Allogeneic grafts for bone tumor

21 cases of osteoarticular and segmental grafts

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We treated 21 aggressive and malignant bone tumors by wide resection and replacement with deep-frozen osteoarticular and segmental (intercalary and block) allografts. Radiologic and histologic studies showed a gradual accretion of new bone on the graft trabeculae, sometimes with total creeping substitution. Substantial resorption of grafted condylar bone occurred in 3 of 14 cases. One of them ended with arthrodesis; in the other 2 the result after augmentation autografts was fair. Radiographically, a gradual joint surface destruction was observed in all the osteoarticular grafts after 5 years, not correlating with joint function, however. Biopsies showed some cartilage regeneration. Each patient underwent, on an average, two operations. Function after osteoarticular grafts at 3–16 years was excellent in 1 case, good in 4, fair in 6, and poor in 1 case; 2 cases were too recent for evaluation. Function 3–12 years after segmental grafts was excellent in 3 cases and poor in 3 cases (1 amputation due to nonunion, 1 amputation due to recurrence, and 1 prosthetic replacement due to recurrence); 1 case was too recent for evaluation. We conclude that an allograft is an acceptable alternative in the reconstruction of large tumor defects. However, it still presents unsolved immunologic and preservation problems, which make the prognosis guarded.

In juxtaarticular bone resection for tumor, the joint can be fused (Enneking et al. 1980, Campanacci 1985) or reconstructed with an osteoarticular allograft (Parrish 1973, Volkov and Imamaliev 1976, Koskinen et al. 1979, Mankin et al. 1987, Alho et al. 1987, Delépine 1988) or replaced with an endoprosthesis (Kotz 1983, Sim and Chao 1987). In a large segmental resection the replacement can be done by using an allograft (Koskinen et al. 1979, Mankin et al. 1987) or a segmental prosthesis (Heck et al. 1986).

We report our experiences during a 16-year period as regards graft incorporation, joint preservation, and limb function in 14 cases of osteoarticular allografts about the knee (Koskinen et al. 1979, Alho et al. 1987) and in 7 cases of segmental (intercalary and block) allografts.

Patients and methods

The preoperative examination (Table 1) included conventional radiography, angiography, ^{99m}Tc-MDP scintigraphy, CT (since 1979), and open biopsy. Standard radiographs, supplemented with tomography and CT, were taken to exclude pulmonary metastases.

The tumors were graded as aggressive benign (G0), low-grade malignant (G1), and high-grade malignant (G2), and were staged according to Alho (1984), Table 1. The histologic diagnoses were giant-cell tumor –10, chondrosarcoma –4 (G1 –3, G2 –1), periosteal osteosarcoma –2, fibrosarcoma –2, chondroblastoma –1, Ewing's sarcoma –1, and metastatic hypernephroma –1.

Simultaneously with the preoperative examinations, an allograft was harvested from a suitable cadaver in accordance with the guidelines of the American Association of Tissue Banks (Friedlaender and Mankin 1981): viz., aged 16–50 years, no known infections, no malignant disease, and no known osteopenia factor. The laboratory studies were ESR, WBC, bacteria in the urine, Australia antigen, and test for syphilis and HIV (since 1987). The bone marrow of the graft and the surrounding periosteum were removed retaining parts of ligaments, and in cases of the proximal tibia, the menisci. Bacterial samples were taken for cul-

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Table 1. Clinical data for osteoarticular (Cases 1–14) and intercalary grafts (Cases 15–20)

Case no.	Sex and age	Diagnosis[a]	Grade[b]	Stage[b]	Type and size[c]	Complications
1	M 34	GCT	0	3	DFB 10	Habitual dislocation of patella
2	M 32	GCT	0	3	DFB 12	"Osteochondritis dissecans"; Ligament insufficiency
3	M 34	GCT	0	3	DFB 12	None
4	F 17	CB	0	3	DFB 9	None
5	M 23	GCT	0	3	PTB 15	Fx of graft-host junction
6	M 42	POS	1	3	DFB 12	Resorption, infection
7	M 26	GCT	0	3	DFB 14	None
8	M 23	POS	1	3	DFB 14	Fx of graft-host junction, Fracture of graft; "Osteochondritis dissecans"
9	F 41	CS	1	3	DFB 13	None
10	F 16	GCT	0	2	DFU 7	Resorption
11	M 33	GCT	0	3	DFU 10	Recurrence, "osteochondritis dissecans"
12	F 28	GCT	0	3	DFU 10	None
13	M 22	GCT	0	2	DFB 15	Resorption, fracture
14	M 35	E	2	2	PTB 16	None
15	F 20	FS	1	2	TI 14	Fatigue fracture
16	F 37	FS	1	3	TI 11	Recurrence
17	M 22	GCT	0	2	FBL 8	None
18	F 49	CS	1	2	TI 10	Non-union
19	M 35	CS	1	3	HI 18	None
20	M 48	CS	2	2	FBL 9	Recurrence
21	M 59	HN	2	4	FI 12	None

[a] GCT giant-cell tumor, CB chondroblastoma, FS fibrosarcoma, HN hypernephroma, POS parosteal osteosarcoma, CS chondrosarcoma, E Ewing's sarcoma.
[b] Grade: 0 benign, 1 low-grade, 2 high grade; Stage:1 intraosseous tumor; 2 intraosseous tumor affecting the cortex, but not extending through the periosteum; 3 tumor extending to surrounding soft tissues; 4 metastatic tumor.

ture before sterile packing. The early grafts were frozen without any cartilage preservative to –70 °C for 48 hours and stored at –20 °C for at least 4 weeks (Koskinen et al. 1979). In the last 5 cases of osteoarticular grafts, we used the slow-freezing, quick-thawing principle (Farrant 1980). The graft cartilage was impregnated with 10 percent dimethylsulfoxide (DMSO) before gradual freezing at +4 °C for 16 hours, at –30 °C for 24 hours, and then stored at –70 °C. The size of the graft was the only matching criterion. Before the transplantation the cartilage was rapidly thawed in warm Ringer's solution.

