CLINICAL ARTICLE

Biological Reconstruction in Bone Sarcomas: Lessons from Three Decades of Experience

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Objective: To review research on all patients treated by biological reconstruction after resection of bone sarcomas between 1987 and 2015 at our hospital.

Methods: One thousand one hundred and sixty-seven cortical allografts and 166 cortical autografts were retrospectively analyzed. Radiological studies had been performed to determine the timing of consolidation of the grafts at both the metaphyseal and diaphyseal osteotomies. A prospective isotopic study with 99 Tc was done in order to evaluate the revascularization of allografts. Histological, immunohistochemistry and fluorescence techniques were used on retrieved allografts to evaluate their integration. Complications, functional results and possible relationships with human leukocyte antigen (HLA) compatibility, were also reviewed.

Results: The mean age of these patients with bone sarcomas was 19 years (range, 3–69 years). The mean length of cortical allografts was 19.5 cm (range, 4–42 cm) and of autografts 8 cm (range, 6–15 cm). The mean consolidation time of diaphyseal osteotomies was 16 months. The mean time to consolidation was 5 months for vascularized autografts and 12 months for non-vascularized grafts. New bone formation was observed at the host bone–allograft junction. Complications included non-union (16.2%), fractures (8.2%) and infections (11.8%). The incidence of complications was higher in the non-compatible group; however, no significant relationship was found between HLA compatibility (or lack thereof) and the occurrence of complications.

Conclusions: Allografts are a good option for reconstruction after removal of larger tumors. It is necessary to take into account the mechanisms of incorporation and the measures that can be taken to reduce complications.

Key words: Allograft; Autograft; Bone integration; Bone sarcoma; HLA

Introduction

Reconstruction surgery after excision of musculoskeletal tumors has advanced greatly in the last few decades. New chemotherapy protocols and imaging techniques have made it possible to surgically remove tumors that were previously unresectable and thus to cure disease and conserve limb function[1]. There are now many long-term survivors after limb salvage procedures and consequently more follow-up information on the outcomes of the reconstruction techniques used.

There are several techniques for limb reconstruction. After resection of a large piece of bone, reconstruction of the limb (when needed) can be achieved with metallic implants, such as prostheses, or with bone, biological reconstruction. In the latter case, bone can come from the patient (autograft) or from a donor (allograft). Autografts can be categorized as vascularized and non-vascularized. There are also reconstruction techniques that utilize combinations of biological and non-biological (allograft–prosthesis composites). The idea of transplanting limbs or bones between individuals of the same species (allogeneic transplanting) or between different species (xenogeneic transplanting) has long been articulated in medical and scientific publications. The first massive

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allograft was undertaken in 1914; since then this type of graft has been employed with varying degrees of success[2–8]. Our hospital has extensive experience in biological reconstruction after resection of bone sarcomas.

In 1986, the first bone bank in Spain was created in our hospital; consequently, since then our experience with biological reconstruction has been broad (Fig. 1). Having a bone bank right next to the operating theatre makes salvage surgery much safer and increases therapeutic possibilities. Allografts can be procured under sterile conditions or sterilized by radiation. However, radiation affects the biomechanical properties of the graft.

Biological reconstruction has the advantages of being osteoinductive and osteoconductive. Incorporation of the insert is a sequential process that begins with inflammation and goes through various stages of revascularization, osteogenesis and remodeling. Osteogenesis, the process of bone formation, can originate in the patient's own bone or in the insert. Fundamental requisites of inserts are that they possess the capacity to form bone or to be substituted for by bone and that they are not rejected by the body in which they are implanted. During osteoinduction the insert does not persist but rather serves to stimulate pluripotential mesenchymal cells to differentiate into osteogenic cells, which in turn induce a creeping substitution of the insert. Massive allografts serve as a scaffold for the ingrowth of new host bone. Repair of allografts is a lengthy process. Remodeling of allograft bone does not necessarily have to be beneficial for the patient in a direct functional way, on the other hand, remodeling is essential for long-term survival of the graft.

Incorporation of allografts together with complications and long-term results has been discussed in various published reports. Systemic chemotherapy and external radiotherapy are known to affect the incorporation of allografts[9,10]. The fact that allograft integration is a slow process accounts for the difficulties in treating the commonest complications. Intercalary diaphyseal reconstruction is one of the more successful forms of allograft reconstruction, although there have been reports of significant complications. To achieve good results, careful preoperative planning and effective soft tissue coverage over the allograft are crucial.

The most frequent complications reportedly associated with allografts are infection, non-union, resorption and fracture. These complications sometimes lead to failure of the reconstruction, and, in most cases, resolution of the complication requires further surgical treatment. The period of highest risk of complications is the first 2 years after surgery; however, late complications have also been described.

Autografts are considered the best option for biological reconstruction[7,8]. With the advent of microvascular surgical techniques, vascularized bone transfer, which addresses some of the deficiencies of non-vascularized autografts and has a broader range of indications, has become a popular procedure.

Another possible technique for biological reconstruction involves "sterilizing" the extracted tumor-affected bone with extracorporeal radiotherapy or freezing and then implanting it back into the patient. This technique has been used successfully, especially in countries where bone banks are not available.

