13 Biological Reconstruction for Extremity Osteosarcoma: Long-Term Results and Current Concept of Intraoperative Extracorporeal Irradiated Bone Graft (IORBG)

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Abstract

Background: The improvement of survival in osteosarcoma has made a demand to get the long-term durability in the reconstruction method after wide resection.

Purpose: The long-term results of intraoperative extracorporeal irradiated bone graft (IORBG) for malignant bone tumors are analyzed to know the long-term durability of this method.

Method: Seventy-two bone tumor patients treated with IORBG for the last 25 years were reviewed. The oncological results, complication, reoperation-free survival, and graft survival were analyzed.

Results: Oncological 5-year and 10 year survival rates were 90 % and 81 %. Local recurrence was detected in one case outside the implanted bone. Major complications, namely, infection, collapse, fracture, and nonunion, were seen within a short term after initial operation. The reoperation rate was as high as 43 %. The graft survival rate was 81 % at 10 years.

Discussion: Although the reoperation rate was high, complications occurred rather in a shorter term compared with that of tumor knee prosthesis (TKR). This IORBG method is less troublesome than the prosthetic replacement which needs maintenance surgery particularly after long-term follow-up. However, as osteosarcoma occurs mostly in the second decade of life, we should continue to seek a better reconstruction method.

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Keywords
Intraoperative extracorporeal irradiation • Autogenous bone graft • Treated recycled bone • Reconstruction method • Malignant bone tumor

13.1 Introduction

The prognosis of osteosarcoma has been improved to about 70–90 % [1, 2]. The reconstruction method of the affected limb after wide resection should be more stable and tolerable for a long term in concordance with prolonged survival. On one hand, the prosthetic reconstruction needs maintenance surgery for the wear of joint parts, loosening of the stem, and breakage after long-term usage. These maintenance surgeries have a risk of infection because of massive prosthesis and bad skin condition [3]. Moreover, in some prostheses, maintenance parts are already not available because of the economic conditions. On the other hand, in order to avoid the need for maintenance surgery, we started to reuse extracorporeally irradiated affected bones. In this paper, we report the long-term results and the current concept of IORBG method in malignant bone tumor patients.

13.2 Patients and Methods

13.2.1 Patients

From 1988 to 2013, 97 patients were treated by IORBG in our three institutions [4–6]. There were 57 males and 40 females. Bone tumor consisted of 72 cases, and soft tissue tumor comprised 25 cases. The mean age of bone tumor patients was younger at 25 years (median 19 years) compared with that of soft tissue tumor patients at 50 years (median 54 years). In this study, the 72 bone tumors were analyzed. The histological diagnoses of the 72 cases are osteosarcoma (48 cases), chondrosarcoma (6 cases), Ewing sarcoma (5 cases), malignant fibrous histiocytoma (MFH) of the bone (3 cases), metastatic carcinoma (3 cases), and others (7 cases). The distribution of the anatomical sites for the application of IORBG in bone tumor is shown in Table 13.1. The tibia was the most frequent site followed by the femur, humerus, etc. This distribution of IORBG is different from

Table 13.1 Anatomical sites of the 72 bone tumors

Tumor site	No. of cases
Tibia	30
Femur	18
Humerus	14
Pelvis	6
Scapula	2
Radius	1
Ulna	1

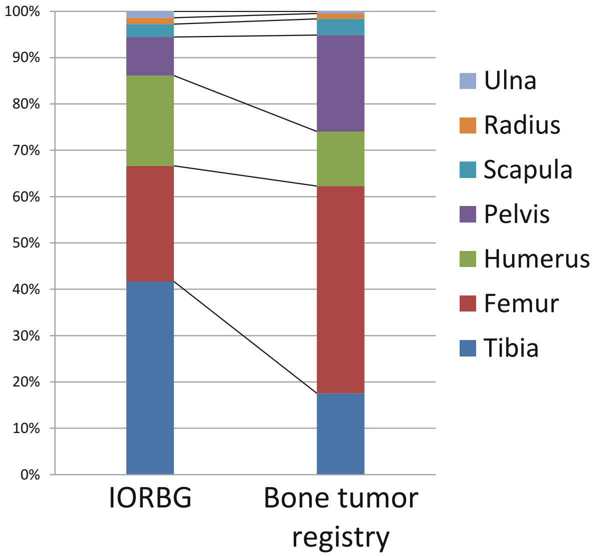

Fig. 13.1 Comparison of tumor site distribution of IORBG to that in the bone tumor registry. The humerus and tibia are preferred sites for the application of this method in order to reconstruct the rotator cuff and patellar tendon