The tumor was removed en bloc, including biopsy scars, with a wide bone and soft-tissue margin, 1 cm transversely and 3–5 cm longitudinally based on the radiologic studies. After the introduction of CT with improved resolution, the 5-cm margin was narrowed to 3 cm.

In the condylar grafts (9 bicondylar and 3 unicondylar femoral grafts, and 2 bicondylar tibial grafts) the knee ligaments were reconstructed either by reinsertion through drill holes to the graft or by sutures to the ligamentous tufts of the graft. The muscles and tendons were reinserted, but the posterior knee capsule was not sutured.

The segmental resections were two trochanteric block resections and five metaphyseal/diaphyseal intercalary removals: one humerus, one femur, and three tibiae (Figure 1). The trochanteric block resections were made by retaining a bridge of intact calcar femorale, with the remainder being intercalary grafts.

In no patient was the main vessel and nerve bundle affected, although most of the tumors were stage T3. The grafts were fixed with AO compression osteosynthesis, except in Case 14, where locked nails were used. A cuff of autogenous cancellous chips from the iliac crest was created around the graft-host junction (Figure 2). Systemic antibiotics for 1–5 days, suction

Case no.	Reoperations	Result[d] M	P	S/D	S	E/F	C	Overall	Knee motion (degrees)	Follow-up (years)	Figure
1	Removal of implant; Patellectomy	E	G	G	E	F	G	Fair	10–110	16	2
2	Suture of lig. and meniscectomy	G	G	G	G	F	G	Fair	10– 75	11	7
3	None	F	G	G	G	F	E	Fair	30– 70	11	11
4	Removal of implant	E	E	E	E	G	E	Good	0–100	11	
5	Reosteosynthesis and autograft	G	E	E	E	G	G	Good	0– 75	11	
6	Total knee replacement; Arthrodesis	P	G	–	G	P	P	Poor	–	10	6
7	None	F	G	E	G	F	E	Fair	5– 55	10	
8	Reosteosynthesis x 2 Fixation of fragment	F	G	G	G	F	F	Good	10– 55	9	
9	Removal of implant	F	G	E	G	G	E	Fair	0– 60	9	5
10	Autograft	E	G	F	G	F	G	Fair	0–115	9	8
11	Curettage, bone cement	E	E	G	E	G	G	Good	0– 95	4	9
12	None	E	E	E	E	E	E	Exc.	5–115	3	3
13	Autograft	F	E	F	G	G	E		10–115	1	
14	None	E	E	E	E	E	E		0–115	1	4, 10
15	Osteosynthesis and autograft: Removal of implant	E	E	E	E	E	G	E		12	1
16	Amputation	–	E	–	E	G	P	P		5	
17	None	E	E	E	E	E	E	E		5	
18	Autograft; Amputation	–	E	–	G	F	P	P		4	
19	None	E	E	E	E	E	E	E		3	
20	Endoprosthesis	G	E	E	G	E	P	P		3	
21	None	E	E	E	G	E	E			1	

[c] DF distal femur, F femur, H humerus, PT proximal tibia, T tibia, B bicondylar, U unicondylar; I intertrochanteric, BL trochanteric block, the length of the graft is given in cm.
[d] Evaluation system of the Musculoskeletal Tumor Society (Enneking 1987): M motion, P pain, S/D stability/deformity, S strength, E/F emotional acceptance/function, C complication. Overall result according to Mankin (1982): E excellent, G good, F fair, P poor.

drainage, and thrombosis prophylaxis were used. In Case 14 of Ewing's sarcoma, adjuvant chemotherapy (Rosen et al. 1981) was given preoperatively and postoperatively.

In the first nine replacements about the knee, the immobilization period in a plaster cast varied from 3 to 8 months, and full weight bearing was allowed between 6 and 14 months (Table 1). Since 1978, we have replaced the plaster cast after 6 weeks with a hinged orthosis for additionally 6–8 weeks. Full weight bearing using a crutch was allowed after 3 months and unprotected weight bearing after 12 months.

In 4 cases the osteosynthesis implant was removed when the host-graft junction was considered strong enough, i.e., 2–3 years after the transplantation. No implant removals have been performed since 1978, and no adverse effects have been found due to this policy.

To determine the incorporation of the grafts, radiography and radionuclide scans were done regularly. Twenty biopsy specimens were taken during operations in 15 cases. CT was used for the late result evaluation.

The overall results 2–16 years after the replacement were evaluated using the classification of Mankin et al. (1982): *excellent* – no evidence of disease and full functional, social, and vocational capacity; *good* – no evidence of disease, stable knee, extension deficit < 10°, range of motion ≥90°, full weight bearing with only occasional pain, and full social and vocational capacity; *fair* – no evidence of disease, slightly unstable knee and/or range of motion less than above, walking aid (cane) and/or restricted social and occupational capacity. Arthrodesis or amputation for graft failure and amputation or prosthesis replacement for tumor recurrence were designated as *poor* regardless of the function.

A B C

Figure 1. Fibrosarcoma of the tibia treated with a segmental resection and intercalary graft (Case 15).
A. Preoperatively.
B. Incorporated graft 2 years later.
C. A fatigue fracture of the graft and plate 5 years after the transplantation was treated by removal of the plate, autogenous subperiosteal graft and plaster cast. The fracture united in 4 months. The result was excellent 12 years later with full function, free knee motion, and 5° reduction in ankle dorsiflexion.