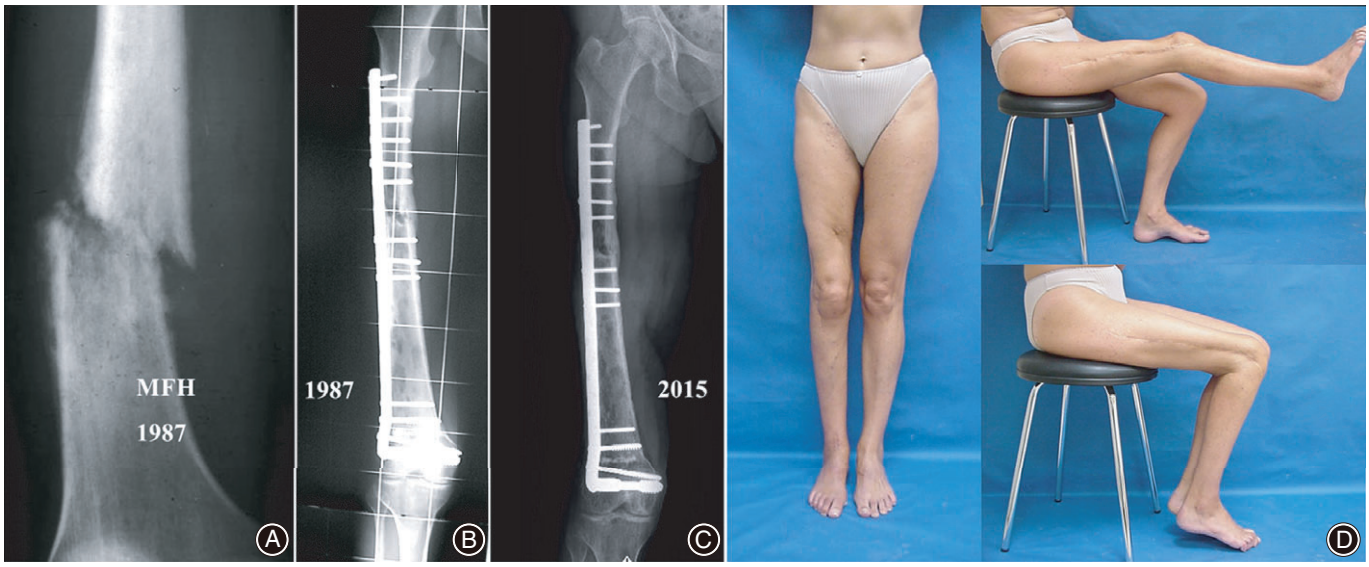

Fig. 1 Representative case showing long-term progress of an intercalary allograft of the distal femur after resection of a malignant fibrous histiocytoma in a 28-year-old woman: (A) Preoperative radiograph showing a pathological fracture in the femoral shaft. (B) Radiograph 5 months after resection of the tumor and reconstruction with an intercalary allograft. (C) X-ray film of the femur 28 years after surgery showing consolidation of the graft and some evidence of resorption. (D) Excellent function of the knee at the last follow-up.

There are fewer complications with autograft reconstruction than with other reconstruction approaches. However, patients who receive autograft reconstruction need to avoid weight loading of their lower extremities for long periods and autografts are limited in terms of availability and can only be used for reconstruction if the tumor resected is small.

The aim of this study was to present a review of our research on patients who have undergone biological reconstruction. To this end, we evaluated incorporation from the radiological, isotopic and histological points of view and assessed complications and results in our patients over the past 29 years. A particular objective was to establish what lessons can be learned to avoid complications and maximize functional results in the future.

Materials and Methods

In this study, 1067 consecutive cortical allografts that had been implanted in 875 patients who had undergone tumor resection at our hospital between April 1987 and April 2015 were reviewed. The series includes all patients treated with cortical allografts after resection of tumors: there were no exclusion criteria.

This series comprises 370 cases of osteosarcoma, 245 of Ewing sarcoma, 117 of chondrosarcoma, nine of giant cell tumor and 134 of other tumor types (e.g. fibrosarcoma, leiomyosarcoma of bone, hemangioendothelioma, and metastatic tumors). Of the 875 patients, 194 (22.2%) required two or more allografts; approximately two thirds of multiple allografts were required as a result of infection or fracture and the remaining third because of polyostotic lesions or bone metastases from bone sarcomas. Chemotherapy was given to 676 (77.3%) patients, and 217 (24.8%) of these also received radiotherapy.

Allografts were procured by an extraction team under sterile conditions. Control cultures were carried out prior to definitive storage at −80 °C in our own bone bank. Prior to implantation, further samples were cultured and checked to reduce the risk of infection.

Allograft incorporation was evaluated by three means: radiological, isotopic and histologic.

Each patient underwent radiological study monthly during the first year of systemic chemotherapy, then every 3 months for another year, and subsequently once a year. International Society of Limb Salvage criteria were used to evaluate consolidation[9]. Multivariate statistical analysis of the following factors that can influence consolidation was performed: host and donor age, allograft length, location, osteotomy and osteosynthesis type, intra-arterial and systemic chemotherapy and intra-operative and external radiotherapy.

In a prospective study of a subgroup of 36 subjects, revascularization of allografts was assessed by isotopic means with 99 Tc MDP at least 2 years after implantation of the allograft. Anterior and posterior views of both limbs were qualitatively interpreted by two experienced physicians. Semi-quantitative measurements were taken with a region of interest technique.

A histological study with hematoxylin-eosin and Mason's trichrome stains was performed on 24 allografts removed because of infection or fracture. Von Willebrand stain was used to assess the viability of the vessels found within the allografts. To ascertain the validity of the latter technique, Von Willebrand staining was also performed on allografts that had been discarded for clinical use because of contamination during extraction (control group). Patients whose allograft was about to be removed received injections of 500 mg oxytetracycline 6, 4 and 2 days before the operation to enable use of fluorescence techniques to study graft integration.

In addition, human leukocyte antigen (HLA) compatibility between donor and recipient was studied in 43 patients who had received allografts from multi-organ donors. This study was conducted to evaluate the possible influence of HLA compatibility on the occurrence of complications (pseudarthrosis, infection or fracture). In this study, the statistical test applied was the Mann–Whitney *U* test.

Functional results were evaluated at the time of follow-up sessions in accordance with MSTS (Musculo Skeletal Tumor Society) standards.

All complications, patient characteristics and tumor types were registered[11,12]. When the donor HLA type was known (i.e., multi-organ donors), histocompatibility between donor and recipient was studied to identify any relationship with occurrence of complications.

Incorporation (by radiological evaluation), functional results and complications of allografts were also compared with those of 166 autografts that had been employed for reconstruction in 165 patients. Twenty-nine (17.5%) of these autografts were vascularized.

Statistical analysis was performed using SPSS v18.0 (IBM). For parametric data, Student's *t*-test was used and for non-parametric data, the χ^2 test. A test result was considered statistically significant if $P < 0.05$.

Results

The mean follow-up time was 188 months (range, 8–344 months). At their most-recent follow-up, 73% of patients with osteosarcoma and 68% of those with Ewing sarcoma were disease-free. These two tumor types were the most frequently encountered in our series: 615 (70.3%) of the total of 875 patients had one of these two tumors.

