

Original article

Pedicle frozen autograft reconstruction in malignant bone tumors

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Abstract

Background. Standardizing limb salvage surgery for malignant bone tumors should result in improved limb function after tumor excision and reconstruction. Recently, we developed and clinically applied a method of biological reconstruction using tumor-bearing autografts treated with liquid nitrogen. We report this newly modified technique using pedicle frozen autografts to save the continuity of anatomical structures.

Methods. We treated 33 malignant bone tumor patients. Diagnoses of the tumors were 17 osteosarcomas, 11 metastatic tumors, 2 Ewing's sarcomas, 2 chondrosarcomas, and 1 undifferentiated pleomorphic sarcoma. The sites of the tumors were 23 femurs, 5 tibias, 4 humeri, and 1 calcaneus. Operative procedures consisted of exposing the tumor, performing one-site osteotomy or joint dislocation, rotating and freezing the tumor lesion in liquid nitrogen for 20 min, and reconstruction using intramedullary nailing, plates, or composite arthroplasty.

Results. Postoperative function was excellent in 25 patients (75.7%), good in 5 patients (15.1%), and fair in 3 patients (9.0%). At the final follow-up, 8 patients had died at a mean of 17 months postoperatively, and 18 patients remained disease-free for a mean follow-up period of 30 months (range 7–69 months). Seven patients were alive but with disease. Complications were encountered in 12 patients, including 4 deep infections, 3 fractures, 3 local recurrences from surrounding soft tissue, 2 nonunions, and 1 collapse. All were managed successfully.

Conclusions. The pedicle frozen autograft, which was newly developed to solve drawbacks of previously reported free frozen autografts, achieved success for reconstruction of malignant bone tumors. This is a new, simple, effective surgical technique for biological reconstruction that is still investigated but has potential for development.

Introduction

Currently, limb salvage surgery is the treatment of choice for malignant bone tumors due to advances in multimodality therapy, diagnostic imaging, radiotherapy, chemotherapy, and operative techniques. Surgeons have multiple alternatives for reconstruction of large bone defects following malignant bone tumor resection, including massive endoprosthesis, allograft, composite arthroplasty, and distraction osteogenesis. Biological reconstruction involving the recycling of resected tumor-bearing bone is popular in some Asian countries for socioreligious reasons. These bone tissues need first to be treated to kill cancer cells that may be present before they are reimplanted into the patient. Treatment methods include irradiation,¹ autoclaving,² and pasteurization.^{3,4} However, these treatment methods require special equipment and strict thermal control. In addition, some treatments cause thermally induced bone weakness with loss of osteoinduction.⁵

Recently, Tsuchiya et al.⁶ reported success with a new method that takes the opposite approach — utilizing hypothermia rather than hyperthermia to treat tumor-containing autografts. Specifically, the method uses liquid nitrogen at -196°C as a cryogenic agent to sterilize tumor cells in the bone. Development of their method was based on in vitro and in vivo studies of the hypothermic effects of liquid nitrogen on osteosarcoma proliferation.⁷ Because liquid nitrogen is a liquid substance that can be contained easily during the operation, we hypothesized that we might be able to develop a new surgical technique that no longer required total en bloc excision of the tumor from an extremity but, instead, would enable us to excise the bone-containing tumor partially from the limb and then rotate the bone so it could be immersed in an adjacent container of liquid nitrogen to create a pedicle frozen autograft.

In prior reports, we identified this method of reconstruction as type 3 based on a comprehensive clas-

sification of frozen autograft reconstructions. Type 1 reconstruction requires cutting ligaments, but the resutured tendon and ligament may not function well after freezing. Type 2 reconstruction does not require resuturing joint structures but does require excising the joint. Type 3 reconstruction keeps the continuity of the joint intact, giving excellent stability and function because no important ligaments are sacrificed. Type 3 is a pedicle frozen method, but few details of this method were previously provided. The purpose of the study reported herein was to assess the feasibility of using pedicle autografts frozen intraoperatively in liquid nitrogen in a clinical setting by examining the outcomes of reconstructions using such autografts in a series of patients with malignant bone tumors.

Patients and methods

We treated 33 patients (19 males, 14 females), whose mean age was 39.5 years (range 9–76 years) (Table 1). Informed consent and a letter of acceptance were obtained from all patients prior to starting treatment; and our institutional review board agreed to publish this article in the journal. Among our study patients, 18 with primary high-grade bone sarcomas underwent preoperative chemotherapy with the K-2 protocol,⁸ which consists of five courses of intra-arterial cisplatin, capecitabine, and doxorubicin at intervals of 3 weeks.

None of the tumors in the 33 patients necessitated total en bloc excision. The tumors were exposed and divided from surrounding soft tissue as we carefully determined the appropriate surgical margins. We ended up performing intentional marginal excisions⁸ in 9 patients with a favorable response to preoperative chemotherapy and wide excisions in the other 24 patients. The bony surgical margins beyond the lesions were determined by preoperative imaging guidance using the same criteria that were used for determining soft tissue surgical margins, and the osteotomy levels were marked. One-site osteotomies were performed in 13 cases (Figs. 1, 2). The other 20 cases were not osteotomized; instead, the bone was mobilized by dislocating it at the joint (Figs. 3, 4).

Soft tissue was divided along the extremity beyond a safe surgical margin until the arc of rotation was adequate. The surrounding soft tissue was protected by surgical sheets while a portion of the tumor was excised from the intramedullary canal, or its soft tissue extension, for histopathology. In cases involving osteotomies, the intramedullary canals were then curetted to remove the bone marrow and tumor content to prevent graft fracture due to watery volume expansion during freezing.

