Cryosurgery and Acrylic Cementation as Surgical Adjuncts in the Treatment of Aggressive (Benign) Bone Tumors

Analysis of 25 Patients Below the Age of 21

MARTIN M. MALAWER, M.D., F.A.C.S., AND WILLIAM DUNHAM, M.D.

This article reviews the clinical experience with cryosurgery (use of liquid nitrogen) and acrylic cementation (polymethylmethacrylate; PMMA) in the treatment of aggressive, benign bone sarcomas and the biologic basis of this technique. The results of 25 patients below the age of 21 treated by cryosurgery, with an average follow-up period of 60.8 months, are reported. Three approaches to surgical reconstruction were used: Group 1 (four patients) had cryosurgery with no reconstruction, Group 2 (13 patients) had bone graft reconstruction alone, and Group 3 (eight patients) had composite osteosynthesis with internal fixation, bone graft, and/or PMMA. The overall control rate was 96% (one recurrence). The tumor types were giant-cell tumor, chondroblastoma, aneurysmal bone cyst, and malignant giant-cell tumor. Nineteen lesions involved the lower extremity, and six lesions were located in the upper extremity. There were two secondary fractures (8%), one local flap necrosis, and one synovial fistula. There were no infections. Two epiphyseodeses were performed. The functional results were excellent (83%), good (13%), and fair (4%). The technique of composite osteosynthesis is recommended for all large tumors of the lower extremity. Cryosurgical results compare favorably with those obtained by *en bloc* resection and demonstrate the ability of cryosurgery to eradicate tumors while avoiding the need for extensive resections and reconstructive procedures.

From The Children's Hospital Medical Center, George Washington University School of Medicine and Health Sciences, Washington, D.C., Surgery Branch, National Cancer Institute, NIH, Bethesda, Maryland, and the Department of Orthopedics, University of Alabama School of Medicine, Birmingham, Alabama.

Reprint requests to Martin M. Malawer, M.D., Orthopedic Surgery, Children's Hospital Medical Center, 111 Michigan Ave. N.W., Washington, D.C. 20010.

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The classic treatment of most benign, aggressive bone tumors has been curettage and bone grafting. The most common aggressive benign bone tumors include giant-cell tumors (GCTs), which have been the subject of most clinical experience, aneurysmal bone cysts (ABCs), chondroblastomas, and osteoblastomas. The literature documents extensive difficulties in obtaining local control of these tumors; consequently, primary resection is frequently recommended for GCTs and less commonly for the other tumors.[10,13,37] Over the past two decades, adjuvant physical modalities, in combination with curettage, have been developed and used in an attempt to decrease the high rate of local recurrence.[4,12,15,20,22–25,31,34,35] The two most common methods are cryosurgery (liquid nitrogen), as developed by Marcove *et al.*,[22–25] and acrylic cementation, as originally described by Persson and Wouters[34] in the early 1970s. Marcove *et al.* have reported extensively on their experience with cryosurgery for benign and certain low-grade malignant tumors; however, this technique has only been used in a few institutions. There are fewer data on acrylic cementation, although it appears to be more widely used, presumably because of the simplicity of this technique.[3,19,35]

Since 1976, cryosurgery has been used in combination with acrylic cementation in the treatment of most benign (aggressive) bony tumors.[20] The aim of the present study has been to decrease the risk of local recurrence following curettage, to avoid the need for major skeletal resections, and to preserve the adjacent joint function. The purpose of this report is (1) to review the clinical and biologic basis of these procedures, (2) to illustrate the surgical technique, (3) to analyze the experience with cryosurgery and cementation in a series of 25 patients below the age of 21, and (4) to present guidelines for patient selection and methods of reconstruction of the tumor cavity.

CEMENTATION (PMMA) AS AN ADJUNCT TO CURETTAGE

The concept of extending the effective margins of a curettage beyond its geographic borders by the use of polymethylmethacrylate (PMMA) was first proposed by Persson and Wouters in the mid-1970s.[34] It was based on the hypothesis that PMMA might kill the residual tumor cells following curettage.

Recently, Persson *et al.*[33] reviewed their experience with curettage and PMMA. Among 20 patients with GCTs treated between 1972 and 1985, there were only three (15%) local recurrences. Two of these were satisfactorily treated with a second curettage and cementation; the remaining patient required an amputation. This technique has now been used by many American and European surgeons. At the Third International Symposium on Limb Salvage Surgery in 1984, a special symposium was held to discuss and evaluate this technique.[34,35,39,40]

The advantages of curettage and cementation, as described by several investigators, have been summarized as follows: (1) The joint is preserved and resection is avoided. (2) The rate of local control increases. (3) The functional result is improved, and there is a quicker return to weight-bearing status. (4) Local recurrence is easier to detect with PMMA than with a bone graft alone. (5) If recurrence occurs, other therapeutic options (resection, amputation) still exist.

The combined results of 240 patients presented at the International Symposium (rated by the Enneking functional classification system) were as follows: 79% were excellent, 16% were good, and 4% were fair or poor. The overall local recurrence rate among these 240 patients was 10%. Surprisingly, there were no local recurrences among patients whose lesions involved the hip, which is generally the most difficult area in which to perform this procedure. The surgeons concluded the functional results were far superior to those following resection with a prosthesis or arthrodesis.

THE ROLE OF PMMA IN TUMOR CONTROL

Limb function and rate of local control have dramatically increased over the past decade with curettage and PMMA compared with curettage alone (historical controls).[15,34,35,40] What accounts for this improvement? There is no question that PMMA immediately stabilizes a large defect and decreases the risk of fracture during healing. The reason for the decrease in local recurrence is not well understood; however, the consensus is that this improvement is at least partially due to advances in the technique of curettage itself. Most surgeons now use a mechanical burr (*e.g.*, Midas-Rex, Fort Worth, Texas) to remove the wall of the tumor cavity, which is the high-risk area for residual tumor cells. Biologically, the wall represents the reactive zone, and it often contains undetected tumor extension. Its adequate removal converts an intralesional procedure into a marginal excision. The mechanical burr is more effective than hand curettes alone. Older reviews of tumor recurrence are usually based on a comparison of simple curettage (nonmechanical) to resections. The basis for improvement in the more recent series is most likely the use of the mechanical burr rather than the tumorcidal effect of PMMA.