those of the bone tumor registry in Japan [7] (Fig. 13.1). The cases on the tibia and humerus were preferred for this method in order to reconstruct the patellar ligaments and the rotator cuff in comparison to the other sites. Median follow-up interval after definitive surgery was 102 months (range 12–299 months).

13.2.2 Methods

The procedure of IORBG is shown in Fig. 13.2. Widely resected tumor material (Fig. 13.2a, b) was trimmed up to the bone and ligaments for reconstruction (Fig. 13.2c) and packed into a sterile plastic container filled with saline (Fig. 13.2d). Then, the bone was irradiated using Liniac with 6 or 10-MV photons (Fig. 13.2e). The irradiation dose was 50–80 Gy in one fraction to the whole wrapped container for about 40 min. After irradiation, the autogenous bone graft was reimplanted to the remaining bone (Fig. 13.2f) with intramedullary rods, plates, screws, and so on (Fig. 13.2g).

13.2.3 Graft Type

The graft types included osteoarticular in 31 cases (lower extremity 17, upper extremity 13, and pelvis 1), intercalary in 18 cases (lower extremity 18), composite with endoprosthesis in 20 cases (lower extremity 14, upper extremity 5, and pelvis 1), and hemicortical in 3 cases (lower extremity 2 and pelvis 1). For the osteoarticular and intercalary grafts, cement augmentation was used in recent cases to avoid collapse of the epiphysis and fracture (Fig. 13.3). For the composite

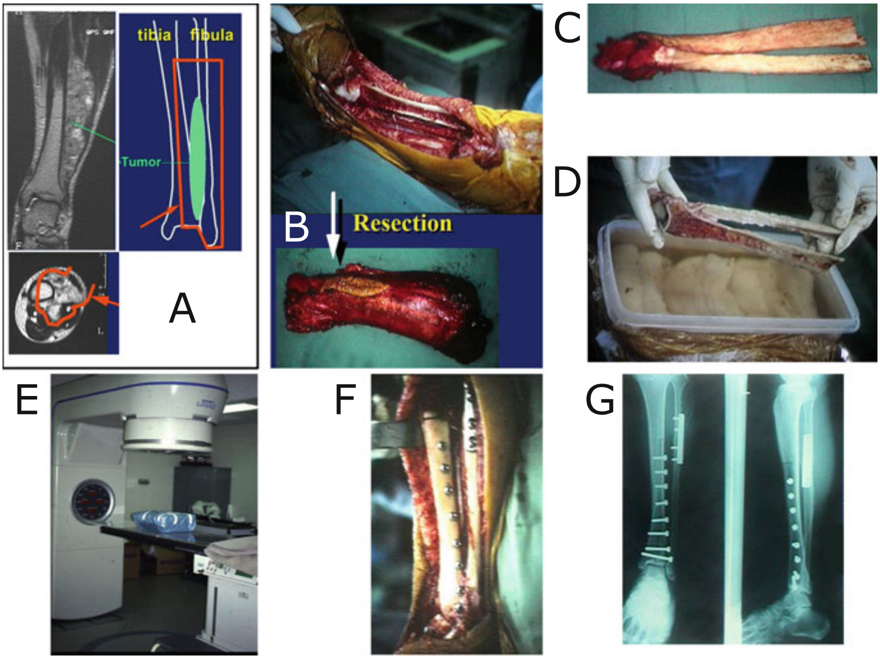

Fig. 13.2 Method of IORBG. (**a**) Wide resection of the tumor. The resection line can be planned in any way for this method. In this intraosseous tumor, the IORBG method was necessary for limb salvage. (**b**) Resected material and host. (**c**) The resected material was trimmed. The muscles were removed while preserving the ligaments. (**d**) The trimmed resected bone and ligaments were soaked in a plastic container filled with saline. (**e**) Irradiation to the whole container for 50 Gy at one time. (**f**) Reimplantation of the bone. Fixation could be done with screws, plates, rod, and so on. (**g**) XP after operation

graft, Link knee prosthesis was used for the lower limb and standard humeral head prosthesis was used for the humerus.