The mean age of patients with bone sarcoma was 19 years (range, 3–69 years). The mean length of cortical allografts was 19.5 cm (range, 4–42 cm); that of autografts was 8 cm (range, 6–15 cm). Table 1 shows the number and type of allografts and autografts.

Evaluation of Incorporation Radiologically

Allografts

The mean consolidation time of diaphyseal osteotomies was 16 months. Consolidation time was significantly associated with the use of systemic chemotherapy ($P < 0.05$), the use of

TABLE 1 Number and types of allografts and autografts used for limb salvage (cases [%])

Type of graft	Cortical allograft	Cortical autograft
Composites graft-prosthesis	321 (36.7)	0
Intercalary grafts	343 (39.2)	106 (63.8)
Osteoarticular grafts	114 (13)	18 (10.8)*
Pelvis	48 (5.4)	15 (9)
Arthrodesis	15 (1.7)†	15 (9)
Spine	28 (3.2)	12 (7.2)
Sternum	6 (0.6)	0

* Upper limb.
†Six ankles and nine knees.

external radiotherapy ($P < 0.01$) and inversely with the age of the recipient ($P < 0.01$): the older the patient, the poorer the consolidation.

Consolidation time was not significantly associated with the use of intra-arterial chemotherapy, intra-operative radiotherapy, donor age, osteosynthesis type (plates *vs.* intramedullary nails), osteotomy type (horizontal *vs.* oblique) or type or location of tumor (Fig. 2).

Consolidation was excellent or good in 82% of cases. Of these, 45% had been stabilized with intramedullary nails and 55% with osteosynthesis plates.

Autografts

The mean consolidation time was 5 months for vascularized and 12 months for non-vascularized autografts. One or more autologous cancellous bone supplementations were required to achieve consolidation in 24% of non-vascularized autografts.

Isotopic Assessment

Table 2 shows the results of the semi-quantitative analysis by isotopic means. In no allograft was uptake rated as 0 (similar to that for soft tissues). Epiphyseal and metaphyseal uptake was the same as in normal bone, and greater than diaphyseal uptake. junction between the allograft and host bone displayed greater uptake than areas within the allograft. It was observed over time that there was greater uptake within the grafts; after sufficient time had elapsed, uptake in the allografts was similar to that in the bone of the contralateral limb (Fig. 3).

Histological Assessment

New bone formation was observed at the host bone–allograft junction; this was mainly periosteal. Allografts contained numerous zones of necrotic bone surrounded by areas of bone in formation. The host bone made use of the bone channels of the allograft to penetrate and carry out a process of resorption and formation of new bone known as "creeping substitution" (Fig. 4A). The external surface of the allograft generally had many vessels arriving from the soft tissues and displayed bone erosion.

The vessels found within allografts (Fig. 4B–D) that had been removed because of infection or fracture reacted positively to Von Willebrand factor, unlike the vessels in

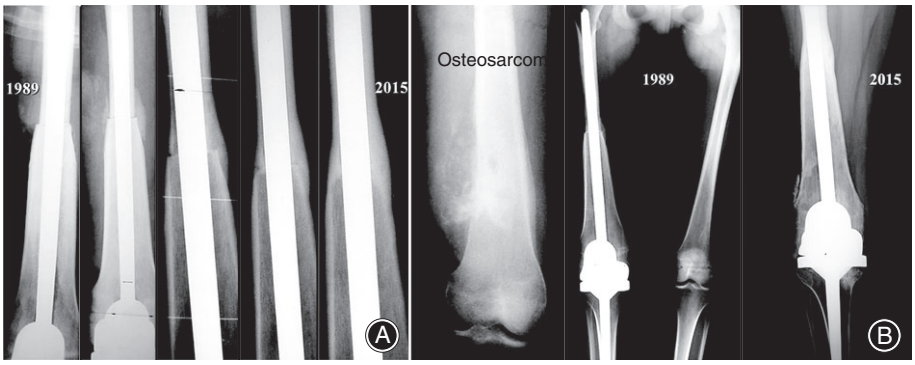

Fig. 2 Example of long-term progress of a composite allograft–prosthesis after resection of a distal femur osteosarcoma in a 14-year-old girl. (A) Consecutive x-ray films showing healing of the diaphyseal osteotomy. (B) Pre-operative, immediate post-operative and last follow-up X-ray films. Note the absence of periprosthetic osteolysis 26 years after the procedure. Healing of the allograft reduces the stress forces on the prosthetic long stem.

TABLE 2 Results of semi-quantitative analysis of isotope uptake in regions of interest

	Mean			Standard deviation			Minimum			Maximum		
	I_1	I_2	I_3	I_1	I_2	I_3	I_1	I_2	I_3	I_1	I_2	I_3
1 (A1/A2)	0.27	0.68	2.31	0.13	0.37	1.41	0.09	0.2	0.42	0.54	1.38	6.00
2 (A1/A3)	0.47	0.98	2.84	0.24	0.45	1.70	0.12	0.2	1.13	0.89	1.90	7.8
3 (A2/A4)	0.91	1.96	4.62	0.59	1.63	2.25	0.41	0.27	2.37	1.94	4.8	8.59

Note: A1, Up-take on allograft; A2, Up-take just above the allograft; A3, The same area as A1, but on the contralateral limb; A4, The same area as A2, but on the contralateral limb; I_1, Index 1, resulting from A1/A2; I_2, Index 2, resulting from A1/A3; I_3, Index 3, resulting from A2/A4.

