Intramedullary, antibiotic-loaded cemented, massive allografts for skeletal reconstruction

26 cases compared with 19 uncemented allografts

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We compared the outcomes of 26 intramedullary cemented massive allografts with 19 allografts without cementation; all allografts were used for reconstruction after excision of bone sarcomas. In the cementation group, 12 allografts were used as osteochondral grafts (proximal humerus 4, proximal tibia 4, and distal femur 4), 7 as intercalary diaphyseal allografts of the femur, and 7 for a knee arthrodesis. In the uncemented allografts, 3 allografts were used as osteochondral grafts (proximal humerus 2, proximal tibia 1), 2 as intercalary diaphyseal allograft of the femur, and 14 for a knee arthrodesis. The average length of follow-up was 40 (25–60) months. 14 of 26 cemented allografts had an excellent (osteotomy line: not visible) or good (fusion ≥ 75% of the cortical thickness) healing of the junction site. Infection developed in 1 allograft. Fracture occurred in 4 of 12 cemented osteochondral allografts due to a subchondral collapse (all in the proximal tibia). Fractures at the junction site in the lower extremity developed in 4 of 22 cemented allografts. In 19 allografts without cementation, 11 had excellent or good healing of the junction. Late infection developed in 4 allografts, fracture of the allograft in 3 cases, and junction fracture in 3 of 17 patients with reconstruction of the lower extremity. Intramedullary graft cementation seems to reduce the fracture and infection rates.

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Infection, fracture, and nonunion are the commonest problems in allograft reconstruction (Tomford et al. 1981, Lord et al. 1988, Berry et al. 1990, Cara et al. 1994, Dick and Strauch 1994, Ozaki et al. 1996). If polymethylmethacrylate (PMMA) is not placed at the junction site, it does not affect the allograft healing adversely in animal experiments (Straw et al. 1992). We have used cement with gentamyicin and vancomycin to fill the marrow cavity of allografts to try to reduce the infection and fracture rates. We report our experience with 26 cases.

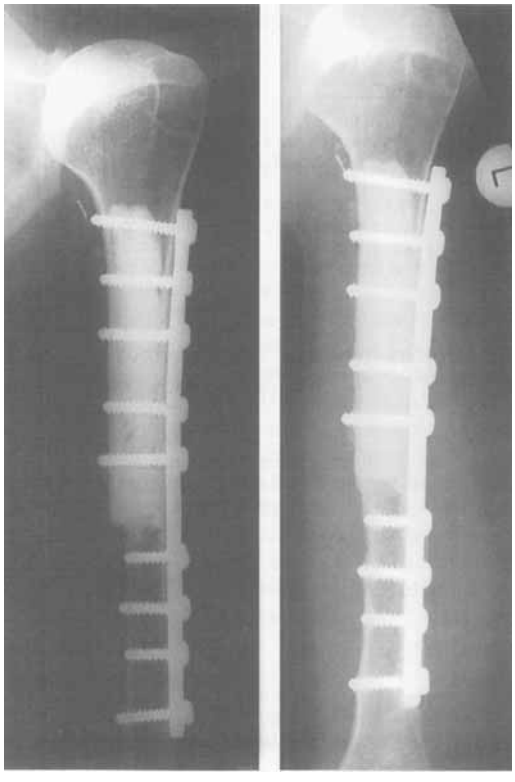
Patients and methods

Between 1991 and 1993, 45 patients who had a bone tumor of the extremities were treated in the Orthopedic Department of Münster University Hospital with excision and allograft reconstruction. From 1989 to 1990, 19 patients underwent allograft implantation without bone cement. These 19 patients were regarded as a control group. Between 1991 and 1993, 26 patients underwent an intramedullary PMMA-packed osteochondral or intercalary allograft (Table 1).

The allografts were used in 3 types of reconstruction: osteochondral allografts, intercalary diaphyseal allograft of the femur, and arthrodesis of the knee joint. At the junction site between the cemented allograft and the recipient bone, osteosynthesis was performed, using 1 or 2 plates with several cortical screws. In the cemented group, 3 of 12 osteochondral allografts, 3 of 7 intercalary allografts of the femur, and 6 of 7 allograft arthrodeses of the knee joint were fixed with 2 plates.