Next, the bony lesions connecting with the limb were

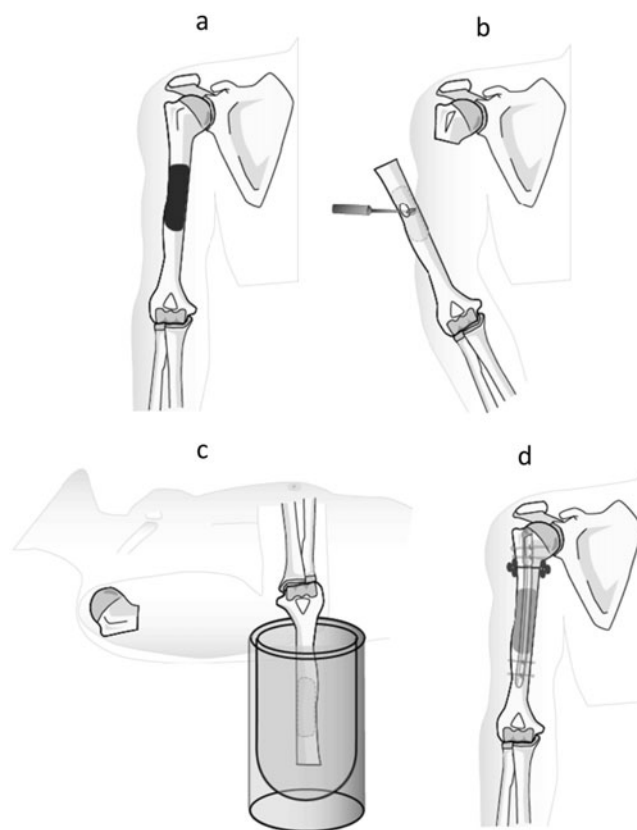


Fig. 1. One-site osteotomy and pedicle freezing. **a** Tumor of the diaphyseal humerus. **b** One-site osteotomy and curettage of tumor. **c** Pedicle freezing in liquid nitrogen. **d** Osteosynthesis using an intramedullary nail with cement and bone graft at the host-graft junction

rotated cautiously and frozen in a liquid nitrogen container while continuing to protect the surrounding soft tissue with surgical sheets. The bony margins were positioned at the surface level of the liquid nitrogen by the surgeons, and the liquid nitrogen was scattered by a spray device at the bony wide (2–3 cm) margin level. All tumors were treated under a one-cycle liquid nitrogen protocol, which consisted of freezing in liquid nitrogen for 20 min, thawing at room temperature for 15 min, and continued thawing in distilled water for an additional 10 min. The steps of this pedicle freezing method were performed under tourniquet to prevent tumor dissemination and bleeding.

Reconstructions after freezing were performed using pressurized intramedullary antibiotic-loaded cementation or artificial bone graft, with nailing or plates attached by screws in 18 cases and with composite prosthetic replacement in the remaining 15 cases. The bone cement mixture consisted of one pack of bone cement (40 g) and 2 g of imipenem/cilastatin sodium or 0.5 g of vancomycin. This cement mixture was used for supplemental nailing and fixing prosthetic components to

Table 1. Treatment results of pedicle frozen autograft reconstruction

Case	Sex/age (years)	Site	Stage	Diagnosis	Reconstruction method		Bony union		Response to chemotherapy ^a		Function	Complication	Follow-up (months)	Outcome
					method	method	Osteotomy	(months)	Chemotherapy ^a	chemotherapy				
1	F/16	Femur (dis)	M0	Ewing's sarcoma	M+IM	M+IM	+	6	K2	Yes	Exc	Local recurrence	19	DOD
2	M/10	Femur (p)	M0	Osteosarcoma	M+prosthesis	M+prosthesis	-	-	K2	Yes	Exc	Nonunion	69	CDF
3	M/60	Femur (dia)	M1	Metastatic tumor (stomach)	W+IM+C	W+IM+C	+	-	-	-	Exc	-	31	NED
4	F/20	Femur (p)	M1	Osteosarcoma	W+prosthesis	W+prosthesis	-	-	K2	No	Exc	-	15	DOD
5	M/73	Femur (dia)	M1	Metastatic tumor (lung)	W+IM+C	W+IM+C	+	-	-	-	Exc	-	4	DOD
6	M/12	Humerus (p)	M0	Osteosarcoma	M+prosthesis	M+prosthesis	-	-	K2	Yes	Exc	Fracture	46	NED
7	F/49	Femur (p)	M1	Metastatic tumor (breast)	M+prosthesis	M+prosthesis	-	-	-	-	Exc	-	47	NED
8	F/18	Femur (p)	M1	Osteosarcoma	M+prosthesis	M+prosthesis	-	-	K2	Yes	Exc	-	55	DOD
9	F/12	Humerus (p)	M1	Osteosarcoma	W+prosthesis	W+prosthesis	-	-	K2	No	Fair	-	6	DOD
10	F/34	Humerus (dia)	M1	Osteosarcoma	W+IM+C	W+IM+C	+	9	-	-	Exc	-	36	AWD
11	M/34	Femur (p)	M0	Chondrosarcoma	W+prosthesis	W+prosthesis	-	-	-	-	Exc	-	36	CDF
12	M/62	Femur (dia)	M0	Osteosarcoma	W+IM+C	W+IM+C	+	-	K2	Yes	Exc	Nonunion	59	CDF
13	F/76	Humerus (p)	M1	Metastatic tumor (colon)	W+prosthesis	W+prosthesis	-	-	-	-	Exc	-	17	DOD
14	F/9	Femur (p)	M1	Osteosarcoma	W+prosthesis	W+prosthesis	-	-	K2	Yes	Good	-	34	NED
15	F/28	Femur (dis)	M0	Osteosarcoma	M+IM+C	M+IM+C	+	9	K2	Yes	Good	-	15	AWD
16	F/18	Tibia (dia)	M1	Osteosarcoma	W+IM+C	W+IM+C	+	4	-	-	Exc	Fracture	35	NED
17	M/73	Femur (p)	M1	Metastatic tumor (liver)	W+prosthesis	W+prosthesis	-	-	-	-	Exc	Infection	12	AWD
18	F/69	Femur (p)	M1	Metastatic tumor (liver)	W+prosthesis	W+prosthesis	-	-	-	-	Exc	-	3	DOD
19	M/15	Tibia (p)	M0	Osteosarcoma	M+IM+C	M+IM+C	+	3	K2	Yes	Fair	Local recurrence	26	AWD
20	M/62	Femur (p)	M0	Chondrosarcoma	W+prosthesis	W+prosthesis	-	-	-	-	Exc	-	25	CDF
21	F/71	Femur (dia)	M1	Metastatic tumor (kidney)	W+IM+C	W+IM+C	+	11	-	-	Exc	-	21	AWD
22	M/28	Tibia (p)	M0	Osteosarcoma	W+IM+C	W+IM+C	-	-	K2	No	Good	Infection	23	CDF
23	M/51	Femur (dis)	M0	Osteosarcoma	W+IM+C	W+IM+C	+	-	K2	Yes	Good	Infection	23	CDF
24	M/14	Tibia (p)	M1	Osteosarcoma	M+IM+C	M+IM+C	-	-	K2	Yes	Fair	Local recurrence, collapse	37	AWD
25	M/20	Tibia (p)	M0	Osteosarcoma	M+IM+C	M+IM+C	-	-	K2	Yes	Exc	Infection	23	CDF
26	M/18	Femur (dis)	M0	Osteosarcoma	W+IM+plate	W+IM+plate	+	9	K2	No	Exc	-	20	NED
27	M/28	Femur (p)	M0	Ewing's sarcoma	W+IM+plate	W+IM+plate	-	-	K2	Yes	Good	-	11	DOD
28	M/69	Femur (p)	M1	Metastatic tumor (lung)	W+plate+C	W+plate+C	+	5	-	-	Exc	-	15	NED
29	F/60	Femur (dis)	M1	Metastatic tumor (kidney)	W+plate+C	W+plate+C	+	10	-	-	Exc	Fracture	16	NED
30	M/61	Femur (p)	M1	Metastatic tumor (lung)	W+prosthesis	W+prosthesis	-	-	-	-	Exc	-	7	NED
31	F/51	Femur (p)	M0	Osteosarcoma	W+prosthesis	W+prosthesis	-	-	-	Yes	Exc	-	10	CDF
32	M/16	Calcaneus	M0	Pleomorphic sarcoma	M+screw	M+screw	-	-	K2	Yes	Exc	-	9	CDF
33	M/66	Femur (p)	M1	Metastatic tumor (kidney)	W+prosthesis	W+prosthesis	-	-	-	-	Exc	-	8	AWD