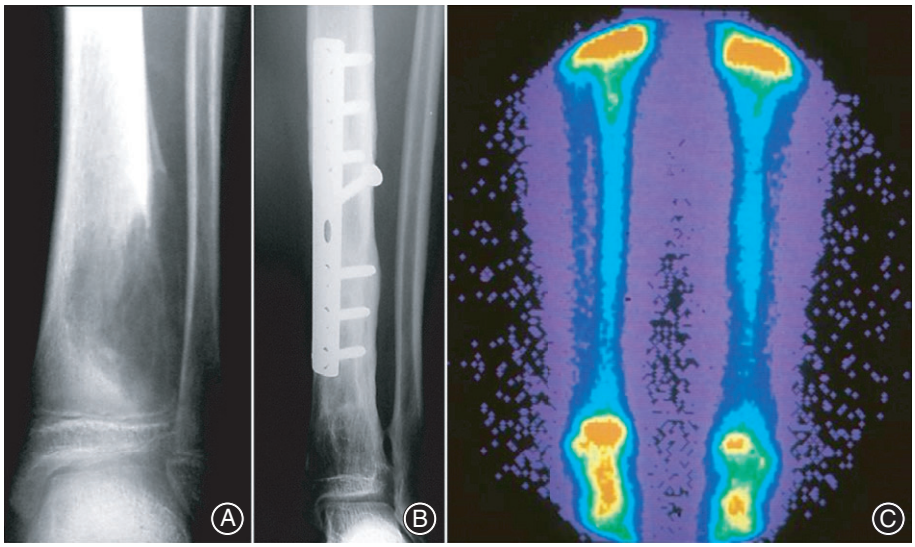

Fig. 3 Example of revascularization of an intercalary allograft of the distal tibia in a 10-year-old girl. (A) Preoperative X-ray film showing a lytic lesion in the distal metaphysis of the left tibia. (B) The tumor was resected by using the Cañadell technique (physeal distraction before excision) and the limb reconstructed with an intercalary allograft. (C) 2 years after surgery, bone scan image showing isotope uptake is similar in both legs.

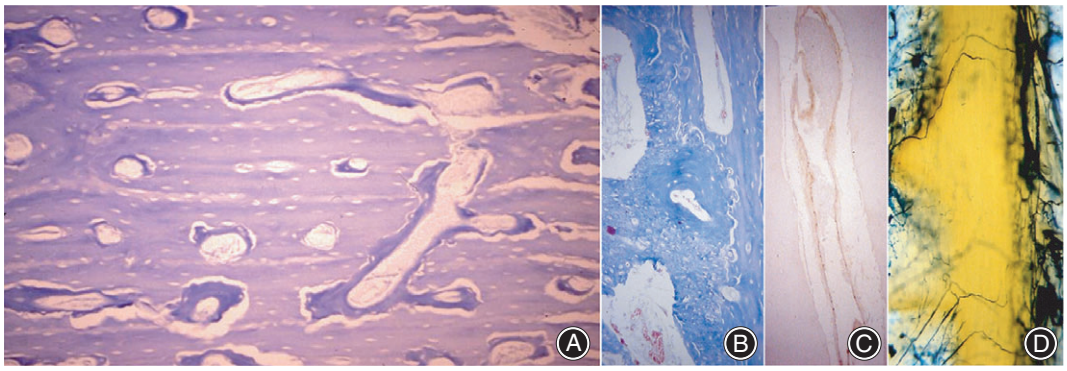

Fig. 4 Histological studies showing integration of a retrieved human cortical allograft 3 years after implantation: (A) Creeping substitution of new bone (dark blue) through allograft vascular channels (Masson Trichrome stain; ×100). (B) Vascular penetration into the allograft (Masson stain; ×150). (C) Immunohistochemistry study: von Willebrand factor demonstrating presence of living endothelial cells inside the allograft (×100). (D) Spalteholz staining shows vessels (dark blue) crossing the allograft cortex (yellow; ×260).

control group allografts, which were negative to this stain. Fluorescent markers confirmed the development of new bone within the allografts (Fig. 5).

Complications

Complications associated with allografts comprised non-union (16.2%), fractures (8.2%) and infections (11.8%).

Infection (11.8%)

The microorganism most frequently isolated was *Staphylococcus epidermidis*, which is most often the bacterium responsible for contamination at the time of extracting allografts. Most infections (>80%) were associated with a reoperation procedure related to another complication, such as non-union or fracture, which means a mean time of 2 years after implantation. In 4% of cases, the infection was late (3–8 years after implantation, mean 4 years) and secondary to another focus of infection (for example, in a tooth). Only 1.6% of all allografts became infected at the time of implantation. There were no significant differences in the rate of infection between types of allograft.

Fractures (8.2%)

Allograft fracture occurred in 14% of patients with non-intramedullary systems of osteosynthesis, in 30% of patients with plate and nail osteosynthesis, and in less than 1% of patients with osteosynthesis by intramedullary nail alone. Fractures occurred in 15.4% of osteoarticular allografts, 12% of intercalary allografts, 4% of composites allograft-prosthesis and 6% of other types of allografts. Most fractures occurred after an injury, usually after the graft had healed to the host bone (mean 2 years after implantation). Half of them were managed successfully by osteosynthesis and autologous bone grafting (Fig. 6), the remaining ones