In 19 allografts without cementation, 2 of 3 osteochondral allografts, 1 of 2 intercalary allografts, and 12 of 14 allograft arthrodeses of the knee joint were fixed with 2 plates. Cement, including gentamicin (Palacos®), was mixed with 1 gram vancomycin per 10 grams of cement. The intramedullary cavity of the allograft was reamed and filled with this antibiotic-loaded cement. The junction sites were free of cement, to provide a close host-allograft bone contact. An additional autogeneic bone graft is not performed

Figure 1. Case 2. 15-year-old girl with osteosarcoma of the proximal humerus.



2 months after surgery.

52 months after surgery showing complete healing of the junction site.

primarily. It was performed 9 times when no evidence of callus at the junction site was noted radiographically at the follow-up examination after the postoperative chemotherapy.

16 patients with osteosarcoma in the cemented group and 12 patients with osteosarcoma in the uncemented group received chemotherapy, according to the COSS protocol (Winkler et al. 1990). 9 patients with Ewing's sarcoma in the cemented group and 2 with Ewing's sarcoma in the uncemented group received chemotherapy according to the CESS protocol (Jürgens et al. 1989). 9 patients with Ewing's sarcoma in the cemented group and 2 patients in the uncemented group received preoperative irradiation: median 54 (45–55) Gy. 1 patient with Ewing's sarcoma in the cemented group received intraoperative 10 Gy brachytherapy (Ozaki et al. 1997).

Allografts were obtained from cadaver donors meeting the selection criteria of the European Association for Musculoskeletal Transplantation (EAMST) (1990). 17 allografts with cementation and 12 without cementation were sterilized by γ-radiation from radioactive cobalt at a dose of 26,000 gray.

All patients received intravenous antibiotic therapy (first generation of cephalosporin) at the start of surgery and continued for 14 days postoperatively. Oral antibiotic prophylaxis was given for 3 months after surgery (first generation of cephalosporin). Hemovac drains were removed after the total volume of the drainage fell below 20 mL/day. In patients who underwent an osteochondral allograft of the distal femur or proximal tibia, partial weight bearing was started between 3 and 6 months postoperatively and full weight bearing began 12–16 months after surgery. In patients who had an intercalary allograft, partial weight bearing started between 2 and 4 months and full weight bearing began between 8 and 13 months after the implantation. Patients were followed routinely as outpatients at 3-month intervals and were studied by means of radiographs. The median length of follow-up was 40 (25–60) months.

At each follow-up examination, the union of the graft to the host bone was classified into 4 grades, according to ISOLS (1991). In cases of postoperative infections, the allograft was removed and the patients underwent extensive debridement plus gentamicin-polymethylmethacrylate (PMMA) bead implantation. After infection control, salvage surgery was planned.

Results

Union

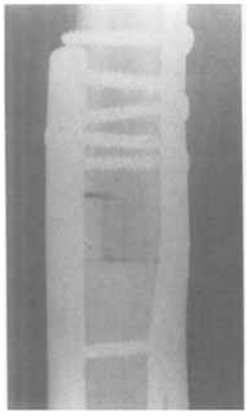
9/26 patients with cemented allografts and 5/19 patients with uncemented allografts had nonunion at the junction site and underwent supplemental autogeneic cancellous bone grafting. The radiological follow-up was performed 2 years after the implantation in all but 4 cases with subchondral collapse or infection. Excellent or good junction healing was noted in 14/26 cemented allografts and 11/19 uncemented allografts (Figures 1 and 2, Tables 1 and 2).

Fracture

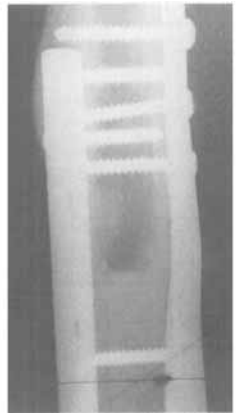
3 types of fractures were noted: a subchondral allograft collapse, a fracture at the junction site between the allograft and the recipient bone, and a fracture of the recipient bone, proximal to the junction.

In the cemented allografts, fractures of the allograft itself were noted only as subchondral collapse of all 4 proximal tibia osteochondral allografts. 3 fractures were located at or near the top of the packed PMMA cement (Figure 3) and 1 fracture occurred at the hole in the allograft which was made for ligament insertion. Subchondral bone collapse did not occur in uncemented allografts in the lower extremity. In all

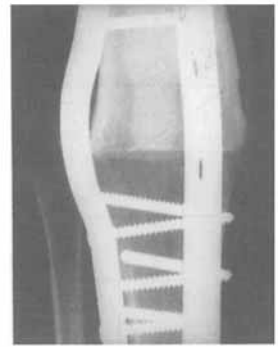
Figure 2. Case 26. 19-year-old man with osteosarcoma of the distal femur.