There are, however, two hypothetical mechanisms for the tumorcidal effect of PMMA: hyperthermia from the heat of polymerization and a possible direct toxic effect of the monomer. Given that PMMA is used simply to pack a defect, both mechanisms are of a short and variable duration and would therefore seem to be of questionable efficacy in the control of bony neoplasms. Experimental data, moreover, show the heat of polymerization drops sharply from the center of the PMMA to the interface with the adjacent cancellous bone.[40] Wilkins *et al.*[39] reviewed the data of heat effects and evaluated necrosis in a dog model. They reported bone marrow necrosis occurs at 60° but not below 48°. Between 50° and 60°, necrosis is variable and time dependent. At 50°, capillary damage occurs at three minutes and bone damage at six minutes. The maximum temperature of the cancellous bone interface in their dog model, using a lateral condyle filled with cement, never exceeded 46°. They concluded that necrosis of tumor cells was questionable under surgical conditions. They strongly recommended not to rely upon PMMA for tumor control and emphasized the need for thorough curettage with a mechanical burr. Malawer *et al.*,[21] using a skeletally mature mongrel dog in a tumor model of the distal femur, compared whole-mount sections with roentgenograms, hematoxylin and eosin sections, and tetracycline fluorescence and demonstrated no evidence of adjacent bony necrosis when the cavity was filled with PMMA alone.

There is a good deal of discussion regarding the necessity for and appropriate timing of PMMA removal.[39] Some believe that the increased stiffness of the PMMA will lead to early degenerative changes. In general, PMMA should not be removed until the high-risk period of local recurrence has elapsed (approximately 24 months). There are few clinical or scientific data to support the need for PMMA removal, even in a subchondral position. Willert[40] compared the stiffness following placement of PMMA versus bone graft in a subchondral position in the lateral condyle of two dogs. Twelve weeks after surgery, he reported only a slight increase of stiffness of the condyles following PMMA. Stiffness had been initially lower in the bone graft model than following the use of PMMA; however, stiffness in the former group increased as healing occurred. Willert concluded that increased stiffness may not be a significant cause of secondary osteoarthrosis.

CRYOSURGERY AS AN ADJUNCT TO CURETTAGE

Cryosurgery is the use of extreme cold to produce tissue necrosis. Cooper[6] described the first direct surgical application and effective instrumentation of a patient by cryosurgery in 1963. Using a cryoprobe, he treated a patient with Parkinson's disease by selectively destroying a portion of the basal ganglia. In 1966, Gage *et al.*[9] demonstrated cryosurgery's effectiveness in destroying bone both clinically and in a dog model. Within the past two decades, cryosurgery has become accepted as an effective therapeutic modality for select benign and malignant lesions in several surgical fields. Cryosurgery, however, has not been widely accepted by orthopedic surgeons; reports of experience have been limited to a few centers. Marcove *et al.*[23-25] have used cryosurgery in the treatment of metastatic and selected benign (aggressive) bone tumors since 1964. They have reported extensively on their experience for more than two decades. In recent years, they have also treated carefully selected malignant bone tumors.

Marcove *et al.* emphasize the efficacy of cryosurgery in obtaining good tumor control (85%–96%) of most benign (aggressive) bony lesions. They emphasized that the advantages of cryosurgery include a high rate of cure, preservation of the adjacent joint, and avoidance of the need for extensive reconstruction by prosthetic replacement, allograft, or arthrodesis. The problems they have reported with cryosurgery are that it kills bone and skin as well as tumor cells, that it has a high fracture rate (11%–28%), and that it may be associated with wound problems (5%–10%). Marcove *et al.*[23–25] described a direct-pour technique in which liquid nitrogen is poured directly into a curetted tumor cavity instead of being introduced through a closed system. This method has the advantage of increasing the contact of the coolant with the irregular walls of a curetted cavity.

BIOLOGIC BASIS OF CRYOSURGERY

The following mechanisms underlie cellular injury at subzero temperatures: (1) thermal shock, (2) dehydration and toxic effects of electrolyte changes, (3) formation of intracellular ice crystals and membrane disruption, (4) denaturation of cellular protein, and (5) microvascular failure.[11,16,17,19,27–29] All of these mechanisms are triggered by changes that result from lowering the temperature of the tissue or by disturbances caused by phase transition when freezing occurs.[26,30,32,36,38] Temperatures between −21° and −60° are needed to obtain cellular necrosis; temperatures below −60° exert no further lethality. In general, the formation of intracellular ice crystals is considered the main mechanism of cellular necrosis. The damage to the microvascular circulation is most likely responsible for late, progressive necrosis after the freeze and for problems associated with subsequent repair of frozen tissue.

There are several modulating biologic and physical influences on the processes of cooling and freezing that also affect cell survival and the pathway of cellular damage. These include the cell type, the tissue density and vascularity, the presence of cryoprotective molecules, the amount and intensity of the heat applied, the rate of cooling, the number of freeze–thaw cycles, the rate of thaw, the absolute temperature obtained, and the duration of the freeze.[1,2,14,26,32,36] All of these factors determine whether the effects of solution changes or intracellular ice formation will exert the greater influence on tissue damage.

In general, a rapid freeze causes intracellular ice crystals to form, whereas a slow freeze causes cellular dehydration. Conversely, a slow thaw will cause intracellular crystalliza-

FIGS. 1A AND 1B. Experimental tumor model of a dog's distal femur used to evaluate the effect of cryosurgery. (A) Distal femur after double freeze-thaw cycle of cryosurgery (with liquid nitrogen), curettage, and bone graft at three weeks. Note the rim of necrotic bone (arrows) and the lack of incorporation of the bone graft. (B) Tetracycline fluorescence (arrows) of the distal femur. Note the absence of fluorescence adjacent to the frozen cavity and no uptake by the graft. In general, peripheral necrosis extended 7–12 mm beyond the cavity after cryosurgery. (Reprinted with permission from Malawer, M. M., Marks, M. R., McChesney, D., Piasio, M., Gunther, S. F., and Schmookler, B. M.: The effect of cryosurgery and polymethylmethacrylate in dogs with experimental bone defects comparable to tumor defects. Clin. Orthop. 226:299, 1988.)

tion and membrane disruption, whereas a rapid thaw will not. This is explained by the physics of crystallization. If there is slow warming, the numerous intracellular crystals will recrystallize into a few large crystals that will damage the cell membrane. Upon fast warming, the intracellular crystals will melt before they can damage the cell. Thus, a rapid freeze and slow thaw, termed a "freeze-thaw cycle," results in the maximum cellular and tissue necrosis.