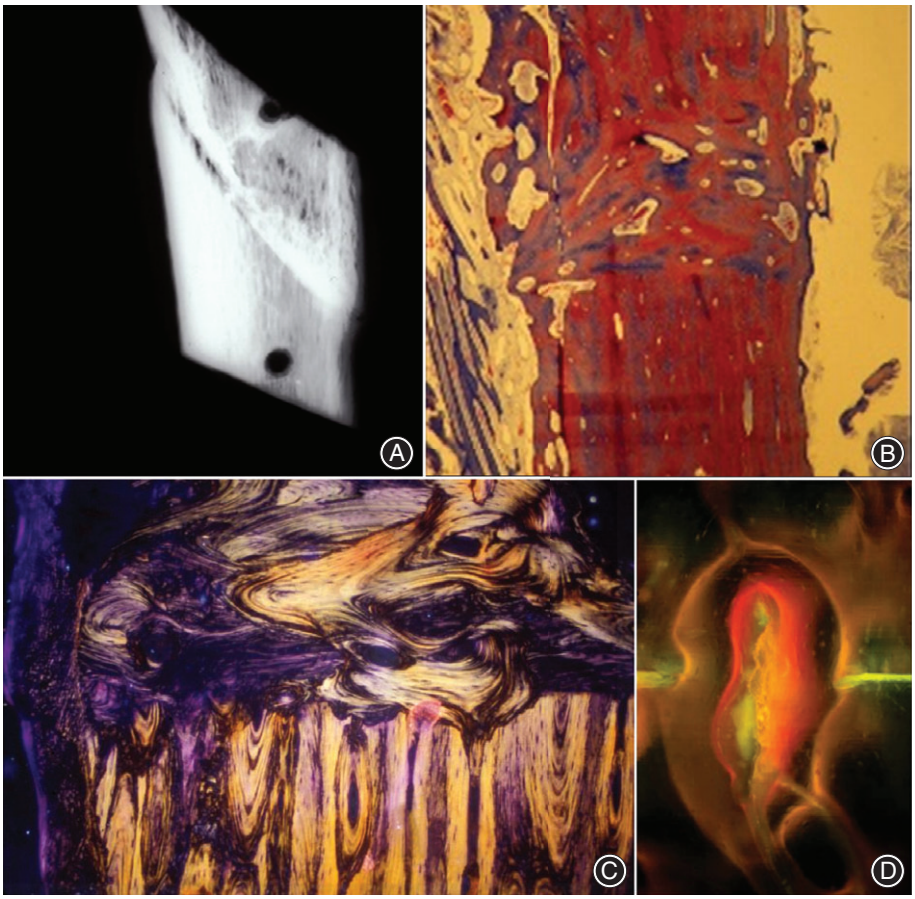

Fig. 5 Example of integration of an allograft. An 18-year-old girl had an osteosarcoma in her right femur removed; reconstruction was carried out with an intercalary allograft. Eight years later, she had a comminuted fracture and a new allograft was substituted. Some days before retrieving the first allograft, tetracycline was given to the patient to enable assessment of the junction between the allograft and the host bone. (A) X-ray film of the diaphyseal osteotomy line showing a perfect junction and some holes denoting the screws of the plate used as osteosynthesis device. (B) Masson staining of the fusion zone (×60). (C) Tetracycline staining showing the osteotomy line (×100). (D) An osteon crossing the osteotomy line in the fluorescence study (×300).

requiring allograft exchange because of comminution (Fig. 7).

Non-union (16.2%)

Eighty-two per cent of allografts consolidated after the initial operation. A further 15% of allografts required the contribution of an autologous insert. The remaining 3% did not consolidate and another allograft was substituted that did.

HLA Compatibility

We were able to study histocompatibility in 43 patients with allografts from multi-organ donors of known HLA type. Their mean follow-up was 2 years. Table 3 shows the relationships between complications and compatibility or non-compatibility of HLA antigens type I and II between donor and recipient. Although the incidence of complications was higher in the non-compatible group, we found no significant relationship between HLA compatibility (or lack thereof) and non-union, fracture or infection of an allograft.

Functional Results

Table 4 shows the functional results (by MSTS score) by allograft or autograft type.

Discussion

Incorporation of Allografts

Incorporation of bone allografts was assessed histologically, by an isotopic method and radiologically. Chemotherapy delays the consolidation of grafts, as does radiotherapy; experimental studies have demonstrated that the latter is because radiation damages the vasculature of adjacent tissues[13]. In our experience, the age of an allograft recipient is a third factor that has a negative effect on achievement of consolidation: the older the patient, the greater the difficulty in achieving consolidation. The same is true for fractures in general, that is, younger patients have a greater capacity for osteogenesis. However, in our series, we were unable to confirm that site, age of donor, allograft length, or type of osteotomy or osteosynthesis influenced the consolidation time.

An isotope uptake study performed at least 2 years after implantation revealed revascularization in allografts. The degree of isotope uptake was similar to that in the same bone of the contralateral limb. We observed photopenia only in allografts that had been in place for a short time. This time-dependency may be related to inhibition of revascularization as a result of chemotherapy in the immediate postoperative period. Uptake in the periphery of the allografts indicated that vessels from adjacent soft tissues had penetrated them. Most

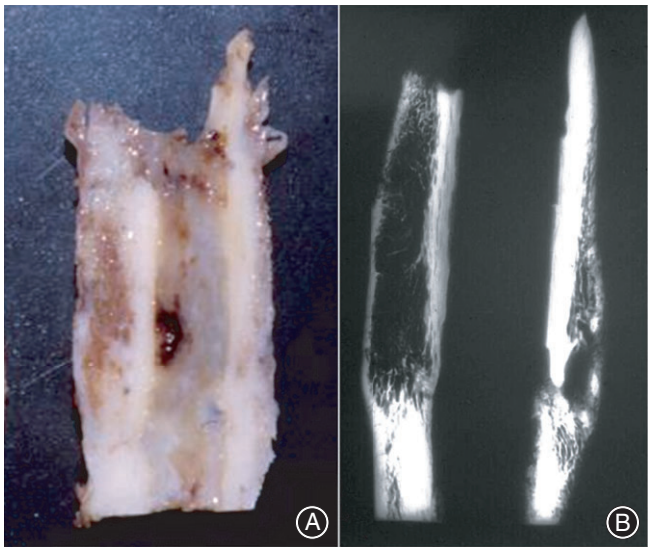

Fig. 6 Representative case demonstrating healing of allograft fracture. The allograft of a 20-year-old woman fractured and was managed by osteosynthesis and bone autograft. Several years later the allograft had to be removed because of another fracture. Images of the healing of a fracture in an allograft: (A) Macroscopic view and (B) X-ray film of the retrieved allograft after a previous fracture. The healing of the fracture occurred through formation of periosteal callus.

of the allografts showed increased uptake at the junction between host bone and allograft, even when consolidation had already taken place. We therefore cannot relate increased uptake to the consolidation process, but rather to greater penetration by vessels at the ends of the allograft than around the periphery. As a result of this revascularization process, allografts therefore have a characteristic bone scan pattern[14].