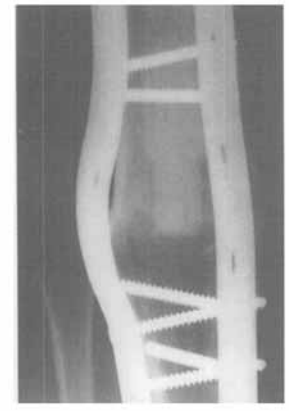
The proximal junction site 3 months after surgery showed clearly visible line of the junction (proximal–recipient site, distal–allograft).



The proximal junction site 36 months after surgery showed complete union of the junction site.

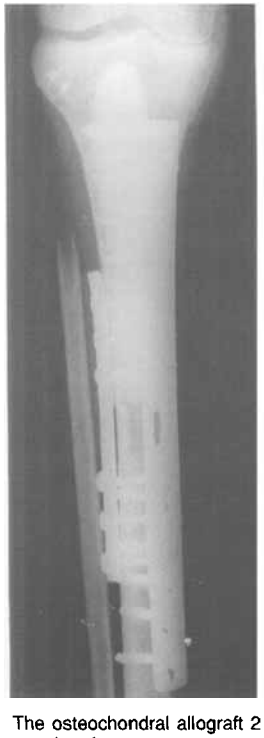


The distal junction site 3 months after surgery showed clearly visible line of the junction (proximal–allograft, distal–recipient site).



The distal junction site 36 months after surgery showed complete union of the junction site.

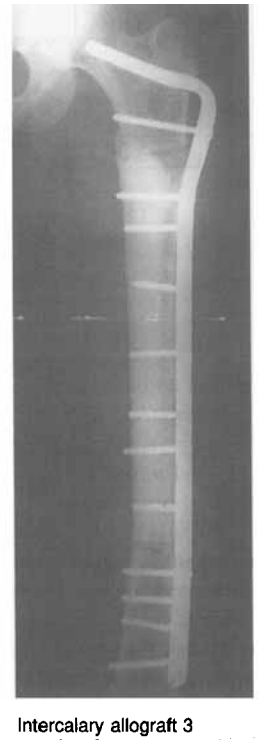
Figure 3. Case 8. 21-year-old man with osteosarcoma of the proximal tibia.



The osteochondral allograft 2 months after surgery.

Subchondral bone collapse at 13 months after implantation.

Figure 4. Case 16. 24-year-old woman with Ewing's sarcoma of the femur.



Intercalary allograft 3 months after surgery.

A fracture at the distal junction 15 months after implantation.

these patients, the allografts were removed and a tumor prosthesis for the proximal tibia was implanted.

Allograft fracture, excluding subchondral bone collapse or junction fracture, was found in none of 26 cemented allografts, but in 3/19 uncemented allografts ($p = 0.04$).

In patients with a cemented allograft, fractures at the junction site were noted in 1 osteochondral al-

Table 1. Clinical data for allografts with and without cement

	No cement n 19	Cement n 26
Mean age (years)	23 (12–48)	18 (11–70)
Sex		
Male	10	16
Female	9	10
Tumor		
Osteosarcoma	12	16
Ewing's sarcoma	2	9
Chondrosarcoma	3	0
Giant cell tumor	1	0
Malignant fibrous histiocytoma	1	1
Site		
Femur		
proximal	2	0
distal	8	8
diaphysis	2	7
Tibia		
proximal	4	4
distal	1	0
Humerus		
proximal	2	7
Reconstruction		
Intercalary arthrodesis	14	7
Intercalary in the femur	2	7
Osteochondral	3	12
Average length (cm)	19 (11–30)	21 (12–40)
Average operation time (hours)	4 (3–6)	4 (3–7)
Average follow-up time (months)	42 (25–60)	39 (27–53)
Junction		
Excellent	5	8
Good	6	7
Fair	4	5
Poor	4	6
Fracture		
Allograft		
Intercalary arthrodesis	2	0
Osteochondral (not subchondral)	1	0
Osteochondral-subchondral	0	4
Junction		
Intercalary arthrodesis	2	0
Intercalary in the femur	1	3
Osteochondral	0	1
Infection	4	1
	(5 months–4 years)	(9 months)

