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ORIGINAL ARTICLE

Result of extracorporeal irradiation and re-implantation for malignant bone tumors: A review of 30 patients

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Abstract

***Aims*:** Extracorporeal irradiation and re-implantation (ECI) has been used as limb salvage surgery for musculoskeletal oncology patients. Biological reconstruction, no risk of disease transmission and immunological reaction, ready availability and preservation of bone stock are the major advantage of this surgical technique. This case series details the outcomes of ECI.

***Methods*:** In total, 30 patients (31 sites) were treated with ECI between 1996 and 2007. The mean survivor follow-up period was 47 months (at least 24 and up to 108). The results of ECI were judged in terms of recurrence and limb function. Surgical failure was defined as local recurrence and the need for amputation, and reoperation for any reasons. Functional status was assessed by three functional assessment systems: Mankin score, the Musculoskeletal Tumor Society score (MTSS) and the Toronto Extremity Salvage score (TESS).

***Results*:** In all, 24 patients (80%) were alive and free from disease at last follow up. Operative failure occurred in two cases (7%) and the main complication was infection in three cases (10%). The mean values of the MTSS and the TESS were 82% (57–98%) and 81% (57–99.), respectively. Excellent or good results were achieved in 27 patients (90%) according to the Mankin score. Patients classified as stage IA and IIA, upper extremity and ECI-prosthesis composite, mostly demonstrated excellent results without any complications.

***Conclusion*:** Our results are encouraging in terms of the orthopedic and oncological outcomes. This indicates that ECI offers a good alternative method for reconstruction in limb salvage surgery.

Key words: bone neoplasm, extracorporeal irradiation and re-implantation, limb salvage, radiotherapy (high-energy), salvage therapy.

INTRODUCTION

The survival rate of patients with malignant bone tumors that are managed by tumor resection and adjuvant therapy (chemotherapy and/or radiation therapy) has improved dramatically in the past 25 years.[1] Multidisciplinary approaches for malignant bone tumors are widely accepted, especially where a limb salvage expectation exists. Although megaprosthesis replacement is the treatment of choice of limb salvage operations currently, long-term survival of the prosthesis and instrumentation availability are disadvantages of this technique.[2] On the other hand, allograft reconstruction has limited use because of concerns about rejection and the transmission of infections.[3–6] Reconstruction with irradiated autogenous bone graft is a procedure that is simple, effective and inexpensive, and has been used as

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an alternative to allograft and megaprosthesis replacement.[2,7] Extracorporeal irradiation and re-implantation (ECI) has been reported to have several advantages.[8–15] This technique also has been performed in Chiang Mai University since 1996 on selected patients in whom the tumor is able to be resected with wide margins, and with enough reconstructable soft tissue and bone stock to perform a reconstruction after tumor removal and irradiation. The procedures were performed in a standard protocol, including neo-adjuvant chemotherapy, a wide resection of the tumor, ECI, re-implantation with appropriate fixations, and a complete adjuvant cycle of chemotherapy. Here, we detail the functional and cancer outcomes of malignant bone tumor using ECI at Chiang Mai University Hospital.

METHODS

Patients

Patients who had malignant musculoskeletal tumor and had undergone a surgical treatment between January 1996 and December 2007 at Chiang Mai University Hospital were retrospectively reviewed. For the selection criteria, the patients who had undergone a tumor resection and reconstruction with ECI, and were available for follow up for at least 24 months were included in this study. Patients requiring an amputation, limb salvage surgery by other reconstruction techniques or who were lost to follow up were excluded. The functional score was evaluated at 24 months after the operation. Outcomes evaluated included time to re-operation for any reason, time to local failure (locally recurrent and requiring amputation). The survival period of the reconstructive procedure was estimated by the Kaplan–Meier method. This study and the treatment protocols were approved by the Research Ethics Committee. All patients were managed in a multidisciplinary clinic involving orthopedic surgeons, radiation oncologists and medical and pediatric oncologists. There were 30 patients (31 sites) in this study. Of these 11 females and 19 males with a mean age at presentation of 26 years (11–60 years) were followed up for at least 24 months after the surgery. The mean survivor follow-up period was 47 months (24 to 108) from the date of surgery. This study group included 21 osteosarcomas, four malignant fibrous histiocytomas, two chondrosarcomas, two Ewing's sarcomas and one synovial sarcoma. The Enneking surgical staging system was used for preoperative evaluation. Six patients were in stage III, 14 patients were in stage IIB, eight were in stage IIA and two were in stage IA.