Repeated freeze–thaw cycles will also increase the extent of necrosis. This is due to the increased conductivity of the cold after the first freeze and the resultant increase in volume of frozen tumor during subsequent freezes. The rate and depth of freeze are increased by repetitive cycles and the rate of thaw is delayed (secondary to delay in heat transfer from impairment of the microcirculation), thus the amount of intracellular crystallization is increased.

HISTOLOGIC EFFECT OF CRYOSURGERY ON BONE

There have been only a few studies of the effect of liquid nitrogen or PMMA on bony necrosis. Gage *et al.*[9] described histologic and roentgenographic findings of 18 dog femora treated by liquid nitrogen. They used a closed system of latex tubes that circulated liquid nitrogen within and around the diaphysis of the femur. Kuylenstierna *et al.*,[18] studied the effect of cryosurgery by applying a probe to the lateral cortex of a rabbit mandible. They described the early histologic effects of and the long response to the cryogenic impact. They demonstrated microvascular failure as well as delayed healing and delayed regrowth of the frozen periosteum.

Using a dog model, Malawer *et al.*[21] developed and reported on an experimental procedure that simulated a tumor cavity of the distal femur (Fig. 1). The purpose of this study was to determine the efficacy of liquid nitrogen and PMMA as surgical adjuvants to curettage. The study evaluated the amount of bony necrosis and the effect on bone graft incorporation and normal formation following cryosurgery, acrylic cementation, or cementation and cryosurgery combined. It was concluded that liquid nitrogen had a profound effect on new bone formation and on bone graft incorporation. In general, a cavity of the distal femur not treated by liquid nitrogen showed no necrosis and demonstrated early and progressive reossification. Those with bone graft also showed good incorporation. Conversely, those treated with liquid nitrogen showed no reossification or bone graft incorporation. In addition, all the animals treated with liquid nitrogen demonstrated extensive circumferential necrosis of the cavity extending from 7 to 12 mm from the center. Those animals treated with PMMA alone showed no necrosis.

The most dramatic effect of the liquid nitrogen was on the appearance of the bone marrow (Fig. 2). Following cryosurgery, the marrow showed extensive necrosis with a minimal inflammatory response. The marrow underwent liquefaction with progressive fibrosis. There was little evidence of

FIGS. 2A AND 2B. Histologic effects of cryosurgery. (A) Photomicrograph of necrotic zone three weeks after cryosurgery. The bone marrow shows extensive necrosis with necrotic trabeculae (N). There is a minimal inflammatory component. A thrombosed vessel (arrow) is seen. (B) Photomicrograph of the necrotic zone eight weeks after cryosurgery. Progressive marrow fibrosis occurred following bone marrow necrosis. There is minimal new bone formation (arrow) upon residual necrotic trabeculae (N). Note the absence of osteoblasts. New bone is formed by direct fibrous metaplasia. (Stain, hematoxylin and eosin; original magnification, ×8 in A, ×21 in B. Reprinted with permission from Malawer, M. M., Marks, M. R., McChesney, D., Piasio, M., Gunther, S. F., and Schmookler, B. M.: The effect of cryosurgery and polymethylmethacrylate in dogs with experimental bone defects comparable to tumor defects. Clin. Orthop. 226:299, 1988.)


A
N
B
N

neovasculature throughout the frozen zone. Large, thickened, thrombosed vessels (an indication of microvascular failure) were occasionally seen in the liquid nitrogen groups, compared with none in the controls.

Liquid nitrogen is a powerful surgical adjuvant, as demonstrated by the amount of bone marrow and trabecular necrosis. PMMA showed only minimal response with no evidence of necrosis (Fig. 3). In general, cryosurgery results in significant necrosis by several mechanisms; the marked delay in reossification and of the reparative process appears to be due to local microvascular thrombosis.

TECHNIQUE OF CRYOSURGERY

The direct-pour method, as described by Marcove *et al.*, and its modifications are listed as follows (Fig. 4).

Wide Skin Retraction. Standard skin incisions are used, and wide retraction is required to prevent inadvertent freezing of the edges and subsequent necrosis, dehiscence, or both.

Retraction of Neurovascular Structures. Adjacent neurovascular structures must be protected from freezing. They must be separated from the involved structures.

Tourniquet. If feasible, a tourniquet should

FIG. 3. Photomicrograph of the wall of a tumor cavity of a dog treated by PMMA alone. The PMMA was removed during the preparation. Note the normal marrow adjacent to the cavity. There is a narrow fibroblastic interface (arrows) lining the cavity. There is no evidence of trabecular or bone marrow necrosis as seen following cryosurgery (see Fig. 2B). (Stain, hematoxylin and eosin; original magnification, ×21. Reprinted with permission from Malawer, M. M., Marks, M. R., McChesney, D., Piasio, M., Gunther, S. F., and Schmookler, B. M.: The effect of cryosurgery and polymethylmethacrylate in dogs with experimental bone defects comparable to tumor defects. Clin. Orthop. 226:299, 1988.)

FIG. 4. Intraoperative photograph demonstrates the direct-pour technique of cryosurgery. A funnel is placed in a thoroughly curetted tumor cavity. Gelfoam (arrow) is used to seal the base and to prevent any spillage of liquid nitrogen. The temperature of the cavity and the surrounding bone is monitored by a thermocouple (small arrow). Wide skin flaps are required and are continuously irrigated with a warm saline solution to prevent inadvertent freezing. A single or double freeze–thaw cycle is used.

be used to decrease the heat-sink effect of the circulation and prevent tumor bleeding, which makes adequate freezing more difficult.

Curettage of Tumor. Thorough curettage of the tumor is performed before cryosurgery. A high-speed burr is routinely used. Care is taken not to push the tumor into the medullary canal.

Coolant. Liquid nitrogen is used as the coolant.

Pouring Technique. A metal funnel is placed in the defect, and the base is sealed with wet Gelfoam (UpJohn, Kalamazoo, Michigan). The liquid nitrogen is poured directly into the cavity via the funnel. The size of the funnel depends on the size of the cavity. The initial pour of the nitrogen lasts only two minutes in order to obtain a seal of the spout of the funnel with bone and the Gelfoam. The wet Gelfoam quickly freezes and produces a seal at the base.