dis, distal; p, proximal; dia, diaphyseal; M0, no metastasis; M1, with metastasis; M, marginal excision; W, wide excision; IM, intramedullary nail; C, cement; Exc, excellent; AWD, alive with disease; CDF, continuously disease-free; DOD, died of disease; NED, no evidence of disease

^a"K2 protocol" consists of five courses of intra-arterial cisplatin/cafeine/doxorubicin at intervals of 3 weeks

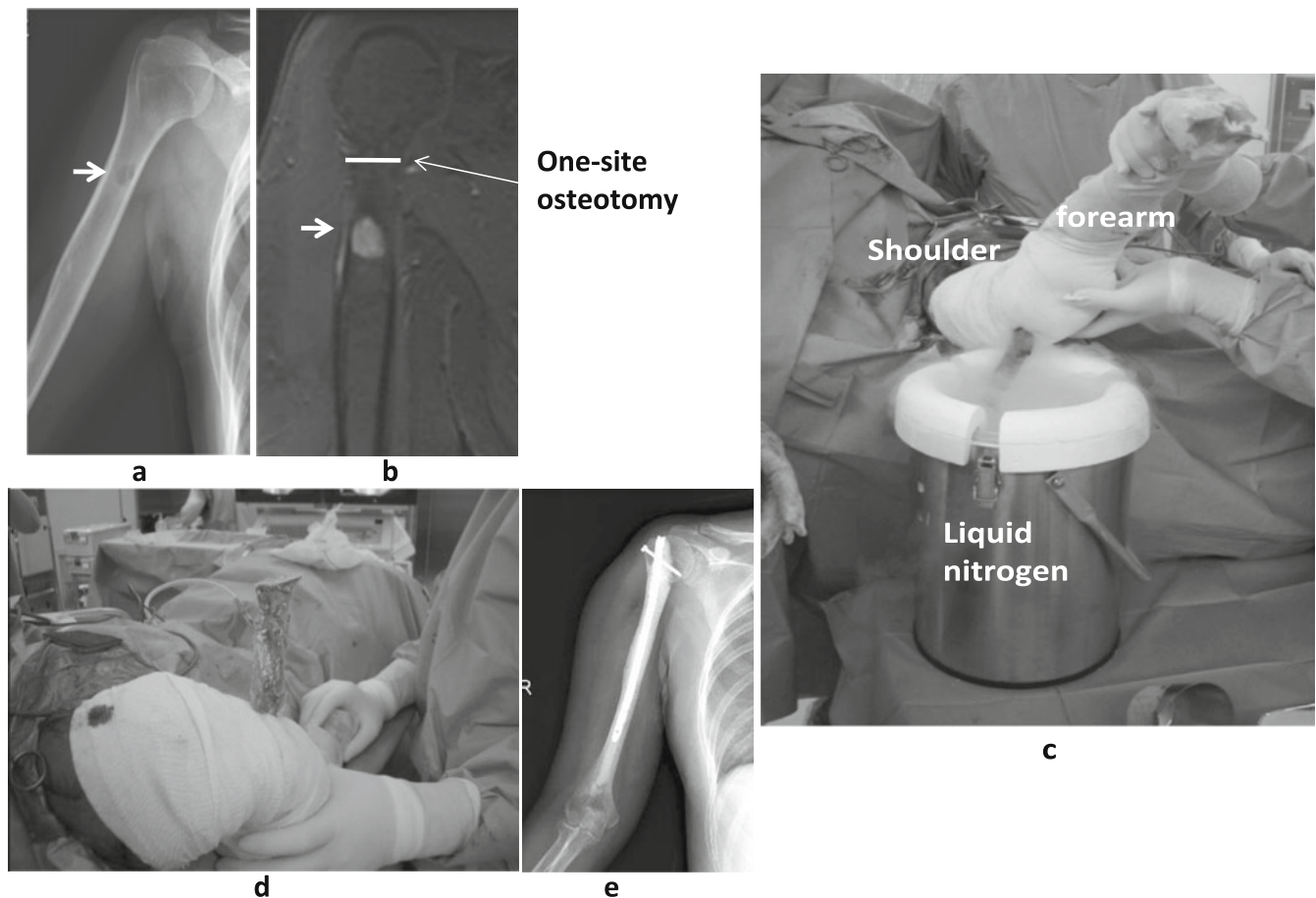


Fig. 2. Case 10, a 34-year-old woman with an osteosarcoma (arrows) of the left diaphyseal humerus. **a** Preoperative radiograph. **b** Preoperative magnetic resonance imaging (MRI). **c** After one-site osteotomy, the bony lesions connecting with the

limb were rotated and frozen in liquid nitrogen. **d** Autograft after freezing. **e** Radiograph 3 years after reconstruction demonstrating bony union at the host-graft junction

increase strength as well as for filling bone defects left behind by the tumor excision.

