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Cryosurgery in the Treatment of Giant Cell Tumor

A Long Term Followup Study

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Between 1983 and 1993, 102 patients with giant cell tumor of bone were treated at three institutions. Sixteen patients (15.9%) presented with already having had local recurrence. All patients were treated with thorough curettage of the tumor, burr drilling of the tumor inner walls, and cryotherapy by direct pour technique using liquid nitrogen. The average followup was 6.5 years (range, 4–15 years). The rate of local recurrence in the 86 patients treated primarily with cryosurgery was 2.3% (two patients), and the overall recurrence rate was 7.9% (eight patients). Six of these patients were cured by cryosurgery and two underwent resection. Overall, 100 of 102 patients were cured with cryosurgery. Complications associated with cryosurgery included six (5.9%) pathologic fractures, three (2.9%) cases of partial skin necrosis, and two (1.9%) significant degenerative changes. Overall function was good to excellent in 94 patients (92.2%), moderate in seven patients (6.9%), and poor in one patient (0.9%). Cryosurgery has the advantages of joint preservation, excellent functional outcome, and low recurrence rate when compared with other joint preservation procedures. For these reasons, it is recommended as an adjuvant to curettage for most giant cell tumors of bone.

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Giant cell tumor of bone first was described in 1818 by Cooper and Travers.[10] Its local aggressiveness was described by Nelaton [53] and its malignant potential by Virchow.[65] During the preroentgen era, most giant cell tumors were treated by radical amputation.[45] Development of precise clinical criteria using radiologic studies permitted better tumor identification and less radical treatment.[4,9]

The descriptor benign first was applied to giant cell tumor by Bloodgood [4] to differentiate these tumors from other bony malignancies that required amputation. He stated that a significant number of patients with giant cell tumor could be cured by multiple excisions. Giant cell tumor now is considered a benign aggressive lesion. This terminology is misleading, because 3% of giant cell tumors are primarily malignant[13,14,16,52,64] or will undergo malignant transformation and metastasize either after radiation therapy[6,51,58] or after several local recurrences.[24,26,31]

Giant cell tumor represents approximately 5% of all primary bone tumors. Seventy percent of these lesions occur in the third or fourth decades of life.[6,13,16,24] The tumor is thought to arise in the metaphyseoepiphyseal junction.[13,16,24,57] Large tumors may extend into the metaphysis and, more rarely, into the diaphysis. The primary areas of involvement are the femoral condyles, tibial plateau, proximal humerus, and distal radius.[16,24,35]

CRYOTHERAPY IN THE TREATMENT OF GIANT CELL TUMOR

In 1966, Gage et al [20] published their initial findings on the biologic effect of cryotherapy on bone. These authors produced bone necrosis in laboratory animals by circulating liquid nitrogen around the femurs and observed subsequent bone regeneration from the periosteum and endosteum. Marcove and Miller [38] first used cryotherapy in the treatment of metastatic carcinoma of the proximal humerus in 1969. They used cryosurgery for treatment of various benign and metastatic bone tumors.[36,37,39,40,42] Marcove et al[41,43] described the use of cryosurgery in the treatment of primary bone sarcomas. During the 1970s, Marcove et al [42] pioneered the development of cryotherapy in the treatment of giant cell tumor of bone and described the effectiveness of a direct pour method in freezing the walls of a curetted cavity. This technique used wide incision, thorough curettage, and repetitive exposure of the curetted area to temperatures below –20° C by liquid nitrogen instillation.[42] They advocated this method as a physical adjuvant in the hope of decreasing the high rates of local recurrence after curettage, thus avoiding the need for extensive resection and reconstruction.[42]

Extensive data within the field of cryobiology show that five mechanisms are involved in the cytotoxicity produced by liquid nitrogen: (1) thermal shock, (2) electrolyte changes, (3) formation of intracellular ice crystals and membrane disruption, (4) denaturation of cellular proteins, and (5) microvascular failure.[23,29,44,47,49] The formation of intracellular ice crystals is considered the main mechanism of cellular necrosis. During cryotherapy, rapid freeze causes intracellular ice crystals to form; this is followed by a slow thaw that causes intracellular crystallization and membrane destruction. Malawer et al [34] emphasized the role of microvascular thrombosis and described a 7 to 12 mm rim of bone necrosis when liquid nitrogen was used in a dog model. A second freeze and thaw cycle is more effective because of the increased conductivity of the cold after the first cycle.[44] Marcove et al[42] stated that three freeze and thaw cycles produce tumor cell death up to 2 cm from the cavity margin.

Cryosurgery has been associated with injury to the adjacent rim of bone, cartilage, and soft tissues caused by exposure to liquid nitrogen with secondary fractures, skin injury with wound healing problems, and temporary neurapraxia (Table 1). The reported rate of local recurrence varies, ranging from 7.1% to 57% (Table 2).