13.2.4 Analysis

Disease-specific survival rates, survival rates of the irradiated bone, and the reoperation-free survival rates were evaluated using the Kaplan-Meier method. The survival of the irradiated bone was considered from the date of implantation to the date of the last follow-up or to the removal of more than half of the bone because of complication or tumor recurrence. Reoperation procedures included any minor operation after the main surgery. The trend of IORBG graft types during the last 25 years was also reviewed and visualized. The NCI's Common Terminology Criteria for Adverse Events (CTCAE) version 4.0 was used for assessment of adverse events.

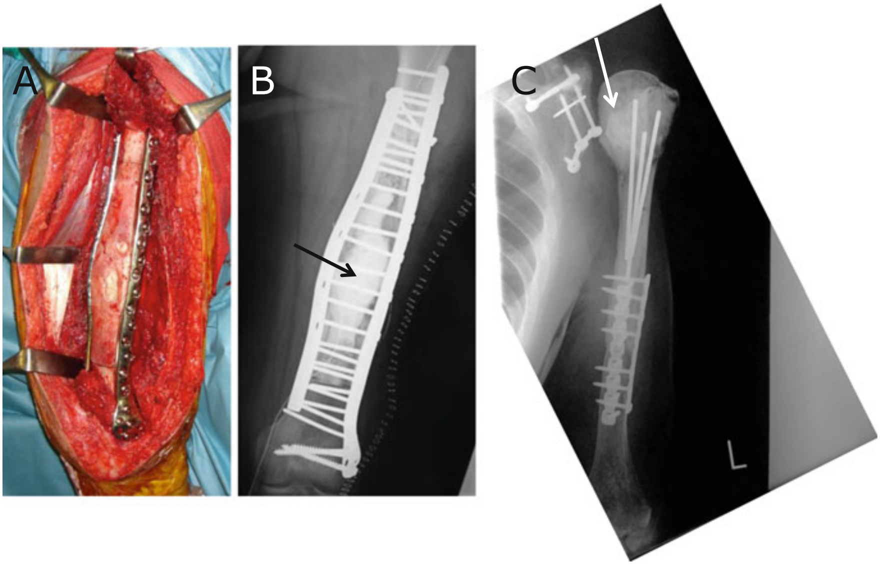

Fig. 13.3 Cement augmentation in intercalary (**a**, **b**) and osteoarticular (**c**) grafts. *White* and *black arrows* indicate the injected bone cement before implantation to the host bone. Note that the osteotomy areas were filled not with cement but with hydroxyapatite in order to achieve bone union

13.3 Results

13.3.1 Disease-Specific Survival and Local Control

The oncological results were CDF 56 cases, NED 6 cases, and DOD 10 cases at mean follow-up of 102 months (range: 12–299 months). Figure 13.4 shows the overall survival curve. The 5-year survival rate was 90 % and the 10-year survival rate was 81 %. There was one case of local recurrence outside the reimplanted bones. We underwent additional wide resection including the implanted irradiated bone and recurrence lesion and total femoral replacement. This case had no further recurrence and remained alive without disease at 19 years post-surgery.