Surgical procedure

After the patients had been completely evaluated by the orthopedists, radiologists and pathologists, a wide resection of the involved bone and surrounding soft tissue was performed after neo-adjuvant chemotherapy for a period of about 4 weeks. After removal of the tumor from the en bloc segment, the bone and the crucial ligament were wrapped with one layer of antibiotic saline-soaked gauze, followed by one layer of sterile draping, and then sealed with a sterile plastic bag. Another sterile plastic bag and sterile drape were used as the outer package before irradiation. All bone segments were placed at the center of a canister and all specimens were given a single midplane dose of 100 Gy at 1.8–2.0 Gy per minute by a 6 MV photon linear accelerator. The total time required from the collection of the bone to returning it to the operating room was within 50 min. Subsequently, the bone segment was soaked with an antibiotic before the re-implantation was carried out.

For pelvic and hip reconstruction, five patients underwent an ECI-prosthetic composite graft (ECI-PC) with hemiarthroplasty (patients no. 2, 18, [Fig. 1] 19, 20 and 30). This procedure was made in three steps: tumor resection, autogenous ECI-PC and re-implantation with soft tissue reconstruction. For tumor resection, a long posterolateral incision and wide margin resection were performed. The femur was dislocated anterolaterally. The femoral osteotomy was performed in a chevron fashion 5 cm distal to the tumor location, as determined

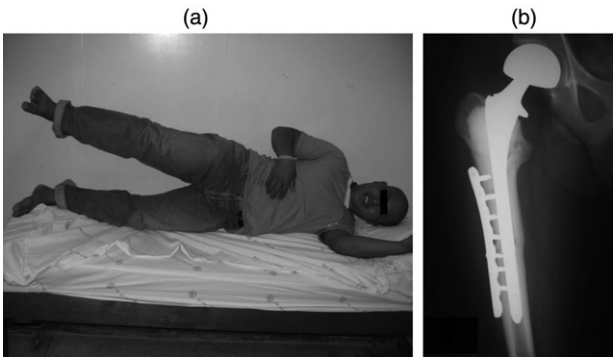

Figure 1 Patient 18. (a) Photograph showing the 2-year post-operative status of a 25-year-old man with osteosarcoma at the femur after extracorporeal irradiation and re-implantation-prosthetic composite ECI-PC re-implantation, demonstrating a good abductor function. (b) Post-operative radiograph of ECI-PC re-implantation and locking compression plate at 24 months showing a good alignment of implant and union of proximal femur.

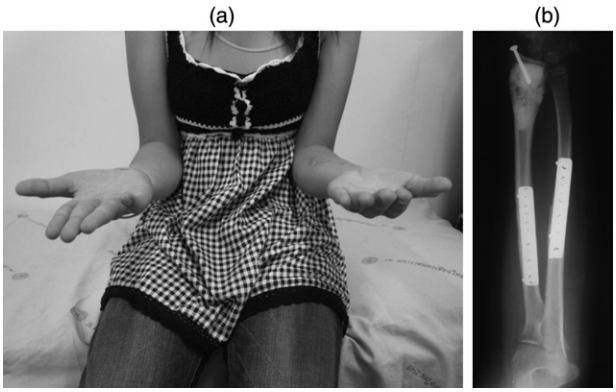

Figure 2 Patient no. 17. (a) Photograph showing 1-year post-operative function of a 14-year-old girl with an osteosarcoma at the left distal radius after osteotomy at the shaft of the radius and ulna and wide resection and extracorporeal irradiation and re-implantation of distal radius. (b) Post-operative forearm radiograph after 24 months showing the union of the radius and ulna after being fixed with small dynamic compression plate and screws.