Thermocouple Monitoring. A thermocouple is used to monitor the freeze and the temperature of the adjacent tissue.

Freeze–Thaw Cycle. A cycle consists of direct freeze with recorded temperatures below $-40°$ for five minutes and a spontaneous thaw until the temperature of the wall of the tumor rises to above $0°$ (approximately three to five minutes). A single or double cycle is used for aggressive or low-grade sarcomas, respectively. If the epiphyseal plate is opened, a single freeze–thaw cycle is recommended.

Wound Irrigation. The wound and skin edges are closely monitored and intermittently irrigated with a warm saline solution to prevent freezing.

Intraarticular Monitoring. The adjacent joint is monitored with thermocouples. If necessary, continuous irrigation with warm saline can be performed to protect the articular cartilage.

Soft-Tissue Reconstruction. It is essential that a good soft-tissue closure be obtained over the frozen bone. The frozen bone must not be left in a subcutaneous location.

Perioperative Antibiotics. Antibiotics are routinely used.

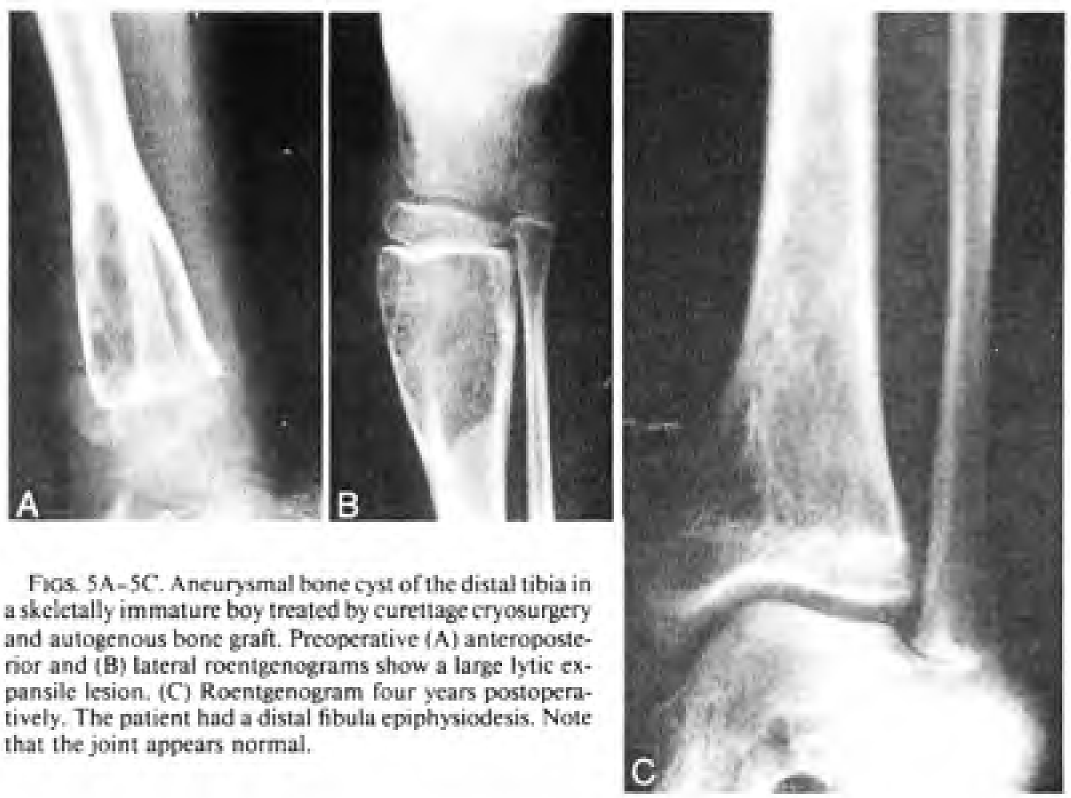
MATERIALS AND METHODS

Between 1976 and 1988, 25 patients below the age of 21 with benign (aggressive) bone tumors were treated with cryosurgery. The average age was 15.3 years (range, six to 21 years). There were 15 females and ten males. There were six upper- and 19 lower-extremity tumors (Fig. 5).

Tumor types are listed in Table 1. The histologic diagnoses were GCT (14), chondroblastoma (seven), ABC (three), and malignant GCT (one). The patients were divided into three groups based on the three types of reconstruction of the resultant surgical defect following cryosurgery. In Group 1, cryosurgery only was performed. In Group 2, bone graft alone was used to reconstruct the defect (Fig. 6). In Group 3, reconstruction consisted of a composite of metallic fixation with PMMA, bone graft, or both. PMMA alone was used in some patients with small lesions, especially those of the upper extremity and foot or ankle (Figs. 7 and 8). The Musculoskeletal Tumor Society functional evaluation system was used to assess function.[7]

RESULTS

Clinical data of the 25 patients are presented in Table 2. The average follow-up pe-



FIGS. 5A–5C. Aneurysmal bone cyst of the distal tibia in a skeletally immature boy treated by curettage cryosurgery and autogenous bone graft. Preoperative (A) anteroposterior and (B) lateral roentgenograms show a large lytic expansile lesion. (C) Roentgenogram four years postoperatively. The patient had a distal fibula epiphysiodesis. Note that the joint appears normal.

TABLE 1. Histogenesis and Anatomic Sites of Tumors in 25 Patients

Data	Patients (n)
Tumor	
GCT	14
Chondroblastoma	7
ABC	3
Malignant GCT	1
Site	
Upper extremity	
Proximal humerus	3
Distal radius	2
Thumb (proximal phalange)	1
Lower extremity	
Pelvis	1
Sacrum	1
Proximal femur	3
Distal femur	5
Proximal tibia	4
Distal tibia	3
Distal fibula	1
Talus	1

riod was 60.8 months. Local tumor control was achieved in 96% (24 of 25) of the patients. One patient developed a local soft-tissue recurrence. She had a malignant GCT and has remained disease free after excision at 95 months.

The complications included secondary fracture in two patients (8%), flap necrosis in one patient (4%), and one synovial fistula. There were no infections. One fracture occurred in the proximal phalange of the thumb and healed nonoperatively, the second fracture occurred in the medial femoral condyle and resulted in a nonunion.