After the bony reconstruction was completed the soft tissue was repaired, and the frozen graft was covered by muscle flaps when necessary. The volume of dead space was diminished as much as possible by soft tissue sutures, and multiple closed suction drains were placed to reduce fluid collection; compressive dressings were applied.

In those patients who underwent preoperative chemotherapy, intravenous chemotherapy was continued during the postoperative period using cisplatin, caffeine, and doxorubicin and/or high-dose methotrexate combined with citrovorum factor and vincristine (three courses each). The patients were followed up routinely, and full weight bearing was permitted after follow-up radiographs based on the degree of bridging callus between the frozen autograft and host bone. In 10 cases of cemented composite prosthetic arthroplasty of the proximal femur, patients were permitted full weight-bearing 3 weeks after surgery because the abductor was resutured using fiber wire. In all patients, the affected

limbs were assessed at the last follow-up according to the functional evaluation system of Enneking,⁹ which consists of six factors for upper extremities (pain, function, emotional acceptance, hand positioning, dexterity, lifting ability) and six factors for lower extremities (pain, function, emotional acceptance, supports, walking, gait).

Results

Details on treatment results are presented in Table 1. At the final follow-up, 8 patients had died at a mean of 17 months postoperatively, 7 patients were alive but with disease, and 18 patients remained disease-free for a mean period of 30 months (range 7–69 months). Bony union was defined as radiographic demonstration of complete cortical bridging. On average, union of the host-graft junction was observed at 7.3 months postoperatively in nine cases, which required only one-site osteotomy. In all, 25 patients had excellent function, 5 had good function, and 3 had fair function.

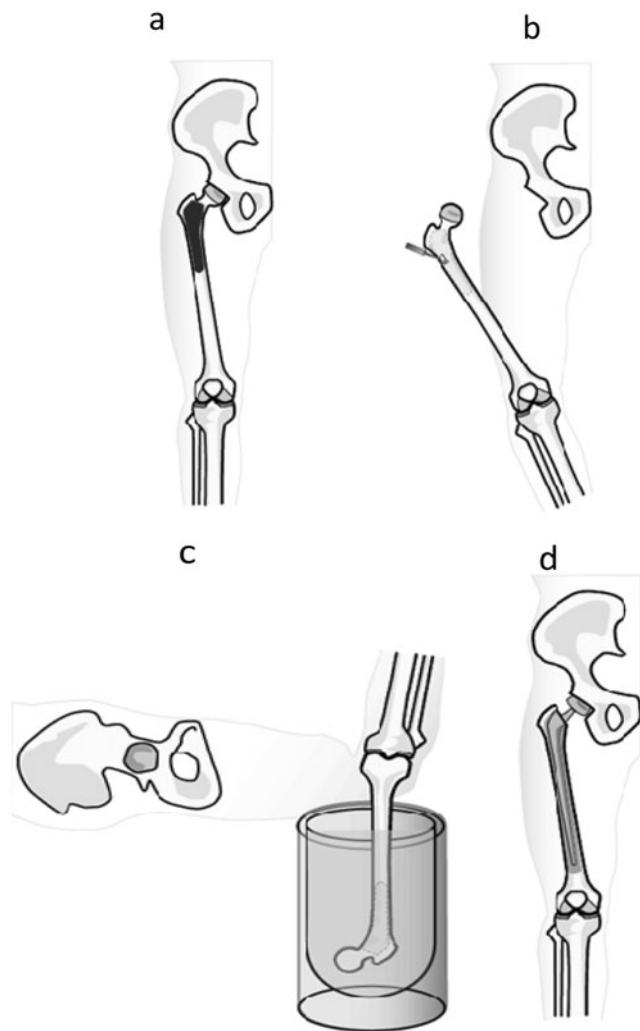


Fig. 3. Joint dislocation and pedicle freezing. **a** Tumor of the proximal femur. **b** Joint dislocation and curettage of the tumor. **c** Pedicle freezing in liquid nitrogen. **d** Composite graft

Altogether, 12 of 14 proximal femoral cases and 3 proximal humeral cases involved dislocating the hip or shoulder joint without osteotomy followed by pedicle freezing. Reconstruction in these cases consisted of a composite prosthesis using hemiarthroplasty. Functional evaluations were excellent in 13 cases, good in 1 case, and fair in 1 case.

Only 1 of the 14 proximal femoral cases, 3 of the 4 proximal tibial cases, and 1 calcaneal case were also treated by dislocating the joint without osteotomy followed by pedicle freezing. It was especially necessary to perform fibular osteotomy at the rotational level in all proximal tibial cases (Figs. 5, 6). These proximal femoral and tibial cases were reconstructed by osteoarticular grafts using intramedullary nails or plates for reinforcement. The calcaneal case involved pedicle freezing that

maintained contact with the body via the Achilles tendon. Reconstruction involved arthrodesis using screws (Fig. 7). Functional evaluations were excellent in two cases, good in two cases, and fair in one case.

In all, 13 cases (5 distal femoral cases, 4 diaphyseal femoral cases, 1 of the 14 proximal femoral cases, 1 of the 4 proximal tibial cases, 1 diaphyseal tibial case, and 1 diaphyseal humeral case) underwent one-site osteotomy of the proximal lesion followed by pedicle freezing. These cases underwent reconstruction by intramedullary nails or plates. Functional evaluations were excellent in 10 cases, good in 2 cases, and fair in 1 case.

There were no intraoperative complications (e.g., surrounding soft tissue damage, neurovascular injuries from freezing effects). Four instances of infected wounds occurred during the early postoperative period. Postoperative graft fractures or implant failures occurred in three patients during intermediate follow-up. Three patients developed local recurrences arising in peripheral soft tissues, which were treated by additional wide excision. Case 1 was Ewing's sarcoma of the distal femur; at 9 months after surgery, local recurrence occurred from the proximal biceps femoris of the operation scar and a wide excision was performed. However, the patient died owing to pulmonary metastases 19 months after surgery. Case 19 was osteosarcoma of the proximal tibia. At 7 months after surgery, local recurrence occurred from the posterior muscle of the frozen bone, and a wide excision was performed. Subsequently, the patient had lung metastases and was treated with chemotherapy. Case 23 was osteosarcoma of the distal femur. At 16 months after surgery, there was a local recurrence from the posterior soft tissue of the frozen bone, and a wide excision was performed. There was no further recurrence and no metastases.