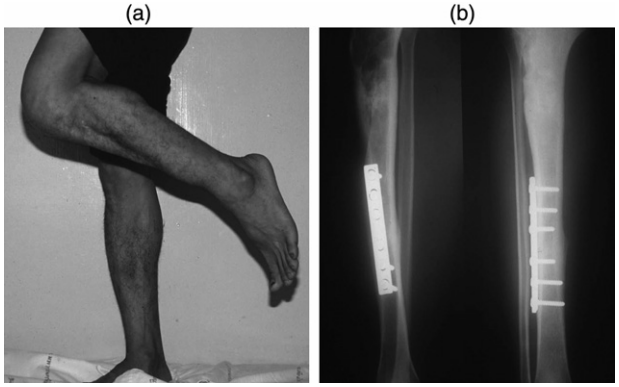

Figure 3 Patient no. 8. (a) Photograph showing 2-year post-operative status of a 26-year-old patient with an osteosarcoma at left proximal tibia after extracorporeal irradiation and re-implantation ECI of osteochondral graft. (b) Post-operative radiograph after wide resection and ECI of an osteochondral graft at proximal tibia in this patient. Stabilization was achieved by a 6-hole narrow plate and screws. Radiograph after 24 months shows a callus and stable implants.

by preoperative imaging studies. Following the resection of the proximal femur, the tumor bone was irradiated extracorporeally with a 100 Gy dose and connected to the femoral component with bone cement. Then the ECI-PC was re-implanted into the host bone. The soft tissue was reconstructed and sutured around the neck of the ECI-PC. The external rotators were reattached to the hip capsule. The abductor and vastus lateralis were repaired together for the abduction function.

For patient no. 25, the iliac bone was fixed with multiple cancellous screws and hip capsule reconstruction was carried out afterward. Diaphyseal resection and intercalary re-implantation of the femur, tibia and upper extremities were performed mostly with plates and screws (patients no. 1, 3, 4, 6, 9, 12, 14, 15, 17, [Fig. 2]) 19, 22 and 24) as well as intramedullary nail fixation (patients no. 11 and 28). Distal femur osteochondral graft with cruciate ligament and tibial bone fragment (patients no. 5, 7, 10, 13, 26 and 29) removed by the intra-articular resection technique were all sent for irradiation. Subsequently the femoral shaft and cruciate ligament were fixed with plate and screws and small cancellous screws, respectively. Extra-articular resection was performed for three patients (no. 16, 27 and 28), and the whole knee unit was irradiated before re-implantation with plate and screws fixation to the femur and tibia. Intra-articular resection at the tibial osteochondral graft was performed for two patients (no. 8 [Fig. 3] and 23) and re-implanted with plate and screws.

Chemotherapy

All cases of osteosarcoma and multiple site mesenchymal chondrosarcoma were treated with cisplatin and adriamycin regimen for adjuvant therapy.

Ewing's sarcoma was treated with multi-agent adjuvant including vincristine, doxorubicin, cyclophosphamide, alternating with ifosfamide and etoposide. For the malignant fibrous histiocytoma and synovial sarcoma, an adriamycin-based adjuvant was used to downstage a large tumor. There was no adjuvant chemotherapy for grade I chondrosarcoma (patient no. 6).

Evaluation

The results of ECI were judged in terms of oncology and limb function. All patients were followed up at monthly intervals in the first year, 3-month intervals in the second year, and every 6 months in the following year. A physical examination was regularly performed to check for local recurrence. In addition for remote metastasis work-up, a chest radiography was done every 3 months, together with a yearly computed tomography chest and bone scan for the first 3 years. A plain radiography was performed to assess the unity of the internal bone and instrument status. The limb salvage functional score including the Mankin score, the Musculoskeletal Tumor Society score (MTSS), and the Toronto Extremity Salvage score (TESS) were evaluated at 24 months after the operation.[16,17]

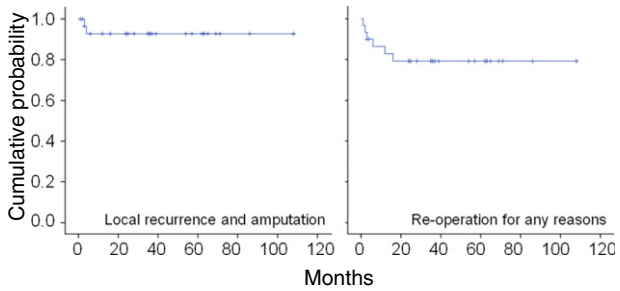

Figure 4 Cumulative probability of operation failure and re-operation showing (a) local recurrence and amputation and (b) re-operation for any reason.