Five patients required one additional procedure each. These secondary procedures were bone graft (one), resection of local recurrence (one), epiphyseodesis (two), and a synovial fistula closure (one). Twenty-four of the 25 patients were evaluated for function. Eighty-three percent (20 of 24) were graded excellent, 13% (three of 24) good, and 4% (one of 24) fair. The latter patient had a fracture of the distal femur and a secondary nonunion. All proximal femoral tumors (three patients) were rated as good. No patients were graded as poor. The type of surgical reconstruction and the functional results were similar for the three groups. There were four Type I, 13 Type II, and eight Type III reconstructions.

DISCUSSION

Classically, aggressive benign tumors such as GCTs, ABCs, chondroblastomas, and osteoblastomas have been difficult to treat because of the high rate of local recurrence following curettage with or without bone graft.[4,7,8,10,13,37] Difficulties in local control following the initial as well as recurrent disease have led investigators to recommend primary resection.[10,13] GCTs have been the most difficult to treat.[10,13] Techniques involving physical adjuncts (cementation and cryosurgery) in combination with curettage have been developed in the hope of decreasing the rate of local recurrence and avoiding the morbidity of a resection.[20–25,34,39,40]

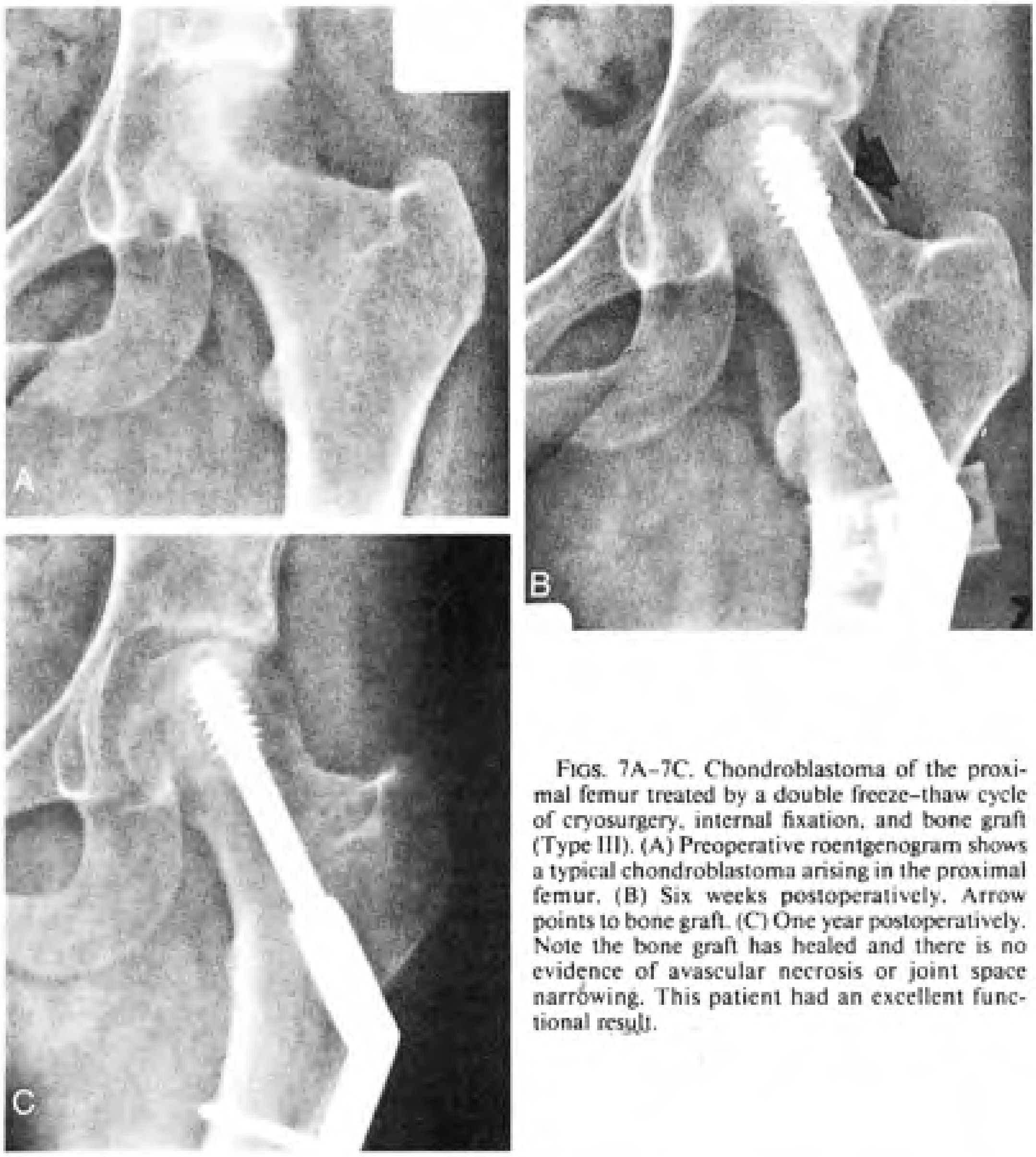
In general, hand curettage (most reports prior to 1980) has been inadequate and has led to the reported high recurrence rates. Mechanical curettage (high-speed burr), combined with cementation, has led to lower rates in the 10%–20% range.[13,27,34,35] The main role of PMMA is probably to stabilize the curetted cavity; its tumorcidal capability is not well documented.[39] Conversely, a large amount of data, as well as the extensive clinical experience as reported by Marcove *et al.*, demonstrates the cytotoxicity of liquid nitrogen (cryosurgery).[1–6,11,16,17,19–29] Cryosurgery is a powerful modality in the treatment of aggressive (benign) and low-grade malignant bone tumors; a local control rate of 96% is reported in this study. Several aspects of the management and technique of these cases deserve special emphasis.