13.3.2 Graft Survival According to the Graft Type

Figure 13.5 shows the survival rate of the irradiated bone according to the applied graft type. There was no significant difference between each graft type. There were only three cases of hemicortical graft, and one case got infected and the graft was removed. The 5-year survival rates were 72.3 % for the osteoarticular graft and 82.6 % for the intercalary graft. All composite grafts survived at mean follow-up of 88 months. The irradiated grafts were removed in 11 patients due to complications

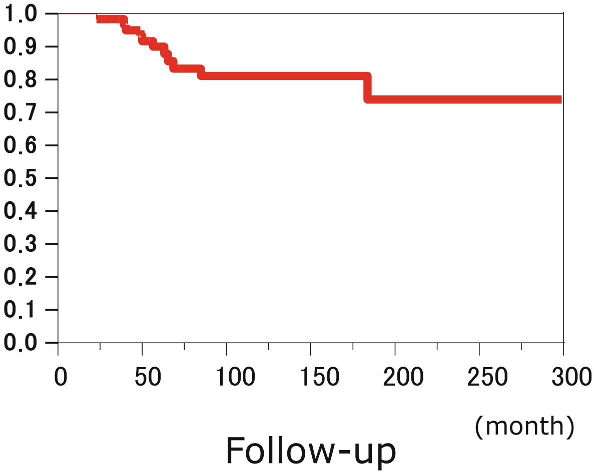

Fig. 13.4 Overall survival curve of 72 bone tumor cases. The 5-year survival rate was 90 % and the 10-year survival rate was 81 %

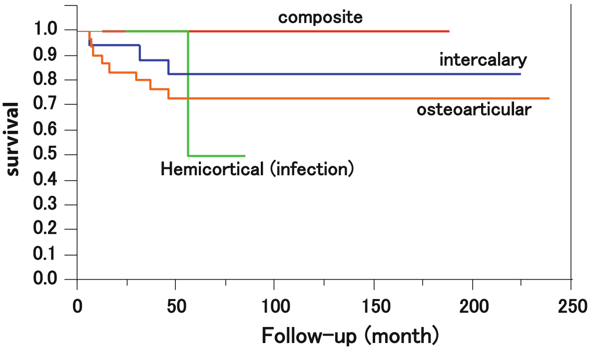

Fig. 13.5 Graft survival curve of 72 bone tumor cases according to graft types. "Survival" is defined as more than half of the graft remaining. The 5-year survival rate of each graft type was as follows: osteoarticular 72.3 %, intercalary 82.6 %, hemicortical 50 %, and composite graft 100 %

or local recurrences outside of the irradiated bone grafts. Eight of the 11 cases were osteoarticular grafts; hence, the survival curve of the osteoarticular grafts declined in a short time after the operation. The overall graft survival for all 72 cases was 81 % at 10 years as shown in Fig. 13.6

13.3.3 Complications

Table 13.2 shows the list of complications of IORBG. Infection was the most frequent (11 cases, 15 %) leading to severe complications, which affected seven osteoarticular, two intercalary, and two composite grafts. Surgical debridement was performed in nine cases corresponding to Grade 3 complication of the CTCAE. Antibiotics were administered in the other two cases. In 5 of the 11 cases, the grafts were removed. Collapse of the epiphysis occurred in nine cases of osteoarticular grafts. Five cases underwent observation without any further treatment because there were no pain and no functional disadvantages as shown in Fig. 13.7. The other

Fig. 13.6 Overall graft survival curve for all 72 bone tumor cases. The 10-year survival rate was 81 %

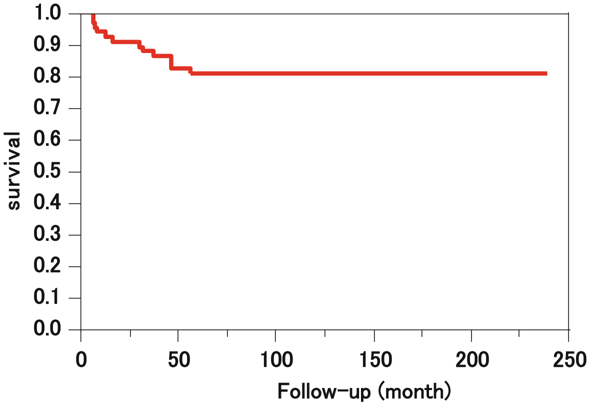

Table 13.2 Lists of complications of 72 cases

Graft related		
	Collapse	9
	Nonunion	7
	Fracture	6
	Resorption	1
	Dislocation	1
Operation related		
	Infection	11
	Recurrence[a]	1
	Neural palsy	2