RESULTS

Oncological outcome

In all, 30 patients (31 sites) were recruited in this study. Two patients (7%) were classified as stage I and 22 patients (73%) as stage II. Six patients (20%) were classified as stage III. A total of 24 patients (80%) were alive and free from disease at 2–9 years. Three of the six (patient no. 22, 24 and 25) with lung metastasis prior to treatment were still alive during evaluation. Two of the six (patient no. 27 and 28) were initially planned for amputation but refused. ECI therefore was the best remaining choice for physiological acceptance but a sufficient margin of tumor resection could not be obtained. These patients had a local recurrence that eventually required amputation. Patient 19 was classified as stage III because multiple site lesions were found in both femurs and the sacrum. Since the patient's treatment with surgery and adjuvant chemotherapy, she has been healthy without evidence of distance metastasis at 35 months follow up.

Orthopedic outcome

The details and functional outcome of patients are summarized in Table 1. The mean values of the MTSS were 82% (57–98%) (Table 1). Excellent or good results were achieved in 24 patients (90%) according to the Mankin score and the mean values of TESS 81% (57 to 99%), the result shown in supplement data. The operative failure from this series (local recurrence and require amputation) was 7%. The cumulative probability of operation failure and re-operation is shown in Figure 4. Patients classified as stage IA and IIA, with upper extremity and ECI-prosthesis composite hemiarthroplasty, mostly demonstrated excellent results without any complications. All but one (10 of 11) intercalary re-implantation sites showed good to excellent functional scores, with the variation in functional ranges depending on the extent of soft tissue removal due to the prior staging. All but two (nine of 11) cases of osteochondral re-implantation provided good to excellent results.

The main complications were infection in three cases (10%). In patient no. 14 this problem was overcome by debridement. Two cases (patient no. 25 and 26) of osteochondral graft and ilium re-implantation underwent debridement and arthrodesis. Two patients (no. 22 and 24) had a delayed union (7%) and one (patient no. 6) had non-union (3%); however, all of these underwent a re-operation with autogenous iliac bone graft. Patient no. 6 showed complete union afterward, and patients no. 22 and 24 are being followed up. There was a fracture of the patella in patient no. 29 through an accidental injury 2 months postoperatively. A re-operation with tension band wiring was performed and the patient eventually has shown good functional activity.

DISCUSSION

Since limb salvage is the treatment of choice for musculoskeletal oncology, ECI has proven to be a useful, convenient and inexpensive technique, providing excellent reconstruction for malignant bone tumor patients.[8–15] Among the 30 patients who underwent treatment with ECI in Chiang Mai University between 1996 and 2007, most had good to excellent results.

Tumor staging, site of tumor and upper extremity location played important roles to provide these favorable outcomes. Early stage tumors (not over stage IIA, 33%) mostly provided an excellent result. Stage IIB (47%) demonstrated more limited functional scores due to the extensive loss of soft tissue. Stage III (20%) demonstrated four good results, two local recurrences, two delayed unions and one infection. Even though stage III patients are not good candidates for treatment, the initially unacceptable amputation narrowed the choices of treatment. ECI was therefore performed to maintain a better physiological status for those patients.

Most cases of intercalary re-implantation provided good functional results because the strut cortical autogenous graft provided an initially strong fixation; hence most patients could immediately begin weight-bearing ambulation. Some osteochondral re-implantation cases had delayed rehabilitation because of major cruciate ligament reconstruction. Subchondral and cancellous