Before surgery, the extent of the tumor must be carefully evaluated. Computed tomography and magnetic resonance imaging are recommended. Soft-tissue extension should be assessed to determine the proxim-

FIGS. 6A AND 6B. A benign GCT of the distal femur treated by cryosurgery and bone graft (Type II). Roentgenograms at (A) two years and (B) four years after surgery. Note the faint cryonecrotic rim (arrows) and the incorporation and retrabeculation at two and four years. This patient has a full range of knee motion. Bone graft incorporation after cryosurgery is delayed.

ity of neurovascular structures and the need for their mobilization and protection. A pathologic fracture is a contraindication to cryosurgery; small, nondisplaced fractures are not. Wide exposure and adequate mobilization of skin flaps and neurovascular bundles, coupled with continuous irrigation of tissues surrounding the funnel, reduced the incidence of skin necrosis to one patient (4%) in this study.

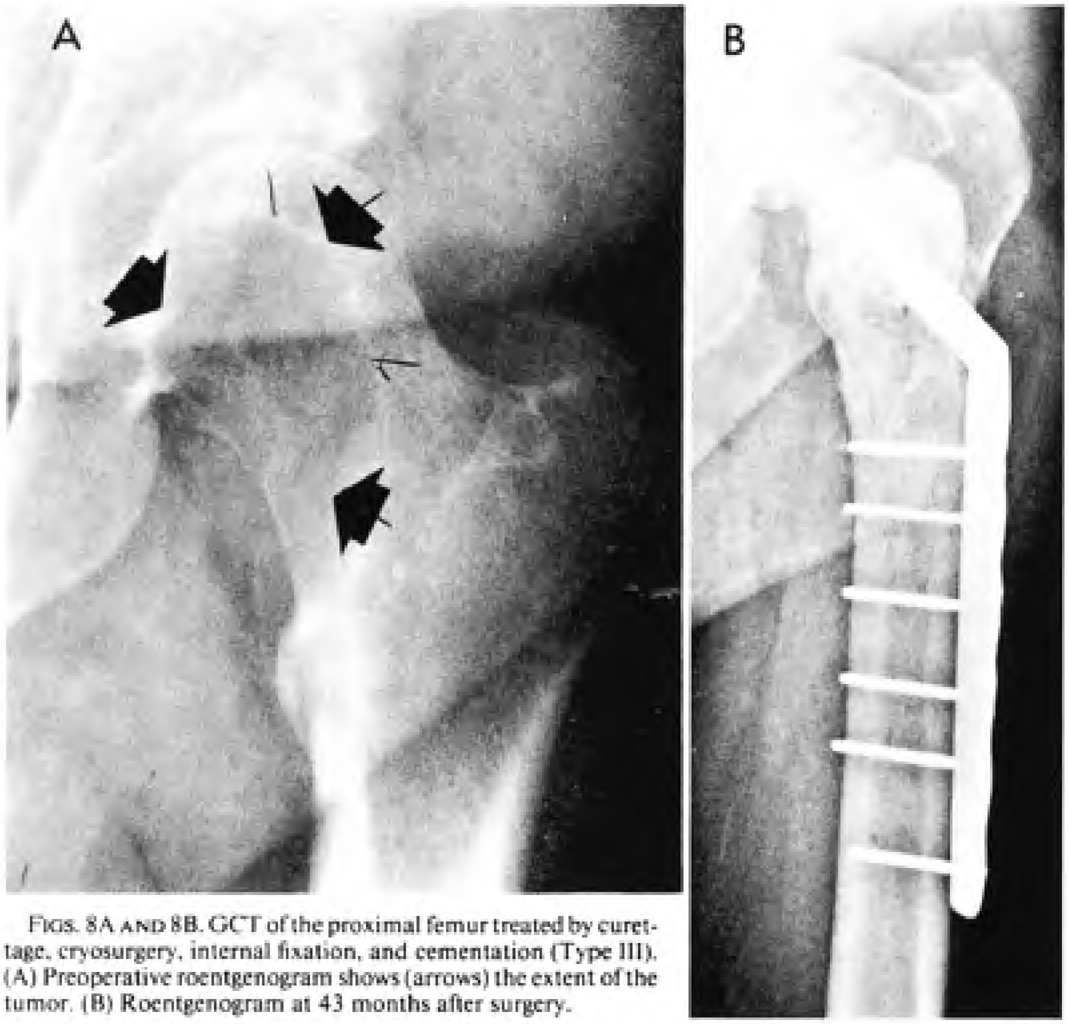
A tourniquet should be used whenever possible to reduce the vascularity and thus the heat supply to the lesion. Several studies have shown that ischemia increases the cytocidal effect of cryosurgery by increasing the rate of cooling and decreasing the rate of thaw.[26–28] Thorough curettage decreases the tumor burden and exposes the residual cells along the wall and those presumed to be between bony trabeculae to the maximum effect of liquid nitrogen. The use of a mechanical burr, in addition to simple curettage, to remove the reactive, sclerotic cavity wall is strongly recommended. After burring, the normal yellowish trabecular bone and marrow should be seen. Mechanical burring alone can substantially reduce the incidence of local recurrence, regardless of whether cryosurgery follows.[5] For maximum contact, the intraosseous cavity must be completely filled



FIGS. 7A–7C. Chondroblastoma of the proximal femur treated by a double freeze–thaw cycle of cryosurgery, internal fixation, and bone graft (Type III). (A) Preoperative roentgenogram shows a typical chondroblastoma arising in the proximal femur. (B) Six weeks postoperatively. Arrow points to bone graft. (C) One year postoperatively. Note the bone graft has healed and there is no evidence of avascular necrosis or joint space narrowing. This patient had an excellent functional result.

with liquid nitrogen at each application. When using the direct-pour technique, one must direct constant attention to the funnel neck to avoid obstruction by ice and formation of a closed system that can lead to a fatal nitrogen embolus. Postoperative elevation (approximately three to five days) is necessary to prevent venous stasis and edema of the flaps and subsequent necrosis, dehiscence, and infection.

There are no differences in indications for the use of cryosurgery in the skeletally immature versus the skeletally mature child. The aim of this technique is to prevent local recurrence and to preserve the adjacent joint that is at a high risk if a recurrence occurs. If



FIGS. 8A AND 8B. GCT of the proximal femur treated by curettage, cryosurgery, internal fixation, and cementation (Type III). (A) Preoperative roentgenogram shows (arrows) the extent of the tumor. (B) Roentgenogram at 43 months after surgery.

epiphyseal closure does occur, an epiphyseodesis of the contralateral epiphysis is recommended. In most instances, the adjacent epiphyseal plate has been destroyed by the tumor before surgical intervention, especially in patients with chondroblastomas and GCTs. In addition, ABCs consistently extend to and involve the epiphyseal plate. Any attempt to limit tumor removal by minimizing curettage adjacent to the plate increases the risk of tumor recurrence. Thus, before surgery, irrespective of the technique used, one must inform the family that the involved epiphysis may be nonfunctional after an attempt at adequate tumor resection. On the other hand, it must be explained that the effect of cryosurgery on the epiphyseal plate is variable, and normal growth may occur.