Results

No wound-healing complications and no infections were experienced after allografting. In 1 case where the graft was removed because of resorption, the total knee replacement was complicated by infection and ended in arthrodesis. Two fractures of the 21 bone-plate constructs were experienced.

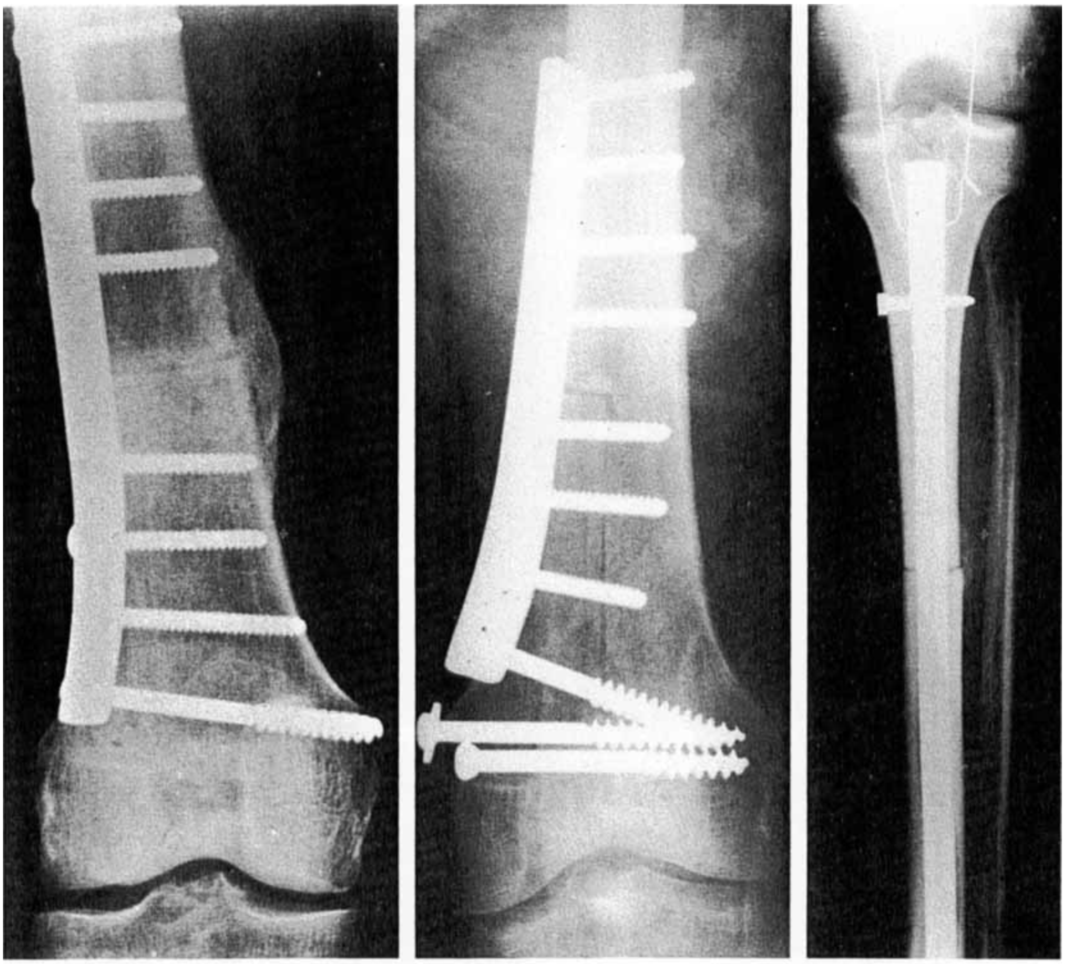
Tumor recurrence

The tumor recurred in 3 cases. A giant-cell tumor was treated successfully with curettage and cementing with polymethylmethacrylate (Case 11). In a case of fibrosarcoma an above-knee amputation was performed (Case 16). The third case a proximal femoral chondrosarcoma was treated with excision and tumor prosthesis without further evidence of disease (Case 20).

Incorporation of graft bone

In most cases, both radiographs (Figure 5) and CT showed an increasing sclerosis of bone. This accorded with the histologic findings (Figure 6) of a gradual accretion of new bone on the necrotic transplant trabeculae. In some of the biopsy specimens, the classical picture of creeping substitution could be seen with a total replacement of the graft matrix by a new, revascularized trabecular network (Figure 7), but this may not be representative for the whole graft.

In the nine osteoarticular grafts, two fractures of the bone plate occurred at the graft-host junction, both during the first year of full weight bearing (Cases 5 and 8). Two patients fractured the graft itself: 1 high-energy trauma after removal of the plate (Case 8), and the other sustained a fatigue fracture of the graft (Case 15, Figures 2–4). All four fractures were successfully