[a]Outside of the graft

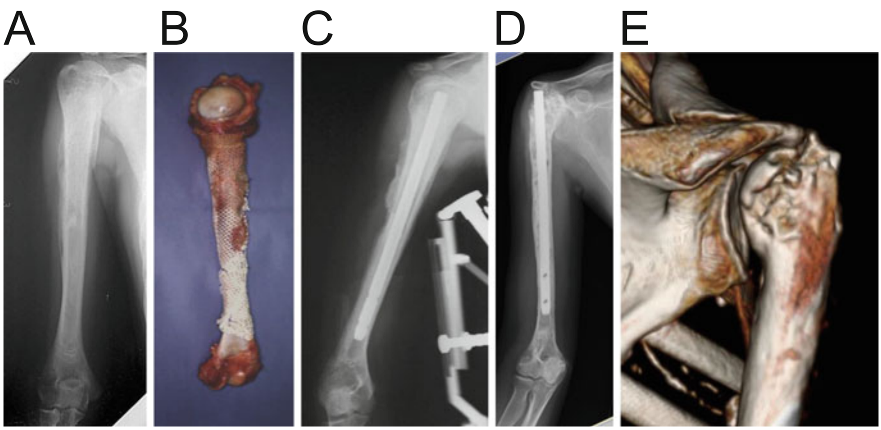

Fig. 13.7 Collapse of humeral head in an osteoarticular graft of the whole humerus. (**a**) Pre-operation XP. (**b**) Implanted irradiated bone. (**c**) Post-operation XP. (**d**) XP at 18 years later. Humeral head is collapsed but the irradiated distal humerus is still healthy. (**e**) 3D-CT shows that the articular surface of the glenohumeral joint is still preserved

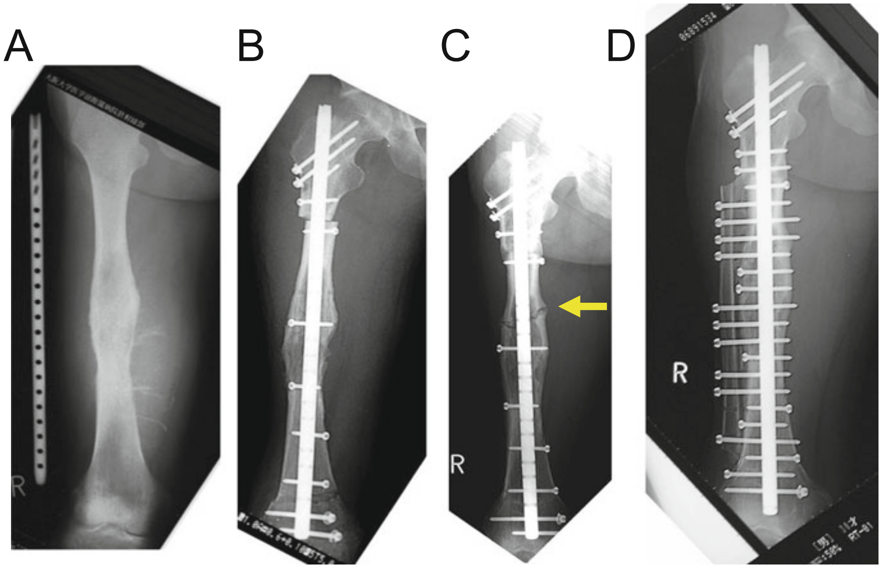

Fig. 13.8 A femoral intercalary graft with fracture at 3 years after initial operation. (**a**) Pre-operation XP. (**b**) Post-operation XP. (**c**) At 3 years post-operation, fracture occurred (*arrow*). (**d**) Free fibular graft was done, and it worked well after 10 years post-reoperation

four cases were treated surgically for partial replacement with prosthesis. Nonunion and fracture occurred mainly in the cases of intercalary graft cases. A femoral case treated with free fibular bone graft showed good function after reoperation (Fig. 13.8). As with this case, nonunion and fracture were salvaged by additional bone grafting with/without additional rigid fixation. Only 1 of 16 intercalary grafts required replacement with prosthesis because of nonunion. Overall, the reoperation rate was as high as 43 %. However, these reoperations due to complications occurred mostly during the short term compared with that of tumor knee prosthesis (Fig. 13.9). There were no Grade 4 or 5 complications.

