Massive autoclaved allografts and autografts for limb salvage surgery

A 1–8 year follow-up of 23 patients

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We performed 23 reconstructions with bone grafts autoclaved at 135 °C for 10 minutes for extensive bone defects after tumor resection. In 15 cases, the resected specimens were autoclaved and used as autografts. In 7 cases, allografts obtained from amputated extremities or cadavers were autoclaved and immediately stored at –80 °C prior to their use. A combination of the two was used in 1 case. The grafts were used in combination with prostheses or other forms of internal fixation. The mean follow-up was 49 (14–98) months. Incorporation of the host-graft junction was observed radiographically after a mean of 11 (6–17) months in all cases. No recurrence due to the autoclaved bone was observed. However, 10 patients suffered complications, including infection, bone resorption, fracture and loosening of the prosthesis. In terms of Mankin's evaluation of bone grafts, 12 patients were evaluated as good or excellent. We conclude that despite the complications, autoclaved autografts and allografts are viable options for reconstruction in many countries because of the difficulty of obtaining large quantities of fresh frozen allografts.

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The reconstruction of extensive bone defects after tumor resection has been accomplished with the use of (vascularized) autografts, prostheses and bone transport.

However, it is difficult to obtain massive fresh frozen allografts in Asian countries because of cultural and religious practices. Therefore, since 1987, we have used massive autoclaved allografts and autografts for reconstruction after resection of malignant bone and soft tissue tumors. In this study, we report the indications, results and complications of this procedure, based on follow-up of patients for 1 year or more.

Patients and methods

Between 1987 and 1994, we used grafts for reconstruction after surgery in 5 osteosarcomas, 3 malignant fibrous histiocytomas (MFH), 2 synovial sarcomas, 1 Ewing's sarcoma, 8 chondrosarcomas, 3 giant cell tumors, and 1 metastatic prostatic tumor. The mean age of the 23 patients was 37 (12–67) years and the mean follow-up was 49 (14–98) months (Table 1). Pre- and postoperative chemotherapy (cisplatin (120 mg/m^2), adriamycin (30 mg/m^2 × 2) and caffeine (1500 mg/m^2 × 3) was given to 11 patients with high-grade sarcomas (Tsuchiya et al. 1994).

We used autoclaved autografts in 15 patients, autoclaved allografts in 7 and a combination of the two in 1 case. Autoclaved autografts were used for tumors with small bony destruction, otherwise autoclaved allografts were used. Autografts were autoclaved at 135 °C for 10 minutes before application. Allografts obtained from amputated extremities or cadavers were immediately stored at –80 °C prior to their use in the sterilized condition after autoclaving at 135 °C for 10 minutes (Johnston et al. 1983, Harrington et al. 1986). The grafts were used as segmental bone grafts and secured with prostheses or other fixation materials. Furthermore, cancellous autografts were placed at the host-graft junctions. We judged incorporation to have taken place when the bridging-callus formation at the host-graft junction seemed homogeneous on both anteroposterior and lateral radiographs.

A wide excision was achieved in 13 cases and a marginal excision in 10. The outcomes were evaluated using Mankin's allograft functional grading system (Mankin et al. 1983). Excellent is defined as no evidence of disease (NED), restoration to normal

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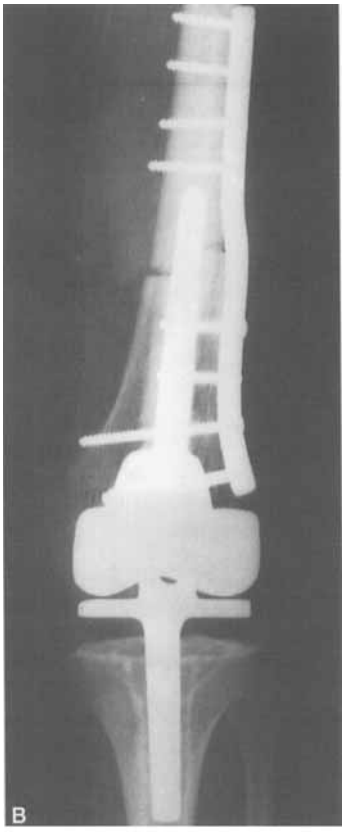
Figure 1. Case 4.