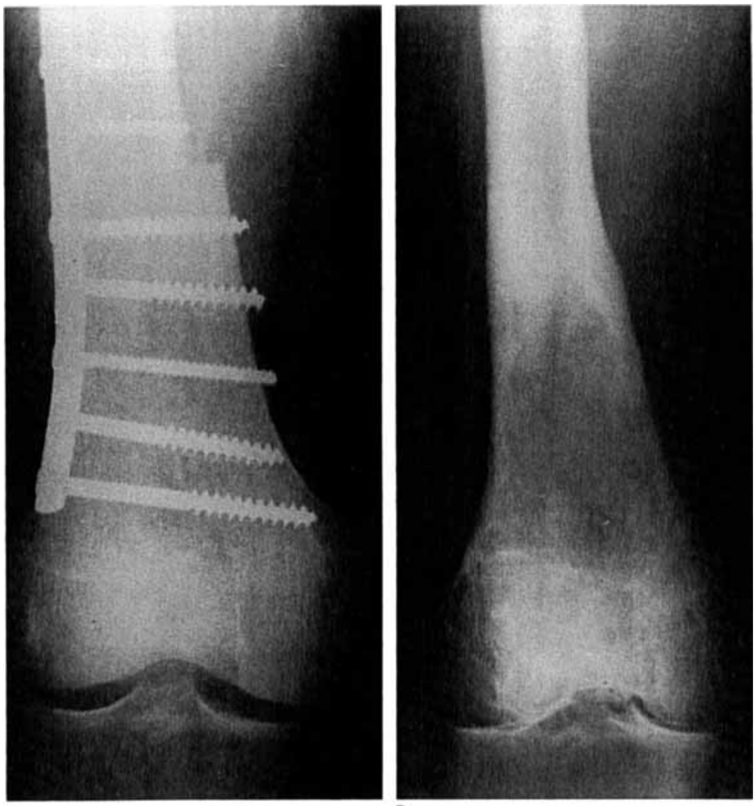
2 3 4

Figure 2. Distal hemijoint allograft fixed with AO compression osteosynthesis. Note the sleeve of autogenous cancellous bone in the graft-host junction. Five years after the operation (Case 1).
Figure 3. Unicondylar femoral allograft replacement. Two months after the operation (Case 12).
Figure 4. Proximal tibial grafting by using locked intramedullary nailing. One year after the operation (Case 14). The result was excellent 12 years later with full function, free knee motion, and 5° reduction in ankle dorsiflexion.

treated with autogenous bone transplantation combined with a new plate fixation in 3 cases. In 1 case the intercalary graft did not incorporate in spite of repeated autogenous sleeve grafting, and the patient preferred an amputation 2.5 years after the allograft replacement (Case 18).

In 3 patients the graft condylar mass showed massive resorption during the first 2 years; in 1 of the patients a total knee replacement was performed (Case 6), whereas autologous bone grafts (fibular struts and cancellous bone) were used in the other 2 patients (Case 10, Figure 8, and Case 13). In 3 other cases a part of the subchondral femoral bone was demarcated as in osteochondritis dissecans (Cases 2, 8, and 11). In Case 8, refixation was carried out using autogenous bone pegs, whereas in the other two no operation was required; in fact, healing of the demarcated fragment could be observed in one of them (Case 11; Figure 9). The subchondral demarcations were observed after the condylar revascularization, as confirmed by biopsy in 2 patients (Cases 2 and 11).

In Case 14 where preoperative and postoperative adjuvant chemotherapy was used for the treatment of Ewing's sarcoma, the radiographs and scintigrams showed increasing incorporation already during the chemotherapy (Figures 1 and 10).



A B

Figure 5. A. Hemijoint allograft replacement after removal of chondrosarcoma (Case 9).
B. The graft was oversized, but the functional result was good 9 years later. Remodeling of the proximal end of the graft and patchy sclerosis as a sign of uneven bone accretion. Narrowing of the joint space in nonweight-bearing radiograph as a sign of cartilage degeneration.

Survival of joint cartilage

Biopsy specimens were taken of cartilage of nine grafts in which no preservative had been used during the deep-freezing process. In five of the specimens, taken during the first year, the cartilage was dead, containing autolyzed chondrocytes. In two specimens, obtained during the third year, islands of living chondrocytes could be seen. In one biopsy specimen, obtained after 1 year, the entire sample consisted of living fibrocartilage; and in another specimen, obtained after 7 years, living cartilage was seen on living subchondral bone (Figure 5). An improved survival of the transplanted chondrocytes after gradual freezing and DMSO preservation was suggested by a biopsy study. However, long-term follow-up is lacking.

Radiography revealed a gradual deterioration of the joint surface (Figure 11). However, this deterioration was not clearly related to the function of the joints (Figure 12).

Function

In the nine osteoarticular grafts where plaster immobilization was used for 3–8 months, the mobility of the knee 1 year after the reconstruction was excellent in 2 cases, good in 6 cases, and fair in 1 case. With the present postoperative care, function at 1 year was excellent in all 5 cases ($P = 0.010$, Fisher's test). Because the knee motion was a decisive factor for the late result, this improvement had an effect on the late results as well. The overall results gradually deteriorated from 5 excellent, 7 good, and 2 fair at 1 year to 4 good, 5 fair, and 1 poor at 8–16 years (Figure 13).

The functional recovery of the segmental (intercalary and block) grafts was excellent in 3 cases. One patient had a below-knee amputation after a 2.5-year treatment of nonunion with orthosis and autogenous bone grafting (Case 18). Two further poor cases were due to tumor recurrence, 1 ending in an above-knee amputation (Case 16) and the other in hip replacement (Case 20) with a good and excellent functional end result, respectively.

Discussion

Attempts to perform an allograft replacement for a bone defect were made anecdotally in the 19th century.