13.3.4 Changes in Applied Graft Types During the Last 25 Years

Figure 13.10 shows the number of cases with changes in applied graft types. The number of osteoarticular grafts apparently decreased in the last 25 years. By comparison, the use of composite grafts increased. The numbers of intercalary and hemicortical grafts used did not change.

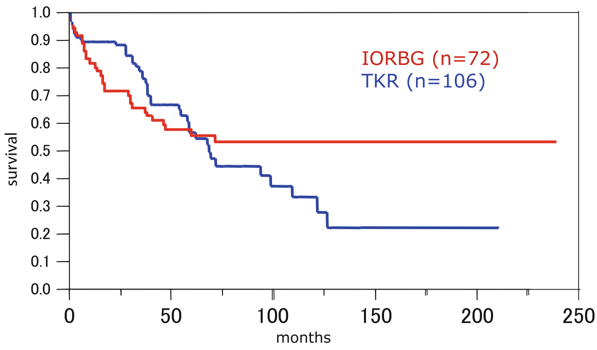

Fig. 13.9 Reoperation survival curve of 72 IORBG cases and 106 tumor knee prosthesis cases. *Red line* is survival curve of IORBG and *blue line* is that of prosthesis. Note the overlap of the reoperation-free survival curve of the two methods

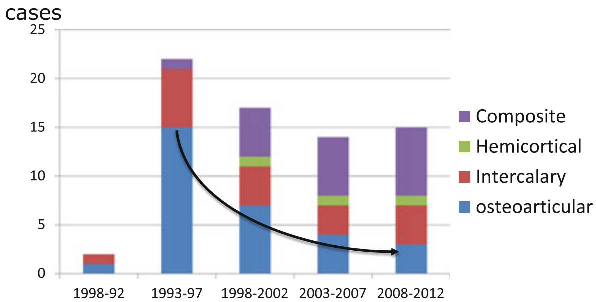

Fig. 13.10 Changes in applied graft types during the last 25 years. The frequency of application of the osteoarticular graft decreased dramatically over 25 years as shown by the arrow. In place of osteoarticular grafts, the use of the composite graft increased. The use of the intercalary and hemicortical grafts did not change

13.4 Discussion

For limb salvage surgery of osteosarcoma, prosthetic replacement is the most common and widely used method. However, prosthesis needs maintenance surgery for the wear of joint parts, loosening, stem breakage, and other complications. Amputation is sometimes required due to a severe complication, such as infection, after these maintenance surgeries [8, 9]. On the other hand, an allograft might be the most widely used biological reconstruction method in foreign countries after a wide resection for osteosarcoma [10]. However, the use of the allograft is difficult in Japan because of the availability of bone based on religious reason. Thus, the treated recycled bones, such as irradiated bone, pasteurized bone (see Chap. 14), and frozen bone (see Chap. 15), are mainly used in Japan. For these treated recycled bones, there are several advantages than allograft with regard to adaptation, disease transmission, availability, usability of attached ligaments, and immunological response. In contrast, the disadvantages of these treated recycled bones compared with prosthesis are problems of absorption and mechanical weakness, as with the allograft [11]. In IORBG, the collapse of the osteoarticular graft and fracture of the intercalary graft represent such conditions. The collapse of the osteoarticular graft was inevitable in our cases; hence, the number of applied decreased in the last 25 years and the application of composite graft increased instead. In particular, for children with growth plates, an osteoarticular graft is not suitable because the growth plate will slip. In this study, the use of the composite graft was shown to be increased with good results. However, we should be aware that this type of graft also requires maintenance surgery for the joint parts the same as prosthesis. For intercalary grafts, the reoperation frequency decreased with cement augmentation, dual plate fixation, and bone grafting, which strengthen the graft. Especially, intercalary graft with vascularized fibular graft showed the best result (Fig. 13.11). This case achieved a normal ADL and the plate could be removed. Although the overall reoperation rate was as high as 43 %, these reoperations due to