Table 1 Details and results for the 30 patients

Patient no.	Diagnosis	Site	Stage	Reconstruction	MTSS	Complications: re-operation
1	Osteosarcoma	Femur	IIA	Intercalary	97.6	
2	Osteosarcoma	Femur	IA	ECI-PC-hemiarthroplasty[§]	93.3	
3	Osteosarcoma	Tibia	IIB	Intercalary	83.3	
4	Osteosarcoma	Femur	IIB	Intercalary	76.6	
5	Osteosarcoma	Femur	IIA	Osteochondral graft	90	
6	Chondrosarcoma	Femur	IIA	Intercalary	93.3	Non-union: iliac bone graft
7	Osteosarcoma	Femur	IIB	Osteochondral graft	76.6	
8	Osteosarcoma	Tibia	IA	Osteochondral graft	93.3	
9	Osteosarcoma	Humerus	IIB	Osteochondral graft	93.3	
10	Osteosarcoma	Femur	IIB	Osteochondral graft	80.3	
11	Osteosarcoma	Femur	IIB	Intercalary	75.3	
12	Ewing's sarcoma	Femur	IIB	Intercalary	75.3	
13	Synovial sarcoma	Femur	IIB	Osteochondral graft	70	
14	MFH[†]	Femur	IIB	Intercalary	56.6	Infection, peroneal nerve palsy: debridement
15	Osteosarcoma	Femur	IIA	Intercalary	96.6	
16	Osteosarcoma	Tibia	IIB	Osteochondral graft	90	Epiphyseal plate separation: knee arthrodesis
17	Osteosarcoma	Radius	IIA	Osteochondral graft	96.6	
18	Osteosarcoma	Femur	IIA	ECI-PC-hemiarthroplasty	90	
19	Chondrosarcoma[‡]	Bilateral Femur	III	Intercalary (Rt) ECI-PC-hemiarthroplasty (Lt)	72.3	
20	MFH	Femur	IIB	ECI-PC-hemiarthroplasty	93.3	
21	MFH	Knee	IIB	Osteochondral graft	70	
22	Osteosarcoma	Femur	III	Intercalary	70	Delayed union
23	Osteosarcoma	Tibia	IIB	Osteochondral graft	93.3	
24	Osteosarcoma	Tibia	III	Intercalary	73.3	Delayed union
25	Ewing sarcoma	Ilium	III	Pelvis	70.6	Infection: debridement and hip arthrodesis
26	Osteosarcoma	Femur	IIB	Osteochondral graft	76.6	Infection: debridement and knee arthrodesis
27	Osteosarcoma	Tibia	III	Osteochondral graft	Failure	Hip disarticulation
28	Osteosarcoma	Tibia	III	Osteochondral graft	Failure	AK amputation
29	Osteosarcoma	Femur	IIA	Osteochondral graft	76.6	Fracture patella: tension band wiring
30	MFH	Femur	IIA	ECI-PC-Hemiarthroplasty	68	

[†]Malignant fibrous histiocytoma, [‡]multiple site chondrosarcoma, [§]extracoporeal irradiation-graft composite hemiarthroplasty. AK, above knee; ECI, Extracorporeal irradiation and re-implantation, Lt, left; MTSS, Musculoskeletal Tumor Society score; PC, prosthetic composite; Rt, right.

bone necrosis in the long-term follow up caused limited functional scores in this group. Nevertheless, preserving the bone stock of the knee joint could be used not only for further prosthesis replacement in long-term survival cases but also for knee arthrodesis in complicated cases. All upper extremity re-implantations provided better results than lower extremity re-implantations. Prosthesis composite with ECI around the hip area mostly presented excellent results. The prosthesis immediately provided good functional activities, similar to regular prosthesis replacement. Composite grafts also maintained the surrounding bone stock for further revision surgery in long-term survival cases.

In the past few decades the number of long-term survivors of bone and soft tissue tumor has increased, the quality of life after limb salvage becomes a major concern. Although the megaprosthesis provides immediate excellent functional results, the problems over

prosthesis survival and revision surgery are still disadvantages of this technique. ECI is one of the biological reconstructions which overcome that limitation. There are several advantages to ECI treatment, including the certain sterilization of tumor cells with radiation; no risk of disease transmission and immunologic reaction; the preservation of the bone stock; the ready availability of the material; a precise anatomic fit of the re-implanted bone segment, being the patient's own bone; anatomical re-attachment of muscles and tendons and natural joint preservation, which ensures that the mobility of the joint is still intact.[9–12,14]

The success of ECI for malignant bone tumors depends on prompt detection, early diagnosis and a coordinated and carefully thought-out sequence of staging. Preoperative treatment, surgical procedures and irradiation and postoperative support and follow up by a dedicated team of caregivers are also major factors in achieving excellent outcomes. This technique should be used only as part of a multidisciplinary approach in which careful follow up is available to assess the orthopedic and oncological outcomes. Complete eradication of the tumor with minimal complications – while maintaining acceptable function, durability and the appearance of the limb – are the goals for our patients. Most patients in our series appreciate having their salvaged limbs. They can enjoy participating in their usual leisure activities and socializing with their friends and family.

Our results are encouraging in terms of both orthopedic and oncological outcomes. This indicates that the technique of ECI and re-implantation offers a good alternative method for reconstruction in limb salvage surgery. A longer follow up in a larger series is needed to confirm this.

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