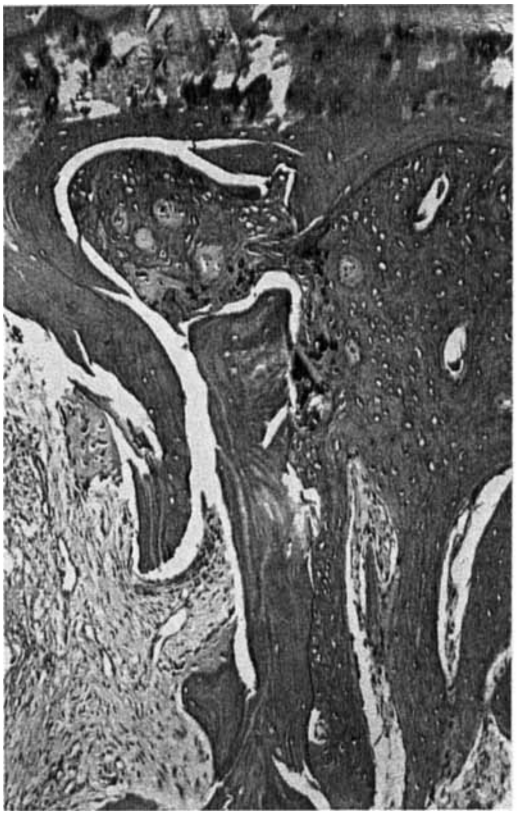


Figure 6. Photomicrograph of biopsy specimen at 18 months showing accretion of new bone (top) onto dead cortical bone, fibrotic tissue (bottom left). The cartilage (right) is dead (Case 6). HE, x280.

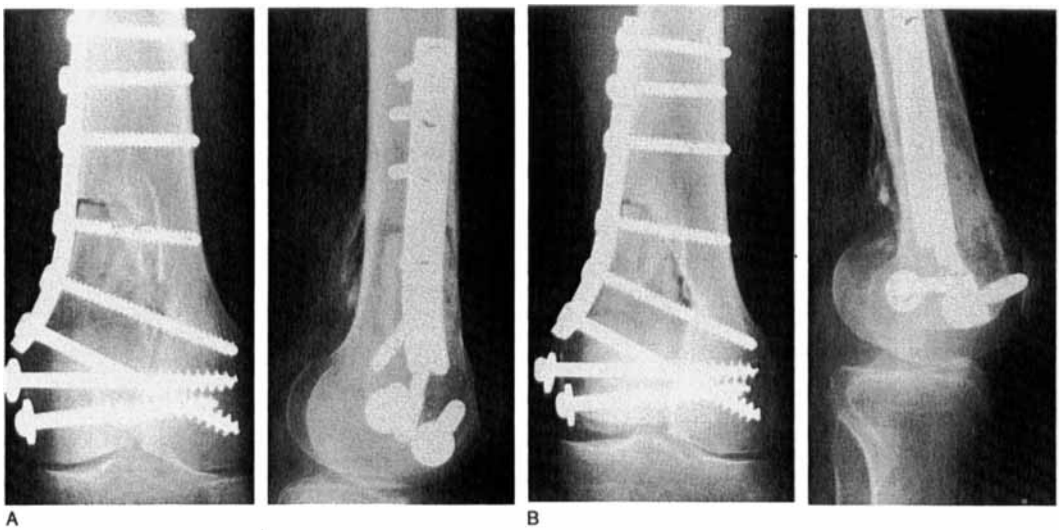
Figure 7. Photomicrograph of biopsy specimen at 7 years showing fibrocartilage (left) and new subchondral bone (right). Note the normal bone marrow in the substituted subchondral bone (Case 2). HE, x140.

Lexer (1908, 1925) used the technique in several cases; he performed his first proximal tibial hemijoint allograft by using a fresh transplant in 1907. More recently, massive osteoarticular allografts preserved by refrigeration have been used in animal experiments and clinically (Parrish 1973, Koskinen et al. 1979, Mankin et al. 1982, 1987, Aho 1985, Søndenaa et al. 1985, Alho et al. 1987).

Allogeneic bone is immunogenic (Chalmers 1959, Bos et al. 1983, Stevenson 1987, Muscolo et al. 1987), and immunosuppression improves the incorporation of experimental bone allografts (Aebi et al. 1987). Freezing also reduces the immunogenicity (Burwell 1969). According to Elves (1978), frozen allogeneic bone does not elicit humoral immune response, but evokes a cell-mediated immune response. Frozen grafts are accepted better than fresh grafts (Burwell 1969, Volkov and Imamalieyv 1976). According to Czitrom et al. (1985), the bone marrow of the graft is especially immunogenic and should therefore be removed. The survival of cartilage is improved either by using fresh grafts (Gross et al. 1984) or by immunosuppression (Aebi et al. 1987).

The slow resorption of graft bone observed in some cases has been interpreted as a retarded rejection (Burchardt 1983). Major rejection reactions have not been observed in the clinical use of massive osteoarticular allogeneic transplantations (Alho 1985, Mankin et al. 1987). However, both slow incorporation of the graft and unexpected resorption may be due to an immunologic mismatch. These problems should be solved for better applicability of allografts. New immunosuppressive agents with few side effects may become useful in selected cases. Also, tissue typing relevant to bone grafting should be improved (Friedlaender and Mankin 1981).