Table 2. Complications

Cementation	Yes (n 26)	No (n 19)	P-value [a]
Junction			
Excellent or good	14/26	11/19	0.9
Fracture			
Allograft	0/26	3/19	0.04
Junction	4/22	3/17	0.9
Subchondral collapse (lower extremity)	4/12	0/1	0.9
Infection			
Early (0–4 months)	0/26	0/19	0.9
Late (> 4 months)	1/26	4/19	0.07

[a] chi-square test

lograft (distal femur) and 3/8 intercalary femur grafts. In these 4 patients, the junction healing was poor in 2, fair in 1, and good in 1. All these patients had internal fixation by 1 plate. Junction fracture did not occur in patients who underwent intercalary knee arthrodesis. In the cementation group, junction fractures in the lower extremity appeared in 4/10 patients with 1-plate-fixation (Figure 4) and 0/12 patients with 2-plate-fixation ($p = 0.02$). 4 patients who had a junction fracture later underwent osteosynthesis with an additional plate and autogenous bone grafts and all the fractures healed. In those with uncemented allografts, junction fracture developed in 2 patients with an intercalary arthrodesis and in 1 patient with an intercalary diaphyseal reconstruction.

Fractures not directly related to the allograft developed in 2 femurs after proximal tibia osteochondral allografts and in 1 femur after an intercalary allograft 6, 12 and 13 months after implantation with cemented allograft. They might have been related to severe osteoporosis of the operated leg. The former 2 fractures were treated and healed by closed treatment with a long leg cast and the other fracture was treated with plate fixation.

Infection

No early infections developed. However, late infections developed in 1/26 cemented allografts and 4 /19 uncemented allografts ($p = 0.07$).

Tumor control

Local relapse developed in only 1 patient (cemented allograft) 27 months after surgery, who underwent a rotationplasty.

Discussion

There are 3 unsolved problems in allograft surgery. First, how to strengthen the allograft itself to avoid graft fractures, secondly, how to prevent infection, and thirdly, how to stabilize the osteosynthesis of the junction site until union is complete. These 3 problems could probably be diminished by filling allografts with antibiotic-loaded bone cement. However, only one small series of 15 patients using cemented allograft has been reported, 4 patients had nonunion and no patients had fracture (Wunder et al. 1995).

As regards bone formation at the junction site between the recipient bone and the allograft, an experimental study showed that intramedullary cementation would not affect the healing of the allograft adversely (Straw et al. 1992). In 14 of our 26 patients with a

cemented allograft, we found good or excellent union. In other series, delayed or nonunion of allografts occurred in between 14% and 27% of the cases (Lord et al. 1988, Cara et al. 1994, Dick and Strauch 1994). The higher rate in our series may be explained by the fact that all patients received intensive postoperative chemotherapy (Friedlaender et al. 1984). We found the same rate of junction healing in cemented and uncemented allografts. Although the bone marrow cavity is packed with cement and endosteal bone formation is disturbed, the fact that most new bone forms from the periosteal rather than the endosteal surfaces of allograft cortical bone implies that intramedullary cementation should not influence healing (Burchardt and Enneking 1985, Urist 1980).

Infection of the allograft is one of the most serious complications (Lord et al. 1988, Wang and Shih 1993). As the allograft has no internal defense against bacteria (Lord et al. 1988), inadequate coverage with soft tissue is one of the main risk factors for infection (Dick and Strauch 1994). 7–13% infection rates of allografts used for reconstruction of malignant or aggressive lesions have been reported (Rosen et al. 1981, Mankin et al 1982, Makley 1985, Lord et al. 1988). In our series, infection developed in 1/26 patients with cemented allograft and in 4/19 with uncemented allografts. Besides elution of antibiotics, bone cement reduces the dead space in the allograft which may reduce the infection risk.

Concerning allograft fracture, special characteristics of each allograft type were noted. There were no fractures (except of the junction) in patients with an intercalary allograft in the lower extremities and an osteochondral allograft of the humerus or femur. The fracture rate, excluding subchondral collapse or junction fractures, was lower in cemented than in uncemented allografts. However, all osteochondral allografts used in the proximal tibia suffered subchondral collapses, probably because only the meta- and diaphyseal regions were reamed and cemented. Better subchondral cement-filling can probably prevent this fracture. The fracture rate at the junction site was higher in patients with 1 plate than in those with 2-plate-fixation. Our findings indicate that cementation of the allograft strengthens the osteosynthesis.

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