The recurrence of all three cases was from the posterior side of the tumor, near the neurovascular sheath, probably from satellite lesions or venous tumor thrombi. Special attention was focused on ablation of tumor tissue around this area especially with the frozen method. Local recurrences were not from the pedicle frozen autografts. We think that curative wide margins have to be performed in chemotherapy nonresponders. Two patients had nonunion of the host-graft junction postoperatively. We performed additional iliac bone graft operations in these patients and bone union was ultimately achieved in both cases. In one patient there was collapse of the frozen bone.

Discussion

The use of liquid nitrogen during surgery was reported by Cooper¹⁰ in 1962. Since then, liquid nitrogen has been used in tumor management in multiple specialties.¹¹⁻¹⁴

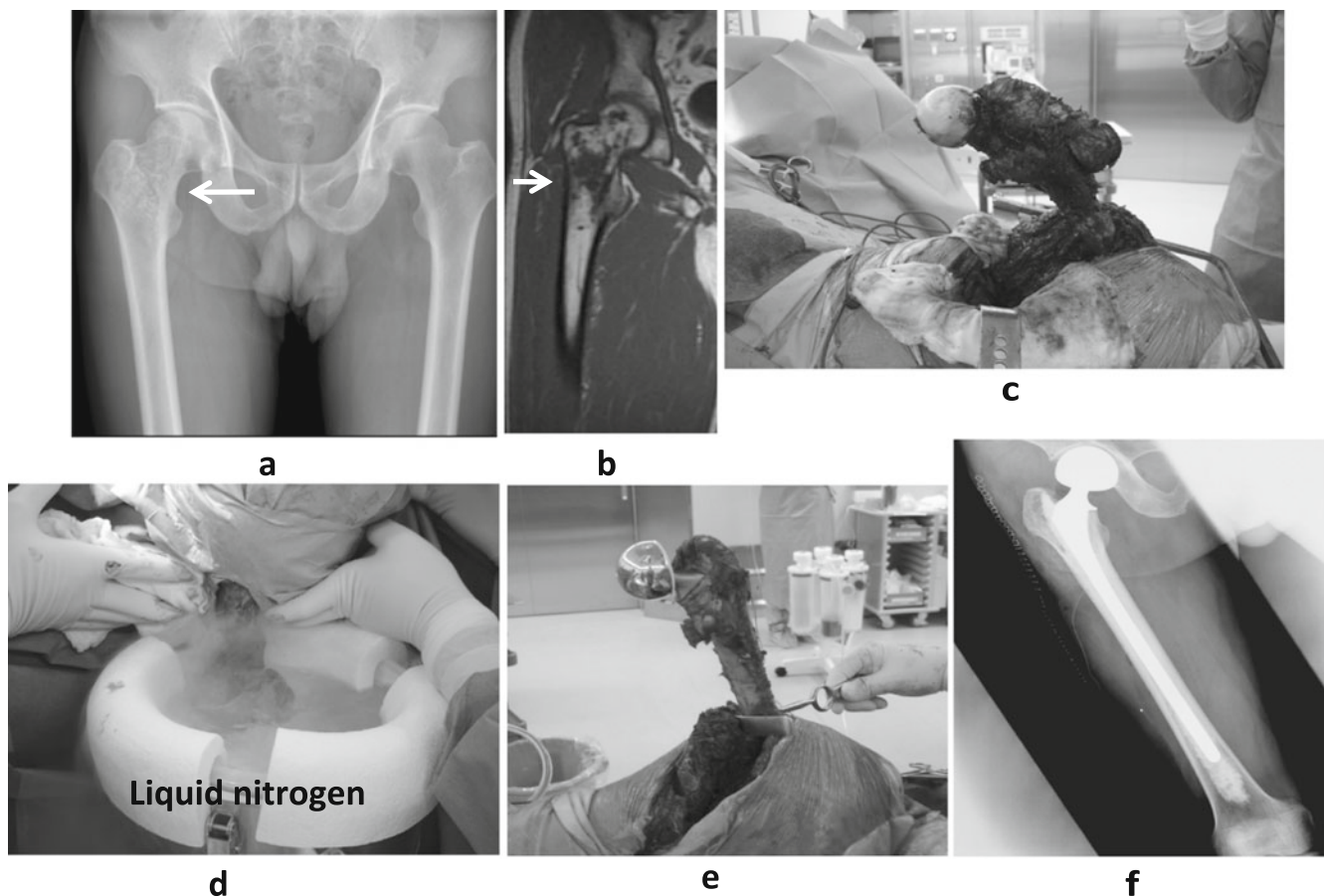


Fig. 4. Case 20, a 62-year-old woman with a chondrosarcoma (arrows) of the right proximal femur. **a** Preoperative radiograph. **b** Preoperative MRI scan. **c** Hip joint following intraoperative dislocation. **d** After femoral neck osteotomy and

tumor curettage, the bony lesions connecting with the limb were rotated and frozen in liquid nitrogen. **e** After freezing the autograft, cemented hemiarthroplasty was performed. **f** Radiograph 2 years after reconstruction

In the field of orthopedics, cryosurgery was first used at Memorial Sloan-Kettering Cancer Center in 1964 for metastatic bone disease.¹⁵ Studies were published describing adjuvant therapy using cryosurgery for benign and malignant bone tumors,^{16,17} but these studies did not include en bloc excision of tumors with reconstruction using tumor-bearing massive frozen autografts treated with liquid nitrogen. A basic research study by Yamamoto et al.⁷ documented the potential effectiveness of liquid nitrogen treatment on osteosarcoma cells, both in vitro and in vivo, and also found that frozen autografts had adequate biomechanical properties. More recently, Tsuchiya et al.⁶ reported successful clinical results from a series of reconstructions using autografts containing tumor treated by liquid nitrogen in patients with malignant bone tumors.