We observed considerable resorption of grafted condylar bone in 3 of our 14 cases. Contrary to the report of Parrish (1973), we did not experience resorption of the shaft portion of the graft. Such resorption may have been due to inadequate stability of the osteosynthesis with impaired bone healing, and not to im-



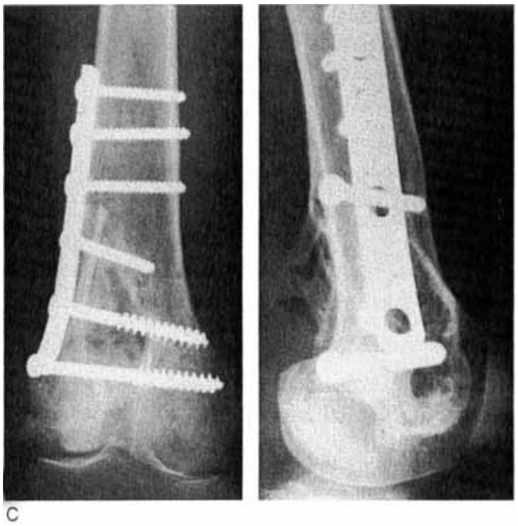


Figure 8 A. Giant-cell tumor treated with unicondylar resection and allograft replacement (Case 10).
A. Beginning of incorporation of the allograft sleeve at 3 months.
B. Disintegration of the graft 8 months after the transplantation.
C. Radiographs 4 years after the reconstruction with fibular struts and iliac cancellous bone. The knee flexion was 0–110°, she had 10° varus and occasional pain after rather long walks.

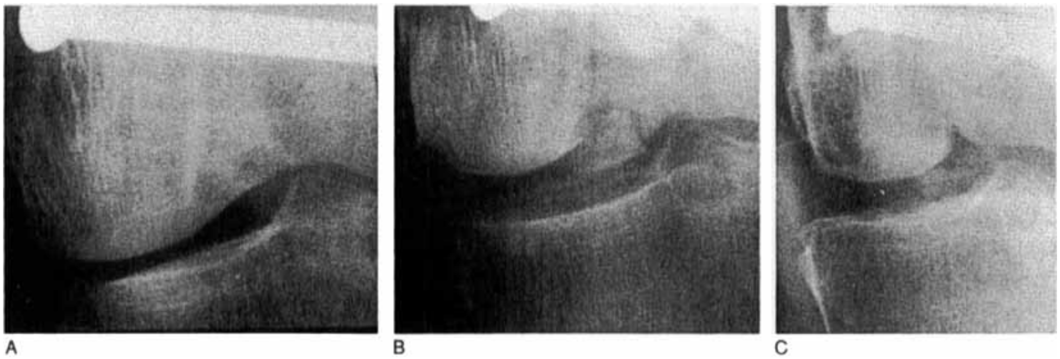


Figure 9. A. Giant-cell tumor treated with extended unicondylar resection at 6 months (Case 11).
B. Demarcation of a subchondral bone fragment at 12 months.
C. Some resorption in the demarcation area with healing by remodeling.

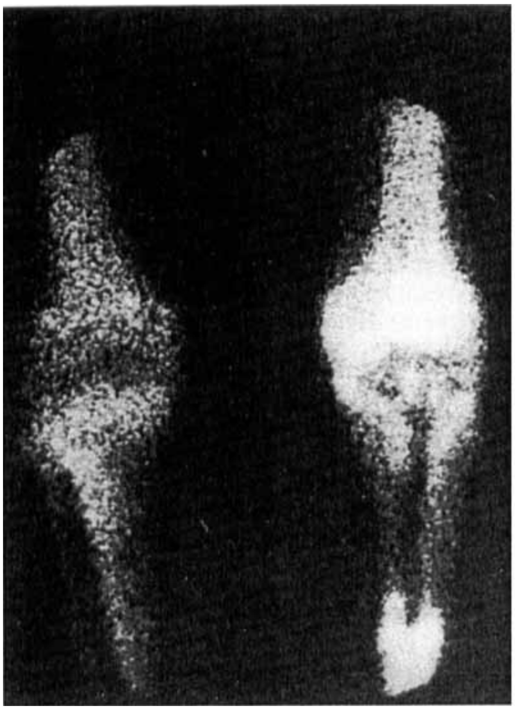


Figure 10. Scintigraphy 3 months after the allograft replacement of a proximal tibial Ewing's sarcoma during adjuvant chemotherapy (oncovin, bleomycin, sendoxan, and actinomycin; Case 14). The reactively increased uptake in the distal femur was present already before the operation.

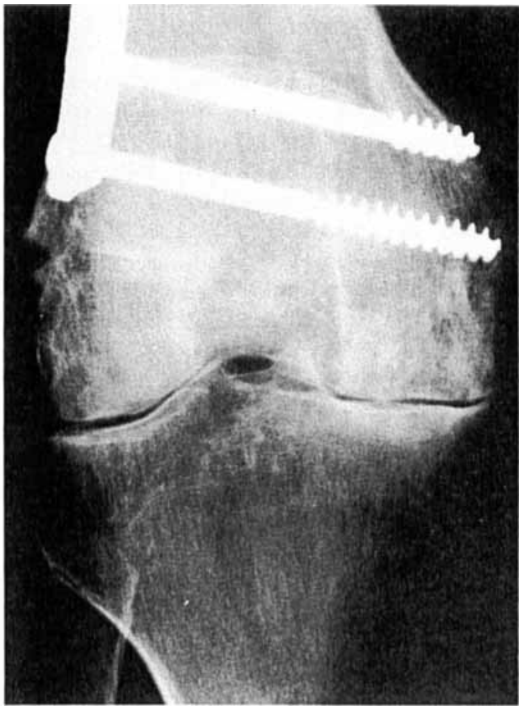


Figure 11. Deterioration of the femorotibial joint surface 10 years after distal femoral bicondylar hemijoint allograft replacement (Case 3). The knee was painless and stable with a range of motion from 30° to 70°. The patient walked without support. The overall result was fair. Nonweight-bearing radiograph.