Basically, there are three aspects to the integration of bone grafts: (i) osteoinduction, which refers to recruitment of multipotent cells from host tissues, requires migration, proliferation and differentiation of the cells surrounding the implantation of a graft; (ii) osteoconduction, which provides back up for bone deposits; and (iii) the graft itself as a source for the formation of bone cells[15,16]. Cortical bone integration is achieved by a mechanism known as creeping substitution, which denotes gradual resorption of the graft with simultaneous replacement by new bone, that is, the new bone creeps into the dead structure[3]. To achieve this, the newly-formed bone makes use of the Haversian and Volkmann channels in the cortical bone and the trabecular spaces in cancellous bone. This is a slow process in which the osteoclasts erode the transplanted bone while the osteogenic cells from the new osteoid simultaneously revitalize the graft. A periosteal bridge is formed from the host bone in the areas of the diaphyso-diaphyseal junction; this bridge tends to engulf the end of the allograft. Rupture and coagulation of the blood vessels of the Haversian systems close to the osteotomy induce bone necrosis, and these areas, which are starved of blood, play a passive part in consolidation. However, in the junction with the metaphysis, the trabeculae grow from the host bone and penetrate the allograft. This growth occurs more quickly than the formation of the periosteal bridge at the diaphyseal junction. In addition to the periosteal and endosteal bridges, vessels penetrate the allograft from the surrounding soft tissues, as shown by the isotope study. Therefore, a twofold vascular invasion takes place from the ends, at the junction between the host bone and graft, and to a lesser extent from the soft tissues surrounding the graft. This clarifies why it is so important that all bone grafts should be well covered by soft tissues.

Two mechanisms act towards revascularization of an allograft. At the endosteal and periosteal surfaces of the allograft, the appearance of mesenchymal cells (fibroblasts) gives rise to osteoclasts that erode the surface of the allograft. These osteoclasts are always accompanied by osteoblasts, which form new bone[15–19]. Our findings are, therefore, in agreement with those of other authors, who state that integration of a cortical bone graft can occur through two mechanisms that generally go together: progressive erosion of the surface of the allograft, and replacement of the intra-cortical bone as a result of long-term penetration of the pre-existing Haversian systems[20–22].

The gradual nature of the process of integration of an allograft accounts for the difficulties in the treatment of the commonest complications: infection, non-union and fracture[9,23,24]. Healing of an infected allograft often requires its removal: the slow penetration of blood vessels into the allograft makes it difficult to achieve a high enough concentration of antibiotics to eradicate the infection. Similarly, development of fractures in a bone that has been partially necrotic for a long time is understandable. Nevertheless, because good stabilization allows periosteal and endosteal bridging, thus helping the fracture to heal, fractures of allografts can be treated by osteosynthesis as though they were normal bones[25]. As other authors have indicated, there seems to be no relationship between HLA compatibility and the incidence of complications, suggesting the ways grafts integrate depend on their compatibility with host bone[5].

Functional Results

We obtained our best outcomes with intercalary auto- or allo-grafts. It was for this reason that Cañadell conceived of and developed the technique of performing epiphysiolysis, which makes it possible to preserve the joint if a tumor is metaphyseal, prior to tumor resection[1]. In many such cases, the functional outcome is so good that patients can recommence sports activities[26,27].

In particular, intercalary autografts are an excellent option for reconstruction in subjects with small tumors that have not invaded the epiphysis[28] (Fig. 8). Long-term results support use of this type of reconstruction. The problem is that with large tumors (as the majority are: the mean length in our series of over a thousand allografts was 19 cm) it is not possible to reconstruct with an autograft because of the limited availability of material. Regarding pelvic tumors, note