The advantages of liquid nitrogen treatment include the following: simplicity, low cost, maintenance of osteoinductive and osteoconductive properties, perfect fit between graft and host bone, sufficient biomechanical strength, no disease transmission, no immunological

rejection, preservation of the cartilage matrix, no need for a bone bank, no requirement of special equipment and strict thermal control, easy attachment of tendons and ligaments to bone, no harmful denatured substances, early revitalization and cryoimmunological effects.¹⁸ Disadvantages include the impossibility of histological analysis of the whole specimen (tumor necrosis analysis) and complications similar to those related to allograft implantation, including degenerative changes in articular cartilage. However, because a frozen autograft used for reconstruction involves recycling tumor-bearing bone, the strength of the autograft depends on the integrity of the remaining structures following cryogenic sterilization. For this reason, one prerequisite for our frozen autograft method is that the tumor is an osteoblastic lesion and that massive osteolytic destruction has not taken place.

Advantages of our pedicle frozen method of autograft include the following: shorter operating time, maintaining the continuity of the joint in selected patients, preserving joint stability and function because

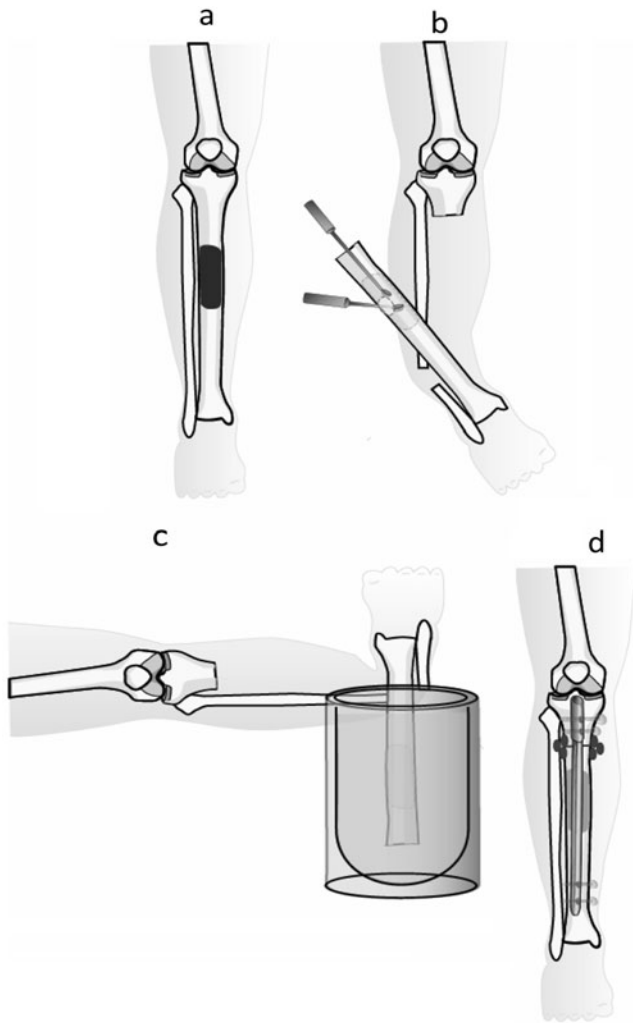


Fig. 5. Pedicle freezing at the shaft of the tibia. **a** Tumor of the diaphyseal tibia. **b** One-site osteotomy of the proximal tibia and distal fibula and curettage of tumor. **c** Pedicle freezing in liquid nitrogen. **d** Osteosynthesis using an intramedullary nail with cement and bone graft at the host-graft junction

no important ligaments need to be sacrificed in selected patients, early functional recovery after operation, decreased osteotomy sites, and a lower rate of graft healing complications. The pedicle method appears to be a good option for extensive intramedullary bony lesions because it is less destructive than total en bloc tumor excision with reconstruction.

Our pedicle frozen autograft method does have some disadvantages. For example, it needs a longer incision and more muscle dissection than en bloc excision owing to the necessity of creating an arc of rotation and employing safety measures to protect adjacent soft tissue. These measures appear to produce more raw surfaces and dead-space volume, which we tried to correct by tight suturing, multiple closed vacuum suction drains, and postoperative compressive dressings. Regarding

soft tissue frozen autograft attachment over the long term, we would expect outcomes comparable to those seen with soft tissue allograft attachment¹⁹ because the two share similar biological properties. The need to keep the tumor lesion in continuity with the limb increases the difficulty of handling the tumor compared with en bloc excision. With en bloc excision, we can perform curettage, partially remove intramedullary bone marrow and soft tissue extensions of the bone tumor, perform intramedullary reaming for fixation preparation, and dry the bone specimen. These procedures aim to prevent fractures due to volume expansion of extracellular fluid during the freezing process. These procedures are more difficult to carry out using the pedicle frozen method because more care needs to be taken to prevent contamination of surrounding tissues from the tumor using a tourniquet. There remains a risk of spreading tumor cells when we curette the canal space under tourniquet. Therefore, this method is still experimental until we clarify the safety regarding contamination by tumor cells. This method also requires special skills to prevent contamination.

Regarding clinical applications, anatomical sites appropriate for the pedicle frozen method include the proximal femur, shaft of the femur, distal femur, proximal humerus, shaft of the humerus, proximal tibia, and shaft of the tibia. With the pedicle frozen method, the proximal side of the tumor is subjected to dislocation or osteotomy, and the distal side is connected to the host extremity. Histological indications are bone tumors of osteoblastic formation such as osteoblastic, chondroblastic, or fibroblastic osteosarcomas. Bone tumors of osteolytic formation such as telangiectatic osteosarcomas can also be subjected to this method using bone cement or bone grafting and internal fixation if the tumor lesion included does not exceed 50%. However, the following cases represent limiting factors for the pedicle frozen method and where en bloc excision would be preferable.