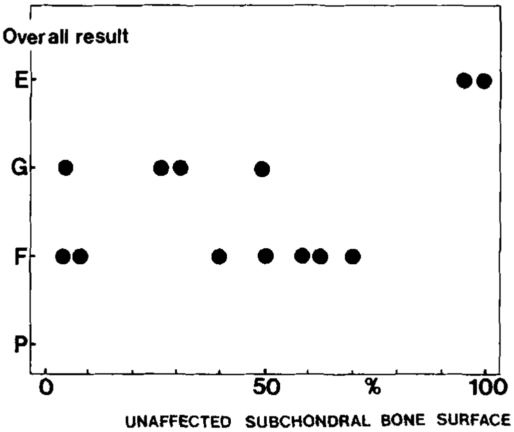


Figure 12. The relation of the radiologically estimated area of functioning graft joint surface to the clinical overall result. The estimation was performed as a mental integration of the findings in the AP and lateral views.

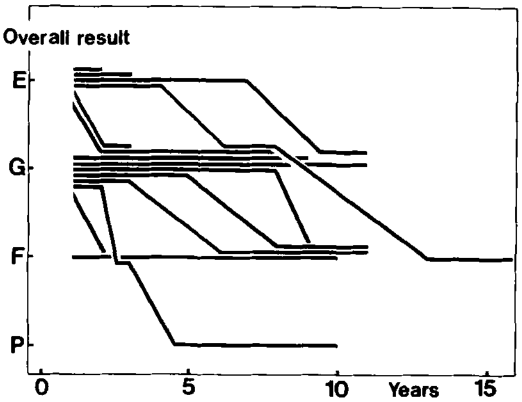


Figure 13. Overall results in the osteoarticular allograft cases according to Mankin et al. (1982).

munologic response. In our cases, stable internal fixation augmented by autogenous iliac grafts usually allowed sufficient time for the incorporation of the shaft.

The fatigue fracture (Case 15) may be explained by the brittleness of the grafted bone and the weakness of the graft-host junction. Therefore, retention of the metal implants seems to be beneficial. Should a fracture occur in the graft-plate-host construct, it is most favorable to have it in the area of the host bone with a normal healing tendency. Based on this point of view, we have stopped removing the osteosynthesis implants.

The survival of transplanted cartilage has been a major problem in many series (Parrish 1973, Alho et al. 1987). Obviously, the chondrocytes survive conventional freezing poorly without a preservative (Salenius et al. 1982). Therefore, based on the reports of the favorable effect of slow freezing with DMSO as a preservative (Farrant 1980, Tomford et al. 1982), we have begun to use such a preservation method.

In our early (Koskinen et al. 1979) and our present analysis, the radiologically demonstrable cartilage destruction was haphazard, and was not correlated with time after transplantation. In accordance with the report of Parrish (1973), the cartilage deterioration was not correlated with the knee function and pain. In this respect the degenerating allograft reminds one of a Charcot joint. It appears that the reinnervation of the graft is poor, which explains the unexpectedly painfree function of the deteriorating graft. Recent pain experienced by some of our first patients may be explained by the secondary destruction of the normal cartilage on the opposite side of the joint after major destruction of the transplanted joint surface. The use of fresh grafts would probably reduce the cartilage survival problem.

Our results are comparable with two previous large series of osteoarticular allograft replacement. Among 17 knee cases with a median follow-up of 3 (2–17) years, Parrish (1973) had two graft failures and one recurrence ending in amputation. Mankin et al. (1987) had 15 percent poor results after 2 or more years.

Among seven segmental grafts, we had one graft failure and two recurrences, one of which could be salvaged with a tumor prosthesis. Mankin et al. (1983) had no failures in 10 grafts. Heck et al. (1986) reported two broken implants among 13 femoral and tibial titanium fiber-metal segmental replacements that were followed for a median of 2.5 (0.5–7) years.

All the series of replacements of large bone defects are loaded with a considerable number of reoperations for various complications. We had 20 reoperations among 21 patients. If the (unnecessary) implant removals are excluded, the reoperation rate was 16 of 21.

An alternative to allograft replacement in juxtaarticular defects is arthrodesis using osteosynthesis and autografts as reported by Enneking et al. (1980) and Campanacci (1985). In their series the reoperation rates were about 50 percent, and the failure rates were approximately 10 percent. Using another alternative, hinged tumor prosthesis of the knee, Sim and Chao (1987) had an 8-year failure rate of 40 percent, reduced to 11 percent by revisions; their reoperation rate was 40 percent.

Except for 1 case of Ewing's sarcoma, our experience from allogeneic grafts is limited to aggressive and low-grade malignant tumors. Only a few reports exist concerning their use in combination with chemotherapy (Dick et al. 1985). Obviously, one has been hesitant to expose the poorly balanced incorporation process of an allograft, with dubiously vital chondrocytes, to the toxic environment of chemotherapy. However, our only case of adjuvant chemotherapy in combination with a massive osteoarticular resection of an Ewing's sarcoma faired excellently with scintigraphic signs of progressive incorporation already during the chemotherapy period.

Lexer (1925) was optimistic when he concluded that allograft transplantation "offers the greatest hope of reestablishing complete function." Clearly, there has been gradual progress in the use of allografts, and there are grounds for guarded optimism. Grafting techniques have improved, and the indications for reconstruction have become clearer. Also, progress is being made in the understanding of cartilage survival and immunologic problems. However, allografts do not present an ideal solution for the problem at present.

References

Aebi M, Schwarzenbach O, Regazzoni P. Long term versus short term immunosuppression in experimental bone allotransplantation. Trans Orthop Res Soc 1987;12:198.

Aho A J. Half joint allograft transplantation in human bone tumours. Int Orthop 1985;9(2):77–87.

Alho A. Staging and management of bone tumours. Acta Orthop Scand 1984;55:580.

