although secondary procedures were needed in some cases. When possible, sparing of the growth plate maximised the growth potential.

Currently, 99 cases on the use of extracorporeal irradiation have been reported in the literature from six centres which have used doses of radiation of between 50 and 300 Gy.^{1,12-19} We used a dose of irradiation of 50 Gy which is

equivalent to 250 Gy in the conventional fraction using the linear quadratic model. The dose is immensely higher than that of the standard fractionated external-beam irradiation treatment for bone tumours and should be sufficient to produce a tumour kill of 100%. There should be no risk of local recurrence or of late radiotherapy-induced malignancy.² We believe that higher doses are unnecessary, take longer to administer and may increase detrimental effects to bone. Bone studies have shown a radiation dose-dependent reduction in strength and also suggest reduced revascularisation and osteoconductive properties, thereby increasing the time to union and incorporation.²⁰⁻²³

When compared with other methods of limb salvage, there was no evidence of increased rate of recurrence with extracorporeal irradiation in our series or other similar studies. Furthermore, local recurrence has not been reported after extracorporeal irradiation. The functional outcome, while variable, is encouraging when compared with other methods, especially the long-term results in the lower limb. When investigating survival, longer follow-up is required, but to date this has not been lower than expected.

One area of concern is avascular necrosis and resorption of the graft. This complication mainly occurred in the areas furthest from revascularisation, was most dramatic in the humeral head but was also seen in the pelvis. Intercalary re-implantations do well since they are revascularised from both ends. Radiological remodelling of the extracorporeal irradiation graft was limited and suggested that complete replacement with living bone did not occur and there remained a framework of dead bone which needed the long-term support of the metalwork. This is why we recommend vascularised fibular graft to supplement the reconstruction.

Another disadvantage was the lack of material for histopathological analysis of the effect of chemotherapy and of

the resection margins. We believe that our marginal biopsies are satisfactory for assessing resection. Our oncologists base post-operative chemotherapy and radiotherapy on the clinical and radiological responses and marginal biopsies. However, our rates of recurrence and mortality have not been increased by these disadvantages.

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. Spira E, Lubin E. Extracorporeal irradiation of bone tumours: a preliminary report. *Israel J Med Sci* 1968;4:1015-19.
2. Hong A, Stevens G, Stalley P, et al. Extracorporeal irradiation for malignant bone tumours. *Int J Radiat Oncol Biol Phys* 2001;50:441-7.
3. Enneking WF. A system of staging musculoskeletal neoplasms. *Clin Orthop* 1986;204:9-24.
4. Enneking WF, Dunham WK, Gebhardt MC, Malawar M, Pritchard D. A system for the functional evaluation of reconstructive procedures after surgical treatment of tumours of the musculoskeletal system. *Clin Orthop* 1993;286:241-6.
5. Enneking WF, Spanier SS, Goodman MA. A system for the surgical staging of musculoskeletal sarcoma. *Clin Orthop* 1980;153:106-20.
6. Davis AM, Bell RS, Badley EN, Yoshida K, Williams JL. Evaluating functional outcome in patients with lower extremity sarcoma. *Clin Orthop* 1999;358:90-100.
7. Davis AM, Wright JG, Williams JL, et al. Development of a measure of physical function for patients with bone and soft tissue sarcoma. *Qual Life Res* 1996;5:508-16.
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. Mondelaers W, Van Laere K, Uyttendaele D. Treatment of primary tumours of bone and cartilage by extracorporeal irradiation with a low energy high power electron linac. *Nuclear Instruments Methods in Physics Res* 1993;70-B:898-900.
10. Ralston A, Estoesta E, Stevens G, Hong A. Extracorporeal irradiation: novel use of a blood product irradiator. *Australia Phys Eng Sci Med* 2001;24:59-62.
11. Enneking WF, Dunham WK. Resection and reconstruction for primary neoplasms involving the innominate bone. *J Bone Joint Surg [Am]* 1978;60-A:731-46.
12. Uyttendaele D, De Schryver A, Claessens H, et al. Limb conservation in primary bone tumors by resection, extracorporeal irradiation and re-implantation. *J Bone Joint Surg [Br]* 1988;70-B:348-53.
13. Araki N, Myoui A, Kuratsu S, et al. Intra-operative extracorporeal autogenous irradiated bone grafts in tumor surgery. *Clin Orthop* 1999;368:196-205.
14. Van Laere K, Casier K, Uyttendaele D, et al. Technetium-99m-MDP scintigraphy and long-term follow-up of treated primary malignant bone tumours. *J Nucl Med* 1998;39:1563-9.
15. Yamamoto T, Akisue T, Marui T, Nagira K, Kurosaka M. Osteosarcoma of the distal radius treated by intra-operative extracorporeal irradiation. *J Hand Surg [Am]* 2002;27:160-4.
16. Chen WM, Huang CK, Chiang CC, Lo WH. Treatment of malignant bone tumours by extracorporeal irradiated autograft-prosthetic composite arthroplasty. *J Bone Joint Surg [Br]* 2002;84-B:1156-61.
17. Sys G, Uyttendaele D, Poffyn B, Berdonk R, Verstraete L. Extracorporeally irradiated autografts in pelvic reconstruction after malignant tumour resection. *Int Orthop* 2002;26:174-8.
18. Bohm P, Fritz J, Thiede S, Budach W. Re-implantation of extracorporeal irradiated bone segments in musculoskeletal tumor surgery: clinical experience in eight patients and review of the literature. *Langenbecks Arch Surg* 2003;387:355-65.
19. Sabo D, Bernd L, Buchner M, et al. Intraoperative extracorporeal irradiation and replantation for local treatment of primary malignant bone tumours. *Orthopade* 2003;32:1003-12.
20. Sabo D, Broacai DR, Eble M, Wannenmacher M, Ewerbeck V. Influence of extracorporeal irradiation on the re-integration of autologous grafts of bone and joint: study in a canine model. *J Bone Joint Surg [Br]* 2000;82-B:276-82.
21. Hamer AJ, Strachan JR, Black MM, et al. Biochemical 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.
22. Currey JD, Foreman J, Laketic I, et al. Effects of ionizing radiation on the mechanical properties of human bone. *J Orthop Res* 1997;15:111-17.
23. Voggenreiter G, Ascherl R, Blumel G, Schmit-Neuerburg KP. Extracorporeal irradiation and incorporation of bone grafts: autogenic cortical grafts studied in rats. *Acta Orthopaedica Scand* 1996;67:585-8.