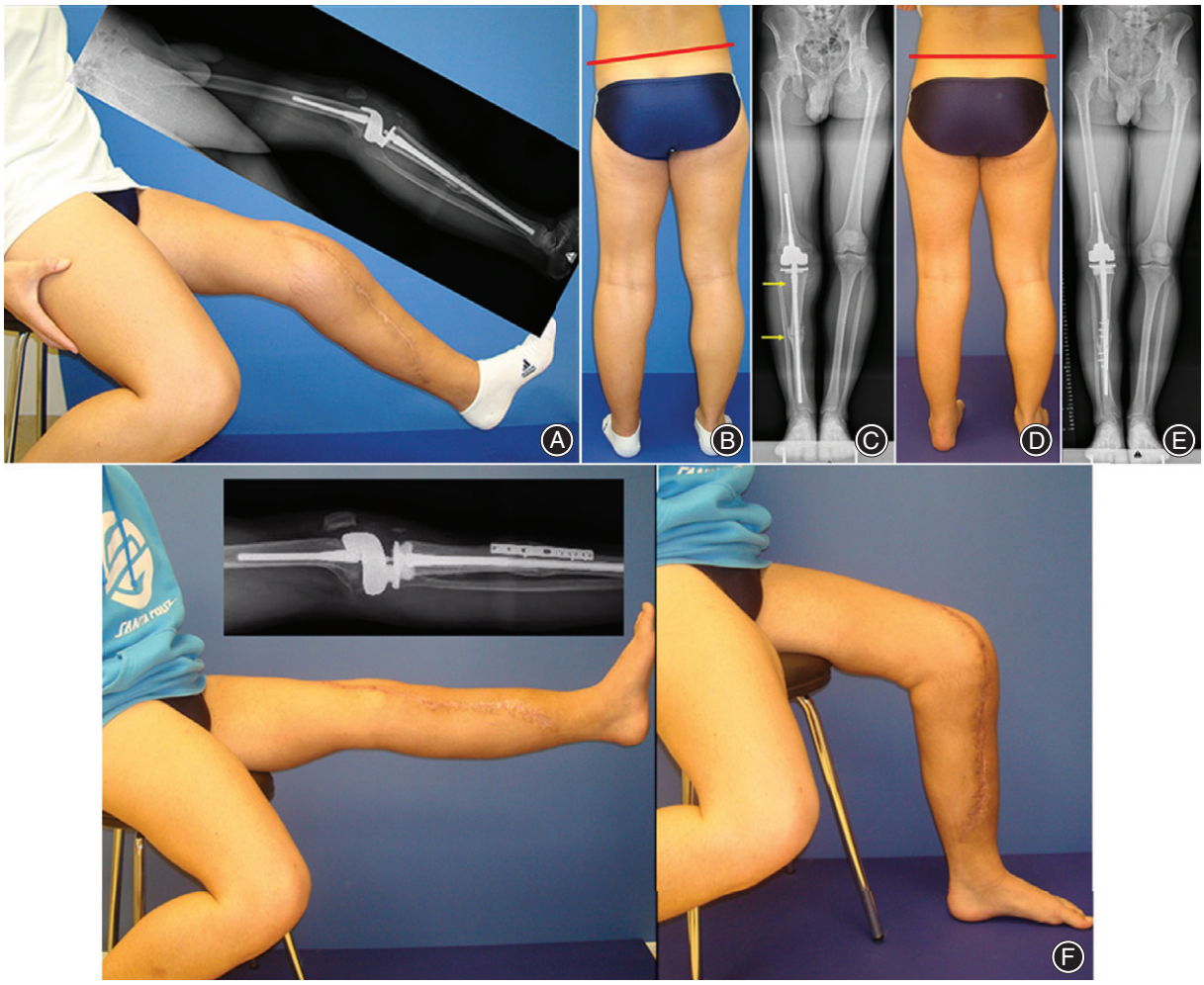

Fig. 7 Representative example of treatment of complications of an allograft. A 17-year-old boy had an osteosarcoma in his left proximal tibia, treated by resection and reconstruction with a composite allograft-prosthesis. This patient had three complications: (A) Detachment of the patellar tendon from the allograft and loss of full extension of the knee. (B) and (C) Limb length discrepancy due to aseptic loosening secondary to non-union and fracture of the allograft (arrows). (D) and (E) Correction by exchanging the allograft, adding a plate and an autologous cancellous graft. (F) X-ray film and function at the last follow-up.

TABLE 3 Number of complications according to histocompatibility (cases)

	Non-union		Fracture		Infection	
Histocompatibility	Yes	No	Yes	No	Yes	No
No compatibility	5	15	4	14	7	13
Compatibility						
Type I	2	8	2	10	1	8
Type II	1	3	1	4	1	4
Type I & II	1	8	1	7	1	8

TABLE 4 Percentage of excellent and good functional results (MSTS scores) according to graft type (%)

Type of graft	Cortical allografts	Cortical autografts
Composite graft-prosthesis	82	–
Intercalary	88	93
Osteoarticular	76	80 (upper limb)
Pelvis	40	82
Arthrodesis	73	76

that we obtained much better functional results with autografts than with allografts; this is largely attributable to the fact that we used autografts for small tumors, which were mainly in zone I (Fig. 9).

Complications

Most infections in our series occurred after reoperation for another complication, such as, non-union or fracture. Consequently, reducing the number of fractures (by protecting the allograft with an intramedullary nail or osteosynthesis plate

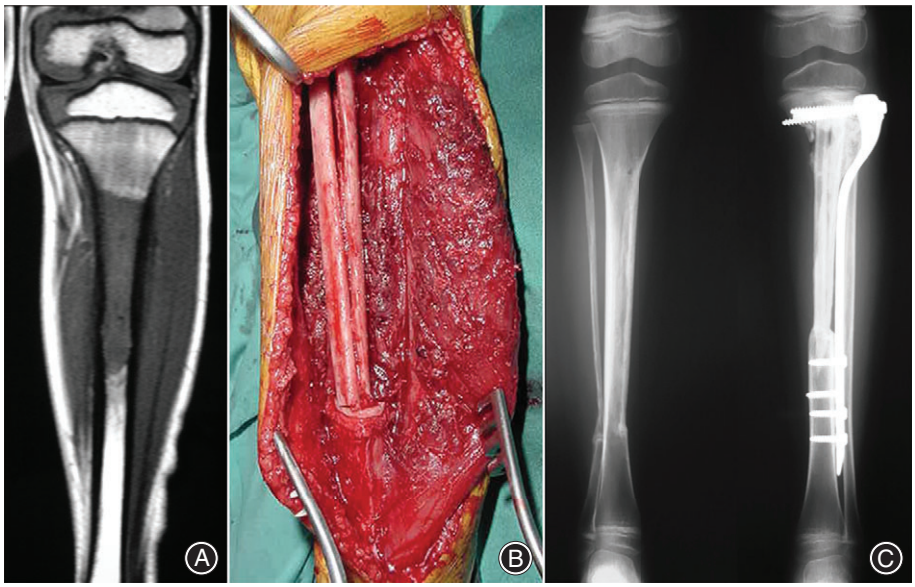

Fig. 8 Example of a resection of a small tumor (Ewing sarcoma in the tibial shaft of a 4-year-old patient) and reconstruction with an autograft. (A) Pre-operative MRI showing a relatively small tumor that is far away from the proximal physis. (B) Reconstruction was performed with a non-vascularized contralateral fibula and a "window" of tibia. (C) X-ray films of both limbs showing healing of the grafts and spontaneous reconstruction of the donor sites.