Alho A, Karaharju E O, Korkala O, Laasonen E. Hemijoint allografts in the treatment of low grade malignant and aggressive bone tumours about the knee. Int Orthop 1987; 11(1):35–41.

Bos G D, Goldberg V M, Powell A E, Heiple K G, Zika J M. The effect of histocompatibility matching on canine frozen bone allografts. J Bone Joint Surg (Am) 1983;65(1): 89–96.

Burchardt H. The biology of bone graft repair. Clin Orthop 1983;(174):28–42.

Burwell R G. The fate of bone grafts. In: Recent Advances in Orthopaedics (Ed. Apley A G). Williams & Wilkins, Baltimore 1969:115–207.

Campanacci M. Knee resection arthrodesis. In: Limb Salvage in Musculoskeletal Oncology, 2nd Bristol Myers / Zimmer Orthopedic Symposium (Ed. Enneking W F). Churchill Livingstone, New York 1987:3–4.

Chalmers J. Transplantation immunity in bone homografting. J Bone Joint Surg (Br) 1959;41:160–79.

Czitrom A A, Axelrod T, Fernandes B. Antigen presenting cells and bone allotransplantation. Clin Orthop 1985; (197):27–31.

Delépine G, Delépine N. Résultats préliminaires de 79 allogreffes osseuses massives dans le traitement conservateur des tumeurs malignes de l'adulte et de l'enfant. Int Orthop 1988;12(1):21–9.

Dick H M, Malinin T I, Mnaymneh W A. Massive allograft implantation following radical resection of high grade tumors requiring adjuvant chemotherapy treatment. Clin Orthop 1985;(197):88–95.

Elves M W. Cell mediated immunity to allografts of fresh and treated bone. Int Orthop, 1978;2(2):171–5.

Enneking W F, Eady J L, Burchardt H. Autogenous cortical bone grafts in the reconstruction of segmental skeletal defects. J Bone Joint Surg (Am) 1980;62(7):1039–58.

Enneking W F. A system for the functional evaluation of the surgical management of musculoskeletal tumors. In: Limb Salvage in Musculoskeletal Oncology, 2nd Bristol Myers / Zimmer Orthopedic Symposium (Ed. Enneking W F). Churchill Livingstone, New York 1987:4–16.

Farrant J. General observations on cold preservation. In: Low Temperature Preservation in Medicine and Biology (Eds. Ashwood Smith M J, Farrant J). Pitman Medical, London 1980:1–18.

Friedlaender G E, Mankin H J. Bone banking: current methods and suggested guidelines. Instr Course Lect 1981; 30:36–55.

Gross A, McKee N, Farine I, Czitrom A, Langer F. Reconstruction of skeletal defects following en block resection of bone tumors. In: Current concepts of diagnosis and treatment of bone and soft tissue tumors (Ed. Uhthoff H K). Springer Verlag, Berlin 1984:163–74.

Heck D A, Chao E Y, Sim F H, Pritchard D J, Shives T C. Titanium fibermetal segmental replacement prostheses. A radiographic analysis and review of current status. Clin Orthop 1986;(204):266–85.

Koskinen E V, Salenius P, Alho A. Allogeneic transplantation in low grade malignant bone tumours. A new operative technique to avoid amputation. Acta Orthop Scand 1979;50(2):129–38.

Kotz R. Possibilities and limitations of limb preserving therapy for bone tumors today. J Cancer Res Clin Oncol 1983; 106(Suppl):68–76.

Lexer E. Die Verwendung der freien Knochenplastik nebst Versuchen über Gelenkversteifung und Gelenktransplantation. Langenbecks Archiv Klin Chir 1908;86:939–54.

Lexer E. Joint transplantation and arthroplasty. Surg Gynecol Obstet 1925;40:782–809.

Mankin H J, Doppelt S H, Sullivan T R, Tomford W W. Osteoarticular and intercalary allograft transplantation in the management of malignant tumors of bone. Cancer 1982; 50(4):613–30.

Mankin H J, Gebhardt M C, Tomford W W. The use of frozen cadaveric allografts in the management of patients with bone tumors of the extremities. Orthop Clin North Am 1987;18(2):275–89.

Muscolo D L, Caletti E, Schajowicz F, Araujo E S, Makino A. Tissue typing in human massive allografts of frozen bone. J Bone Joint Surg (Am) 1987;69(4):583–95.

Parrish F F. Allograft replacement of all or part of the end of a long bone following excision of a tumor. J Bone Joint Surg (Am) 1973;55(1):1–22.

Rosen G, Caparros B, Nirenberg A, Marcove R C, Huvos A G, Kosloff C, Lane J, Murphy M L. Ewing's sarcoma: ten year experience with adjuvant chemotherapy. Cancer 1981;47(9):2204–13.

Salenius P, Holmstrom T, Koskinen E V, Alho A. Histological changes in clinical half joint allograft replacements. Acta Orthop Scand 1982;53(2):295–9.

Sim F H, Chao E Y O. Prosthetic implants in limb salvage after musculoskeletal tumor resection. Report. Dept Orthop, Mayo Clinic, Rochester, MN 55905, 1987.

Stevenson S. The immune response to osteochondral allografts in dogs. J Bone Joint Surg (Am) 1987;69(4): 573–82.

Søndenaa K, Alho A, Nielsen R. Cryopreservation of osteo chondral grafts in rabbits. Acta Orthop Scand 1985; 56(3):218–22.

Tomford W W, Fredericks G R, Mankin H J. Cryopreservation of intact articular cartilage. Trans Orthop Res Soc 1982;7:176.

Volkov M V, Imamaliyev A S. Use of allogenous articular bone implants as substitutes for autotransplants in adult patients. Clin Orthop 1976;(114):192–202.