- Tumor adhering to major neurovascular structures from which the tumor cannot be dissected and/or it is impossible to bypass the major artery
- Pathological fractures
- Severe osteolytic lesion with an impending fracture (because of the higher risk of intraoperative fracture with the pedicle frozen method)

The criteria for using this method were determined by whether the joint could be preserved. Diaphyseal osteotomy was performed on all cases where the joint could be preserved. Joint nonpreserved cases of the proximal femur and humerus underwent composite reconstruction because of early osteonecrosis and collapse. Cases around the knee were subjected to osteoarticular reconstruction when the subarticular structure

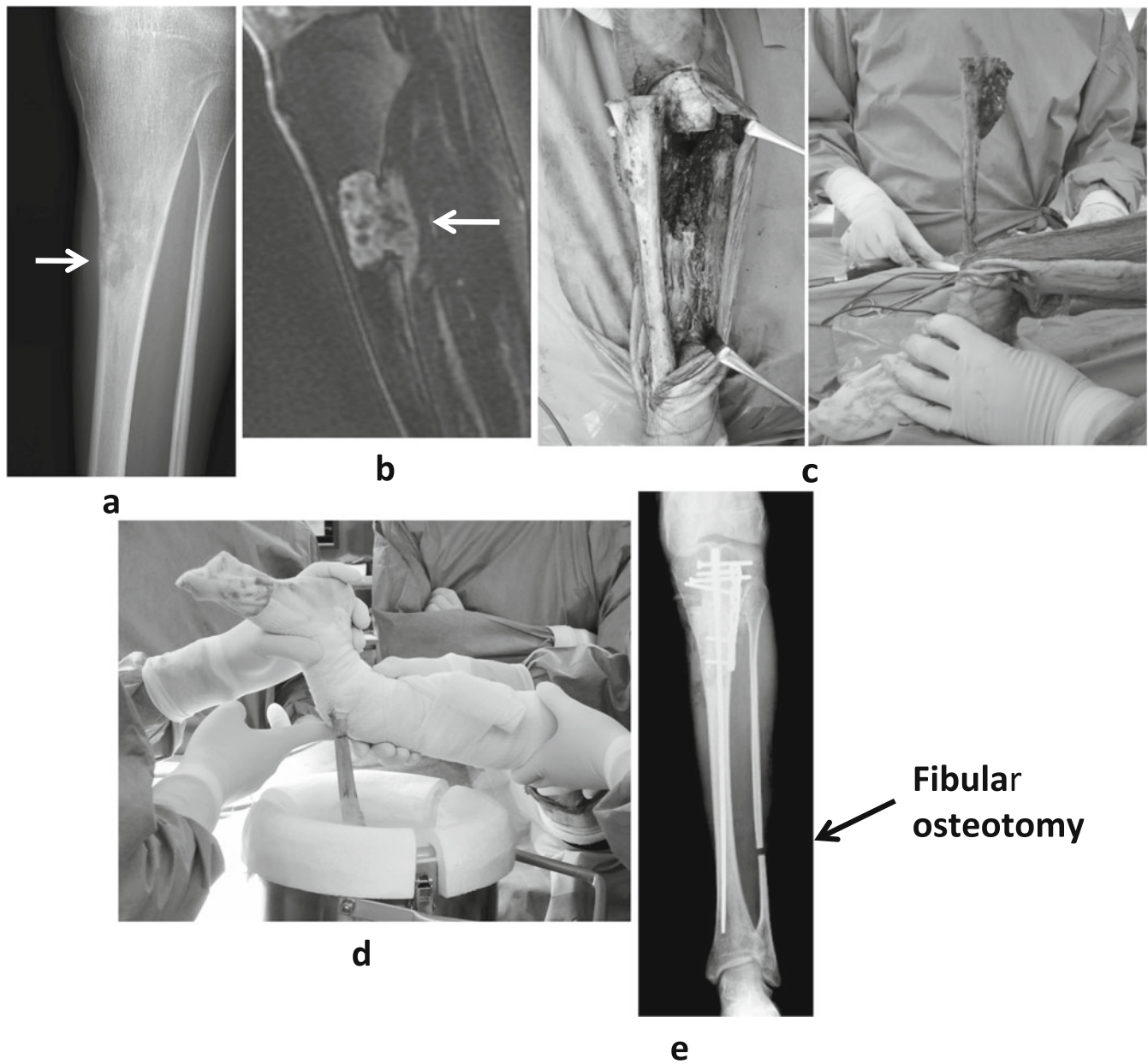


Fig. 6. Case 16, an 18-year-old man with an osteosarcoma (*arrows*) of the left diaphyseal tibia. **a** Preoperative radiograph. **b** Preoperative MRI scan. **c** One-site osteotomy of the proximal tibia and subsequent fibular osteotomy at the rotated

level. **d** The bony lesions connecting with the limb were rotated and frozen in liquid nitrogen. **e** Radiograph 1 year after reconstruction demonstrates bony union at the host-graft junction

was well preserved. Osteotomy cases regained range of motion 3 weeks after surgery and partial weight bearing 3 months after surgery. On the other hand, nonosteotomy cases started partial weight bearing 1 month after surgery when patients had recovered from the soft tissue injury.

Regarding the use of frozen bone for reconstruction, structural graft fractures are a potential problem with biological reconstructions of musculoskeletal tumors due to biomechanical properties of the biological mate-

rials themselves, a problem that could become a greater concern as tumor patients start to survive longer. For allografts, one study encountered a graft fracture rate of 17.7% at a mean of 3.2 years postoperatively.²⁰ Multiple factors may raise the risk of allograft fractures, including increasing the length of structural allografts, the use of plate fixation, chemotherapy, and penetration of graft cortices by the fixation device.²¹⁻²³ Plating requires many screws for secure fixation. The observation that 33% of allograft fractures occur through screw



Fig. 7. Case 32, a 16-year-old boy with a pleomorphic sarcoma (arrows) of the left calcaneus. **a** Preoperative radiograph. **b** Preoperative MRI scan. **c** After preoperative chemotherapy, we performed surgery through a horizontal incision in the

foot. **d** The excised calcaneus-containing tumor remains connected to the limb via the Achilles tendon. **e** Autograft at the end of pedicle freezing. **f** Radiograph 6 months after reconstruction

holes raises a concern that screw holes may lead to abnormal stress that could predispose the graft to fracture.

We have taken a number of measures to reduce the rate of complications from our procedure. Prior to immersing the graft in liquid nitrogen, we curetted the intramedullary canals to remove the bone marrow and tumor content, thereby hoping to prevent graft fractures due to watery volume expansion during freezing. With regard to tumor recurrence, surgical margins remain a controversial issue in musculoskeletal sarcoma surgery. We endeavored to reduce the possibility of tumor contamination by taking certain precautions, including protecting adjacent tissues with surgical sheets, performing curettage carefully, and using operative instruments separately. In our basic research and prior clinical series,

we determined that liquid nitrogen effectively sterilized tumor cells. In our current series, only three patients had local recurrences from adjacent soft tissue and they had all presented with a substantial amount of soft tissue extension. Thus, our liquid nitrogen and pedicle frozen method appears to be safe.