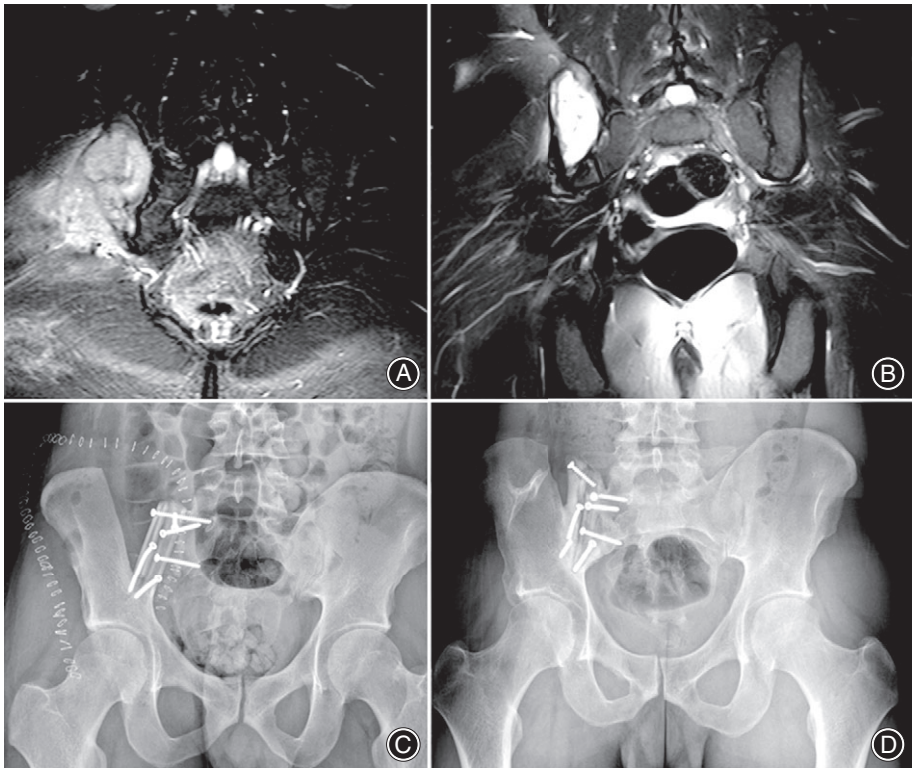

Fig. 9 Example of the use of autografts to reduce complication rates in difficult locations like the pelvic ring: 19-year-old boy with a Ewing sarcoma of the pelvis (sacroiliac joint) resected and reconstructed by autograft: (A) Pelvic MRI at diagnosis. (B) MRI after neoadjuvant chemotherapy showing a very good response to neoadjuvant chemotherapy. (C) Postoperative X-ray film showing reconstruction of the pelvic ring with autologous fibula (×2) and screws. (D) Current X-ray film 4 years postoperatively. Despite some screws having broken, the grafts have healed. The patient is completely asymptomatic and is unrestricted in his sports activities.

that bridges it without perforating it) and/or reducing the chances of non-unions (by using stable osteosynthesis approaches, especially in the diaphyso-diaphyseal union), reduces the risk of infection. It is also necessary to know the timing of allograft incorporation. Some authors consider it necessary to add cancellous autograft to the union zones if consolidation is not evident 6 months after implantation[28,29]. The data from our series lead us to disagree because consolidation did not usually occur until after completion of chemotherapy treatment, which normally takes a year. Thus, we can avoid the risks of re-operating as well as the risks at the donor site.

If possible, aseptic and antiseptic measures as well as prophylaxis should be even greater when performing reoperations than for the primary operation. A small percentage (4%) of infections occurred late and was related to

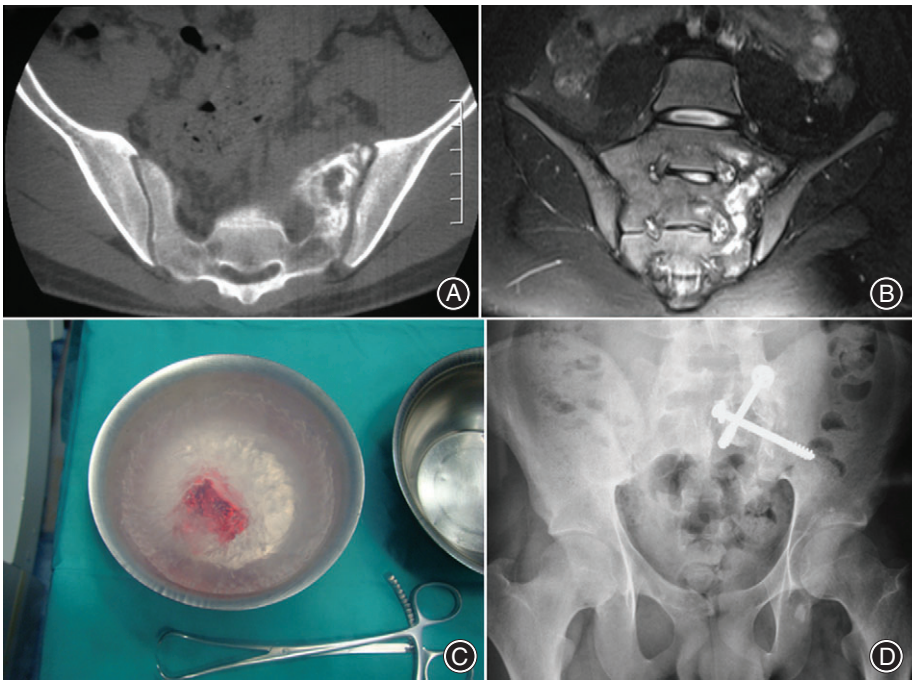

Fig. 10 Example of re-implantation of a tumoral autograft treated by freezing. (A) CT scan showing a destructive lesion in the left side of the sacrum (Ewing sarcoma). (B) MRI after neoadjuvant chemotherapy, showing a good response. (C) Freezing of the resected specimen in liquid nitrogen. Samples of the piece were assessed histologically and no viable cells identified. (D) Re-implantation of the "sterilized" specimen.

bacteremia resulting from an infection at a focus, such as a tooth, other than the original tumor site. Patients should be alerted to this possibility so that if they do have any bacterial infection they can receive suitable treatment in a timely manner, thus avoiding contamination of the allograft. With learning such measures through experience, we have been able to reduce the number of complications[7,30]. Another consideration regarding infection is sterility of the allograft. We consider that individuals who have died as a result of high-energy trauma with visceral injuries are not a good source of allograft material because of the possible blood-borne contamination of the allograft with microorganisms[31].

Most patients with infection required a two-step procedure to change the allograft and resolve the complication.

With non-vascularized autografts, the consolidation success rate was higher in our series; however, the need for autologous cancellous bone was greater. Overall, the infection rate was much lower, as was the incidence of fractures, from which patients recovered much more easily. Fractures of autografts were easily resolved with conservative treatments; it was rarely necessary to replace an autograft as a result of infection. Furthermore, there were no cases of late infection in patients with autografts.

As alternative procedures, we used vascularized fibular grafts periosteum grafts or reimplantation of tumoral bone after it had been extracorporeally "sterilized" with cold or radiation[32–37] (Fig. 10). Vascularized fibular grafts are primarily used for reconstruction of the upper limbs because grafts in the lower limbs must be broader so that they can support the heavier loads. The duration of surgery is considerably longer; however, consolidation is faster than with non-vascularized autografts. Reimplanted tumor-affected bone carries a greater risk of local recurrence of tumor and is structurally more fragile as a result of the sterilization procedure employed. A further interesting option is to use a vascularized autograft in conjunction with an allograft[38].

Conclusions

Non-vascularized intercalary autografts achieve the best functional results for small tumors (up to 10–12 cm in length). Although such grafts need the support of autologous bone to consolidate, in the long term their performance is similar to that of normal bone. Despite the higher incidence of complications, allografts are a good option for reconstruction after resection of larger tumors. To optimize functional results, it is necessary to understand and take into account the mechanisms of incorporation and the measures that can be taken to reduce complications.

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