A. A 17-year-old girl with osteosarcoma of the distal femur.

B. Reconstruction with an autoclaved allograft in combination with a rotating-hinge knee prosthesis.



strength and pain-free function of the part, normal activities and life-style. Good is defined as NED, restoration to limited but pain-free functional motion and strength, mild-to-moderate reduction in capacity to perform life activities. Fair is defined as NED, marked limitation of range of motion, strength of the part that requires braces and/or cane or crutches for function, restricted capacity to perform life activities. Failure is defined as amputation, removal of the graft, local recurrence of tumor, metastasis or death as a result of the tumor.

The period of graft effectiveness was equal to the follow-up period which was finished when grafts were removed or patients died of disease, according to Mankin's evaluation.

The Student's t-test was used for the comparison of mean values, and Fisher's exact probability test was used to compare frequencies. A value of $p < 0.05$ was considered significant.

Figure 2. Case 13.

A. A 36-year-old woman with chondrosarcoma of the proximal humerus.

B. Reconstruction with an autoclaved allograft in combination with Neer's prosthesis.

C. Graft resorption without prosthetic loosening.

Table 1. Demographic and clinical data on patients undergoing autoclaved allo- or autograft reconstruction for limb salvage

A	B	C	D	E	F	G	H	I	J	K	L	M
1	17	M	O	III	femur	W	auto + intramedullary nail	+		failure	DOD	15
2	14	F	O	II	femur	W	auto + hinge TKA	+		excellent	CDF	91
3	18	M	O	II	tibia	M	auto + hinge TKA	+		failure	DOD	19
4	17	F	O	II	femur	M	allo + hinge TKA	+		excellent	CDF	66
5	16	M	O	II	tibia	M	auto + plate	+	infection	failure	NED	44
6	55	F	C	I	pelvis	M	auto + plate		recurrence	failure	AWD	81
7	57	M	C	I	humerus	W	auto + Neer's prosthesis		bone absorption	good	CDF	86
8	48	M	C	I	tibia	W	auto + plate		infection	excellent	CDF	63
9	34	F	C	I	pelvis	M	allo + screw			excellent	CDF	51
10	52	M	C	I	pelvis + femur	M	allo (pelvis) + auto (femur) + THA		dislocation	fair	CDF	50
11	49	F	C	I	pelvis	W	auto + plate + THA		fracture and dislocation	failure	CDF	24
12	59	F	C	I	pelvis	W	allo + plate + femoral head prosthesis			excellent	CDF	34
13	36	F	C	I	humerus	M	allo + Neer's prosthesis		bone absorption	good	NED	49
14	47	F	MFH	II	tibia	W	auto + hinge TKA	+		good	CDF	85
15	21	M	MFH	II	femur	W	allo + hinge TKA	+	recurrence	failure	DOD	34
16	60	M	MFH	III	femur	W	auto + intramedullary nail	+		failure	DOD	30
17	36	M	GCT	III	pelvis	W	auto + sacral bar			good	CDF	98
18	30	M	GCT	III	femur	M	allo + screw		recurrence	failure	NED	20
19	29	F	GCT	III	humerus	M	allo + Neer's prosthesis		bone absorption	good	CDF	54
20	12	M	E	II	femur	W	auto + intramedullary nail	+		excellent	CDF	14
21	46	F	S	II	femur	W	auto + hinge TKA	+	fracture and loosening	good	CDF	63
22	16	M	S	II	femur	W	auto + femoral head prosthesis	+	infection	failure	NED	50
23	67	M	M		pelvis	M	auto + plate + THA		dislocation	fair	NED	26

A Case
B Age
C Sex
D Diagnosis
  O osteosarcoma
  C chondrosarcoma
  MFH malignant fibrous histiocytoma
  GCT giant cell tumor
  E Ewing's sarcoma
  S synovial sarcoma
  M metastatic carcinoma
E Stage
F Location
G Margin
  W wide
  M marginal
H Reconstruction
  auto autoclaved autograft
  allo autoclaved allograft
I Chemotherapy:
  5 courses of cisplatin (120 mg/m^2), adriamycin (30mg/m^2/day × 2 days) and caffeine (1500mg/m^2/day × 3 days) before and after surgery
J Complication
K Evaluation
L Prognosis
  CDF continuously disease-free
  NED no evidence of disease
  AWD alive with disease
  DOD died of disease
M Months follow-up

Results

Incorporation at the host-graft junction occurred in all patients after a mean of 11 (6–17) months.