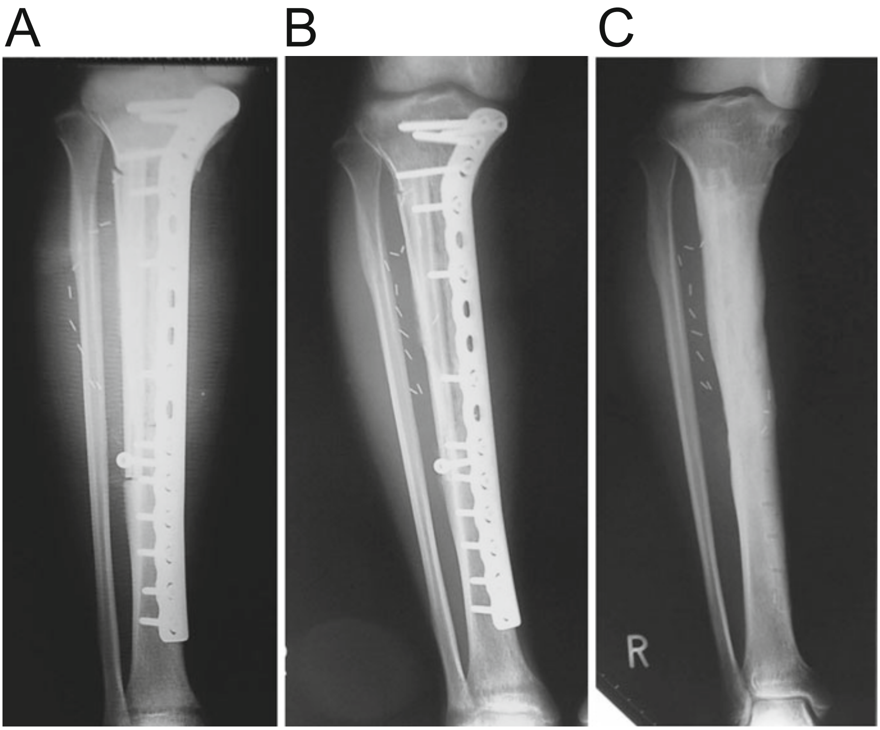

Fig. 13.11 Intercalary graft with vascularized fibular graft. (**a**) Post-operation XP. (**b**) XP at 6 months after operation. (**c**) XP at 65 months after the operation The plate could be removed

complications occurred rather in a shorter term compared with that of tumor knee prosthesis (TKR) (Fig. 13.9). The reoperation-free survival of IORBG overcomes that of TKR after 5 years. This is the advantage of biological reconstruction compared with prosthetic reconstruction, which requires maintenance surgery over the long term. Compared to the survivorship of prostheses of 35–71 % at 10 years reported in previous studies [9, 12, 13], the survivorship of irradiated bone of 81 % at 10 years is very attractive. The irradiated bone graft, once it has healed, is less troublesome compared with the prosthesis, particularly after long-term follow-up. Stable condition in the long term is the best advantage of IORBG. Another advantage of IORBG is the feasibility to reconstruct tendons, joints and small bones for which good prosthesis is not available. IORBG can be used to reconstruct any sites in the body, such as the hand, elbow, ankle, toe, tendons, and ligaments [6, 14].

In conclusion, the long-lasting stability of IORBG can be seen after 5 years, and the subsequent complication rate will decrease. The long-term effectiveness, safety, and reliability of irradiated bone grafting are advantages of IORBG as compared to prostheses, especially for the young patients with osteosarcoma who deserve a long survival period. However, we still need to create a maintenance-free reconstruction method for the knee joints instead of a composite graft.

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