Reasons for reoperation were fractures of frozen bone, nonunion of the osteotomy site, and osteoarthritis in osteoarticular reconstruction cases. Fractures and nonunion cases were generally treated by internal fixation and iliac bone grafts because of early bone remodeling²⁴ and sufficient strength of the frozen bone. If this measure was impossible, a mega tumor prosthesis was used. Osteoarthritis of hip and knee joints underwent total knee or hip arthroplasty with a long stem. It was not necessary to use a mega tumor prosthesis.

Given that our series is limited by the relatively small number of patients and an intermediate duration of follow-up, we recognize that this report of a new surgical technique in limb salvage surgery is only a preliminary study, one in which we focused on tumor treatment, ability to preserve important structures, and reducing unnecessary complications from a one-site operation. We found that pedicle frozen autografts can be used successfully for type 3 reconstruction in patients with malignant bone tumors. This simple, effective operative procedure has good potential for avoiding unnecessary complications. Pedicle frozen autografts show promise as an alternative option in limb salvage surgery. Long-term follow-up studies should provide additional useful information.

References

- Araki N, Myoui A, Kuratsu S, Hashimoto N, Inoue T, Kudawara I, et al. Intraoperative extracorporeal autogenous irradiated bone grafts in tumor surgery. *Clin Orthop* 1999;368:196–206.
- Asada N, Tsuchiya H, Kitaoka K, Mori Y, Tomita K. Massive autoclaved allografts and autografts for limb salvage surgery: a 1–8 year follow-up of 23 patients. *Acta Orthop Scand* 1997;68:392–5.
- Manabe J, Ahmed AR, Kawaguchi N, Matsumoto S, Kuroda H. Pasteurized autologous bone graft in surgery for bone and soft tissue sarcoma. *Clin Orthop* 2004 419:258–66.
- Sakayama K, Kidani T, Fujibuchi T, Kamogawa J, Yamamoto H, Shibata T. Reconstruction surgery for patients with musculoskeletal tumor, using a pasteurized autogenous bone graft. *Int J Clin Oncol* 2004;9:167–73.
- Urist MR, Dawson E. Intertransverse process fusion with the aid of chemosterilized autolyzed antigen-extracted allogeneic (AAA) bone. *Clin Orthop* 1981;154:97–113.
- Tsuchiya H, Wan SL, Sakayama K, Yamamoto N, Nishida H, Tomita K. Reconstruction using an autograft containing tumor treated by liquid nitrogen. *J Bone Joint Surg Br* 2005;87:218–25.
- Yamamoto N, Tsuchiya H, Tomita K. Effects of liquid nitrogen treatment on the proliferation of osteosarcomas and biomechanical properties of normal bone. *J Ortho Sci* 2003;8:374–80.
- Tsuchiya H, Tomita K, Mori Y, Asada N, Yamamoto N. Marginal excision for osteosarcoma with caffeine assisted chemotherapy. *Clin Orthop* 1999;358:27–35.
- Enneking WF. A system for functional evaluation of surgical management of musculoskeletal tumors. In: Enneking WF, editor. *Limb salvage in musculoskeletal oncology*. New York: Churchill-Livingstone; 1987. p. 5–16.
- Cooper IS. Cryosurgery surgery of the basal ganglia. *JAMA* 1962;181:600–4.
- Shafir M, Shapiro R, Sung M, Warner R, Sicular A, Klipfel A. Cryoablation of unresectable malignant liver tumors. *Am J Surg* 1996;171:27–31.
- Uchida M, Imaide Y, Sugimoto K, Uehara H, Watanabe H. Percutaneous cryosurgery for renal tumors. *Br J Urol* 1995;75:132–7.
- Popescu V, Spirescu E. Bone resection, extra-corporeal cryotherapy and immediate reimplantation in the treatment of mandibular tumors. *J Maxillofac Surg* 1980;8:8–16.
- Leipzig B, Cummings CW. The current status of mandibular reconstruction using autogenous frozen mandibular grafts. *Head Neck Surg* 1984;6:992–7.
- Marcove RC, Miller TR. The treatment of primary and metastatic localized bone tumors by cryosurgery. *Surg Clin North Am* 1969;49:421–30.
- Malawer MM, Bickels J, Meller I, Buch RG, Henshaw RM, Kollender Y. Cryosurgery in the treatment of giant cell tumor: a long-term follow-up study. *Clin Orthop* 1999;359:176–88.
- Veth R, Schreuder B, van Beem H, Pruszczynski M, de Rooy J. Cryosurgery in aggressive, benign, and low-grade malignant bone tumors. *Lancet Oncol* 2005;6:25–34.
- Nishida H, Tsuchiya H, Tomita K. Re-implantation of destructive tumor tissue treated by liquid nitrogen cryotreatment induces anti-tumor activity against murine osteosarcoma. *J Bone Joint Surg Br* 2008;90:1249–55.
- Enneking WF, Campanacci DA. Retrieved human allografts: a clinicopathological study. *J Bone Joint Surg Am* 2001;83:971–86.
- Sorger JI, Hornicek FJ, Zavatta M, Menzner JP, Gebhardt MC, Tomford WW, et al. Allograft fractures revisited. *Clin Orthop* 2001;382:66–74.
- Thompson RC Jr, Garg A, Clohisy DR, Cheng EY. Fractures in large-segment allografts. *Clin Orthop* 2000;370:227–35.
- Hornicek FJ Jr, Mnaymneh W, Lackman RD, Exner GU, Malinin TI. Limb salvage with osteoarticular allografts after resection of proximal tibia bone tumors. *Clin Orthop* 1998;352:179–86.
- Vander Griend RA. The effect of internal fixation on the healing of large allografts. *J Bone Joint Surg Am* 1994;76:657–63.
- Tanzawa Y, Tsuchiya H, Shirai T, Hayashi K, Yo Z, Tomita K. Histological examination of frozen autograft treated by liquid nitrogen removed after implantation. *J Orthop Sci* 2009;14:761–8.