Late fracture is the most common and potentially serious reported complication associated with cryosurgery. Marcove *et al.*[22-25] reported a 28% fracture rate for their first 25 patients with GCTs and 18% for the second 25 patients. Fracture is an inherent risk of cryosurgery. Frozen bone shows trabecular necrosis with disruption of the osteoid seams and extensive marrow necrosis extending a minimum of 1 cm from the periphery of the

TABLE 2. Clinical Data of 25 Patients Below the Age of 21 Treated With Cryosurgery

Case	Diagnosis	Follow-Up Period (months)	Site	Group	Function
1	GCT	156.2	Talus	2	Excellent
2	GCT	156.2	Proximal tibia	2	Excellent
3	ABC	121.7	Distal fibula	1	Excellent
4	GCT	118.7	Distal tibia	1	Excellent
5	CB	110.5	Proximal tibia	1	Excellent
6	GCT (malignant)	95.3	Distal femur	3**	Excellent
7	ABC	80.1	Proximal tibia	2	Excellent
8	GCT	61.8	Distal femur	3	Excellent
9	GCT/ABC*	55.7	Distal tibia	2	Excellent
10	GCT/ABC*	55.7	Proximal tibia	2	Excellent
11	CB	53.7	Distal femur	2	Excellent
12	ABC	49.7	Sacrum	1	Excellent
13	ABC	49.7	Distal tibia	2	Excellent
14	CB	48.7	Proximal femur	3	Excellent
15	GCT	43.6	Thumb	2	N/A
16	GCT	30.4	Distal femur	3	Excellent
17	GCT	23.3	Humerus	2	Excellent
18	GCT	16.2	Pelvis	1	Excellent
19	CB	14.2	Proximal humerus	2	Excellent
20	CB	13.1	Proximal femur/humerus	3	Good
21	CB	10.1	Proximal femur/humerus	3	Good
22	CB	8.0	Proximal humerus	3	Excellent
23	ABC	8.0	Distal radius	3	Excellent
24	GCT	80.1	Distal radius	2	Excellent
25	GCT	88.2	Distal femur	3	Good

* Aneurysmal bone cyst arising in a GCT.
** Local recurrence.

frozen defect. Frozen bone reossifies slowly and often incompletely; it tends to act like an autograft. Gage *et al.* termed this as an "autograft *in situ*."[9] The fracture rate of the present study was 8%. To reduce the possibility of fracture, reconstruction of large defects to support the tumor cavity and articular surface is recommended. PMMA and internal fixation provide immediate stability. Corticocancellous grafts are required to strengthen the subchondral bone, whereas fibular struts reconstitute the cortical defect. The present study compared the complication rate in a group of 25 pediatric patients with the overall experience of 74 patients (unpublished data). Interestingly, the fracture rate and incidence of flap necrosis were lower in the pediatric group: 8% versus 18%, and 4% versus 10%, respectively. In general, tumors of children are smaller, and the well-known ability of children to reossify and heal bony defects is reflected in a lower fracture rate.

The overall functional results in the 25 patients were 96% good and excellent. Surprisingly, tumors of the hip were all rated good; there were no cases of secondary fracture or avascular necrosis. Epiphyseodesis, when required, reliably equalized potential leg-length discrepancies in the younger patient.

Cryosurgery extends the margin of a simple curettage, making it biologically equivalent to a wide (intracompartmental) resection. Cryosurgery entails using a wide excision *in situ* but without the morbidity of an *en bloc* resection and the need to sacrifice a joint. Compared with other techniques, cryosurgery not only preserves bone stock and joint function but also is accompanied by a significant decrease in the local recurrence rate. Routine resection of benign (aggressive) bone tumors is not warranted; a large number of these lesions can be cured by cryosurgery. In general, a primary resection is reserved for extremely large lesions and for patients with a significant pathologic fracture. PMMA is used to obtain immediate fixation and stabilization of these large defects, especially in the weight-bearing bones. This study agrees with Willert[40] that PMMA alone probably does not provide adequate tumor control. The improved results of the present study, compared with those associated with hand curettage alone, may be attributed to combining mechanical burring and cryosurgery to extend the margin of resection.