4 patients died of pulmonary metastases, 13 were continuously disease-free, 5 had no evidence of disease and 1 was alive with disease. Local recurrence occurred in 3 patients with MFH, chondrosarcoma, and giant cell tumor. Recurrent tumors did not develop from the autoclaved bone grafts. The patient with the recurrent giant cell tumor underwent further extensive tumor resection and reconstruction. The others were amputated (Table 1).

According to Mankin's evaluation, 6 were excellent, 6 were good, 2 were fair and 9 were failures. The mean period of graft effectiveness for the 12 patients with excellent or good outcome was 63 months and for the others 36 months ($p = 0.008$). The mean age of the good result group was 36 years and of the poor result group 37 years. Whether the margin was marginal or wide had no effect on Mankin's evaluation ($p = 0.3$). Nor was there a difference whether an allograft or autograft had been used ($p = 0.4$), or whether chemotherapy had been given ($p = 0.3$). As for location, the number of excellent or good outcomes for the femur was 4 /9, for the pelvis 3 /7, for the humerus 3 /3 and for the tibia 2 /4 (Table 2).

Regarding complications, cases 7, 13 and 19, all of which involved the proximal humerus, had partial graft resorptions but no loosening of the prostheses. These patients are asymptomatic so far. 3 cases of pelvic reconstruction with cemented total hip arthroplasty were complicated by dislocated hip prostheses. In case 11, an autoclaved autograft was replaced by an autoclaved allograft, in combination with a cemented acetabular cup which failed and was removed because of a deep infection. Finally, as a salvage operation, the hip joint was fused and the tibia was lengthened by 5

Table 2. Comparison of clinical factors based on Mankin's evaluation of results

		Good result	Poor result
Number of cases		12	11
Age, years [a]		36 ± 16	37 ± 20
Period, months [a]		63 ± 25	36 ± 19 [b]
Margin	Wide	8	5
	Marginal	4	6
Reconstruction	Auto	7	8
	Allo	5	3 [c]
Chemotherapy	(+)	5	7
	(–)	7	4
Location	Humerus	3	0
	Femur	4	5
	Tibia	2	2
	Pelvis	3	4 [d]

Good result: excellent + good, Poor result: fair + failure.
[a] Mean ± SD
[b] $p < 0.05$
[c] One patient had both an allograft and an autograft
[d] In one patient, both the pelvis and femur were involved

cm, using the Ilizarov external fixator. In case 10, a revision of the acetabular cup was performed. Case 23 was not reoperated. 3 cases developed deep infections, case 8 was treated with antibiotics, the other 2 were treated with bone transport after resection of the dead bone. In case 5, the defect of more than 20 cm long was reconstructed by the Ilizarov method and the salvage surgery resulted in healing. In case 22, a hip disarticulation was finally performed.

Discussion

In Europe and North America, fresh frozen allografts are commonly used in tumor surgery (Bloem et al. 1991). However, in Japan and other Asian countries, autoclaved allografts and autografts are used because of the difficulty of obtaining massive fresh frozen allografts. If allografts were available, they would be obtained mostly from amputated limbs with a risk of infection.

Autoclaved autografts have worked well in cases with osteoblastic tumors, where more than two thirds of the cortex was intact. Osteoinduction is lost by autoclaving, but osteoconduction kept and incorporation at the host-graft junction is a result of the periosteum of the host, and forms around autoclaved bone (Johnston et al. 1983, Shimozaki et al. 1993).

The advantages of autoclaved bone include technical ease and immediate availability. It is also possible for tendons and ligaments to be attached to autoclaved bone grafts (Sugiura et al. 1993). Furthermore, allografts at risk for infections can be used for grafting after autoclave sterilization, unlike fresh frozen allografts which may be contaminated with HIV, HCV or other viruses (Tomford 1995). Autoclaving at 60 °C for 30 minutes (Manabe 1993) or at 70 °C for 15 minutes (Nakanishi et al. 1992) can preserve osteoinduction while achieving total tumor-cell kill.

The complication rate unrelated to tumor recurrence in our study was 10/23. Similar rates have been reported with autoclaved bone grafts (Harrington et al. 1986) and fresh allografts (Bloem et al. 1991).

We conclude that, despite the complications, autoclaved autografts and allografts are viable options for reconstruction in many countries because of the difficulty of obtaining large amounts of fresh frozen allografts.

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