REFERENCES

1. Asahina, E., and Emura, M.: Types of freezing and the post-thawing survival of mammalian sarcoma cells. Cryobiology 2:256, 1966.
2. Barner, H. B.: The vascular lesion of freezing as modified by dimethyl sulfoxide. Cryobiology 2:55, 1965.
3. Berggren, R., Ferraro, J., and Price, B.: A comparison of cryoprophylactic agents for the pre-treatment of frozen rat skin. Cryosurgery 3:272, 1966.
4. Biesecker, J. L., Marcove, R. C., Huvos, A. G., and Mike, V.: Aneurysmal bone cysts, a clinicopathologic study of 66 cases. Cancer 26:615, 1970.
5. Blackwood, J., Moore, F. T., and Pace, W. G.: Cryotherapy for malignant tumors. Cryobiology 4:1, 1967.
6. Cooper, I. S.: A new method of destruction or extirpation of benign or malignant tissues. N. Engl. J. Med. 268:743, 1963.
7. Enneking, W. F.: Limb-Sparing Surgery in Musculoskeletal Oncology. New York, Churchill-Livingstone, 1987, pp. 5–16.
8. Enneking, W. F., Spanier, S. S., and Goodman, M. A.: A system for the surgical staging of musculoskeletal sarcoma. Clin. Orthop. 153:106, 1980.
9. Gage, A., Greene, G. W., Neiders, M. E., and Emmings, F. G.: Freezing bone without excision. An experimental study of bone cell destruction. JAMA 196:770, 1966.
10. Goldenberg, R. R., Campbell, C. J., and Bonfiglio, M.: Giant cell tumor of bone. An analysis of two hundred and eighteen cases. J. Bone Joint Surg. 52A:619, 1970.
11. Harris, L., and Griffiths, J.: Relative effects of cooling and warming rates on mammalian cells during the freeze-thaw cycle. Cryobiology 14:662, 1977.
12. Hoekstra, H. J., Koops, H. S., Oeseburg, H. G., and Oldhoff, J.: Two extensive giant cell tumors of the proximal humerus treated by resection–reconstruction of excochleation-cryosurgery. Arch. Chirurgicum Neerlandicum 31:49, 1979.
13. Hutter, R., Worchester, J., Francis, K. C., Foote, F. W., Jr., and Stewart, P.: Benign and malignant giant cell tumors of bone. Cancer 15:653, 1962.
14. Jennings, J. W., Sr.: Production and control of low temperatures in cryosurgery. Assoc. Oper. Room Nurs. 7:41, 1968.
15. Johnston, J.: Treatment of giant cell bone tumors by aggressive curettage and packing with bone cement. *In* Enneking, W. F. (ed.): Limb-Sparing Surgery in Musculoskeletal Oncology. Churchill-Livingstone, New York, 1987, pp. 512–516.
16. Karow, A. R., and Webb, W. R.: Tissue freezing, a theory for injury and survival. Cryobiology 2:99, 1965.
17. Kreyberg, L.: Local freezing. Proc. R. Soc. London 147:546, 1957.
18. Kuylenstierna, R., Nathanson, A., and Lundquist, P.-G.: Effects of cryosurgery on the healing pattern of rabbit mandibular bone. Acta Otolaryngol. 92:569, 1981.
19. Luyet, B. J., and Gehenio, M. P.: Life and Death at Low Temperatures. Normandy, Missouri, Biodynamica, 1940, p. 341.
20. Malawer, M. M., and Dunham, W. K.: Cryosurgery in the management of benign (aggressive) and low grade malignant tumors of bone: Analysis of 40 consecutive cases. *In* Enneking, W. F. (ed.): Limb-Sparing Surgery in Musculoskeletal Oncology. Churchill-Livingstone, New York, 1987, pp. 498–510.
21. Malawer, M. M., Marks, M. R., McChesney, D., Piasio, M., Gunther, S. F., and Schmookler, B. M.: The effect of cryosurgery and polymethylmethacrylate in dogs with experimental bone defects comparable to tumor defects. Clin. Orthop. 226:299, 1988.
22. Marcove, R. C., Lyden, J. P., Huvos, A. G., and Bullough, P. B.: Giant cell tumors treated by cryosurgery. A report of twenty-five cases. J. Bone Joint Surg. 55A:1633, 1973.
23. Marcove, R. C., Searfoss, R. C., Whitmore, W. F., and Grabstald, H.: Cryosurgery in the treatment of bone metastases from renal cell carcinoma. Clin. Orthop. 127:220, 1977.
24. Marcove, R. C., Stovell, P. B., Huvos, A. G., and Bullough, P. G.: The use of cryosurgery in the treatment of low and medium grade chondrosarcoma. A preliminary report. Clin. Orthop. 122:147, 1977.
25. Marcove, R. C., Weis, L. D., Vagharwalla, M. R., and Pearson, R.: Cryosurgery in the treatment of giant cell tumors of bone. A report of 52 consecutive cases. Clin. Orthop. 134:275, 1978.
26. Mazur, P.: Theoretical and experimental effects of cooling and warming velocity on the survival of frozen and thawed cells. Cryobiology 2:181, 1966.
27. Mazur, P.: Cryobiology: The freezing of biological systems. Science 168:939, 1970.
28. McGann, L. E., Kruuv, J., Frim, J., and Frey, H. E.: Factors affecting the repair of sublethal freeze-thaw damage in mammalian cells. Suboptimal temperature and hypoxia. Cryobiology 12:530, 1975.
29. Miller, R. H., and Mazur, P.: Survival of frozen-

thawed human red cells as a function of cooling and warming velocities. Cryobiology 13:404, 1976.

30. Neel, H., Ketcham, A., and Hammond, A.: Requisites for successful cryogenic surgery for cancer. Arch. Surg. 102:45, 1971.
31. Oeseburg, H. B., Rogge, C. W. L., Koops, H. S., and Oldhoff, J.: Cryosurgical treatment of aneurysmal bone cysts. J. Surg. Oncol. 10:20, 1978.
32. Pegg, D. E.: Cryobiology, review article. Phys. Med. Biol. 2:209, 1966.
33. Persson, B. M., Rydholm, A., Berlin, O., and Gunterberg, B.: Curettage and acrylic cementation in surgical treatment of giant cell tumors. *In* Enneking, W. F. (ed.): Limb-Sparing Surgery in Musculoskeletal Oncology. Churchill-Livingstone, New York, 1987, p. 476.
34. Persson, B. M., and Wouters, H. W.: Curettage and acrylic fixation cementation in surgery of giant cell tumor of bone. J. Bone Joint Surg. 120B:125, 1976.
35. Taminiau, A. H. M., and Wouters, H. W.: Treatment of giant cell tumors by curettage and cementation. *In* Enneking, W. F. (ed.): Limb-Sparing Surgery in Musculoskeletal Oncology. Churchill-Livingstone, New York, 1987, p. 477.
36. Taylor, A. C.: Effect of rate of cooling on survival of frozen tissues. Proc. R. Soc. London 147:466, 1957.
37. Tillman, B. P., Dahlin, D. C., Lipscomb, P. R., and Stewart, J. R.: Aneurysmal bone cyst: An analysis of ninety-five cases. Mayo Clin. Proc. 43:478, 1967.
38. Walton, A.: Cold shock of spermatozoa. Proc. R. Soc. London 147:508, 1957.
39. Wilkins, R. M., Okada, Y., Sim, F. H., Chao, E. Y. S., and Gorgki, J.: Methylmethacrylate replacement of subchondral bone: A biomechanical, biochemical, and morphologic analysis. *In* Enneking, W. F. (ed.): Limb-Sparing Surgery in Musculoskeletal Oncology. Churchill-Livingstone, New York, 1987, pp. 479–485.
40. Willert, H.-G.: Clinical results of the temporary acrylic bone cement plug in the treatment of bone tumors: A multicentric study. *In* Enneking, W. F. (ed.): Limb-Sparing Surgery in Musculoskeletal Oncology. Churchill-Livingstone, New York, 1987, pp. 445–458.