The purpose of this study was to evaluate the efficacy of cryosurgery as a physical adjuvant in the treatment of giant cell tumor of bone. Particular attention was given to the rate of local recurrence and the extent of complications that have given this modality a poor reputation. The study was performed at three oncology centers, using the same technique of curettage, cryosurgery, and reconstruction. It is the largest report published of giant cell tumors treated by cryosurgery with long term followup. This is a timely subject in the face of surgical advances with cryotherapy in the treatment of other cancers.[66,70,71]

MATERIALS AND METHODS

One hundred two consecutive patients with giant cell tumor of bone were treated between January 1983 and June 1993 at three institutions. All participating surgeons trained together and used the same technique of curettage, resection, cryotherapy, and reconstruction. There were 52 male and 50 female patients. Ages ranged from 15 to 72 years (average, 27 years). The average followup

TABLE 1. Literature Review on Complication Rate After Cryosurgery

Author	Cases	Fracture	Infection	Joint Degeneration	Nerve Palsy	Other
Marcove et al[37,42]	52	13	8	2	4	—
Marcove et al[41]	18	7	—	—	4	Joint stiffness (3)
Jacobs and Clemency[25]	12	6	—	—	—	—
Malawer and Dunham[33]	25	2	—	—	—	Flap necrosis (1) Synovial fistula (1)
Aboulafia et al[1]	9	—	—	—	—	—
Marcove et al[39]	7	—	2	—	—	Rectal fistula (1)
Marcove et al[40]	51	5	—	—	1	—
Schreuder et al[61]	26	1	2	—	1	—
Total	200	34	12	2	10	
Percent		17	6	1	5	

was 6.5 years (range, 4–15 years). Sixteen patients (15.9%) presented with local recurrences; these patients had undergone one to three previous surgical procedures. All patients underwent staging studies that included plain radiography, computed tomography (CT), and chest radiograph. Figure 1 shows the anatomic distribution of the tumor. Using Campanacci's staging system for giant cell tumor of bone,[5] 15 tumors were classified as Stage I, 47 tumors as Stage II, and 40 tumors as Stage III.

If the clinical presentation and the imaging studies were compatible with diagnosis of a classic benign giant cell tumor of bone, the biopsy (frozen section) and surgery were performed during the same session. In case of atypical clinical or radiologic presentation, either CT guided core needle or open incisional biopsy were performed and surgery was delayed until histopathologic evaluation had been completed.

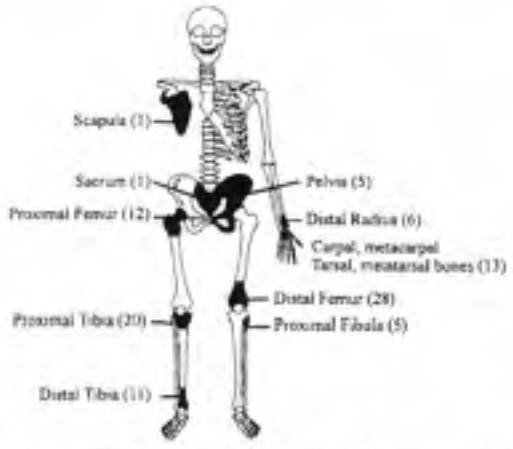

Fig 1. Anatomic site of giant cell tumor in 102 patients treated with cryosurgery.

Three patients presented with a closed pathologic fracture of the distal femur after minor trauma. This group of patients was treated with an open reduction, curettage, burr drilling, and internal fixation. Cryosurgery, as described in the surgical technique section, was performed 4 to 6 months later when fracture healing was established clinically and radiologically.[2]

Surgical Technique

When possible, a pneumatic tourniquet was used during the procedure to decrease local bleeding and prevent blood from acting as a heat sink and being a thermal barrier for the cryotherapy. Because of the metaphyseoepiphyseal location of giant cell tumors in long bones, cryosurgery, with the exception of the proximal femur, is an extracapsular procedure. Violation of the joint cavity must be avoided because of the possibility of contamination of the joint cavity with tumor cells and potential injury to the cartilage after direct exposure to liquid nitrogen. Pelvic lesions were approached using the utilitarian incision, described by Enneking.[17] Sacral and scapular lesions were approached using a longitudinal posterior incision. After exposure of the involved bone and soft tissues, a cortical window the size of the longest longitudinal dimension of the tumor was made. A large cortical window is essential to expose the entire tumor and avoid in-

TABLE 2. Literature Review of Local Recurrence Rate After Curettage, Curettage and Burr Drilling, Resection, and Cryosurgery for Giant Cell Tumor of Bone

	Curettage		Curettage and Burr Drilling		Resection		Cryosurgery	
Author	*n*	*LR*	*n*	*LR*	*n*	*LR*	*n*	*LR*
Johnston and Dahlin[27]	71	41	—	—	14	2	—	—
Hutter et al[24]	—	—	—	—	9	4	—	—
Mnaymneh et al[51]	23	13	—	—	21	0	—	—
Johnson and Riley[26]	16	8	—	—	—	—	—	—
Dahlin et al[12]	17	4	—	—	6	4	—	—
Goldenberg et al[22]	136	73	—	—	66	22	—	—
McGarth[48]	20	9	—	—	7	0	—	—
Marcove et al[37,42]	—	—	—	—	—	—	52	12
Larsson et al[32]	30	14	—	—	—	—	—	—
Persson and Woulers[56]	12	3	—	—	5	2	—	—
Enneking and Shirley[19]	—	—	—	—	10	0	—	—
Sung et al[63]	52	14	—	—	75	8	—	—
Jacobs and Clemency[25]	—	—	—	—	—	—	12	2
McDonald et al[46]	85	29	—	—	27	2	—	—
Campanacci et al[6]	151	41	122	10	58	0	—	—
Malawer and Dunham[33]	—	—	—	—	—	—	14	1
Gitelis et al[21]	—	—	—	—	20	0	—	—
Sanjai et al[60]	9	5	—	—	6	0	—	—
Aboulafia et al[1]	—	—	—	—	—	—	6	1
Marcove et al[39]	—	—	—	—	—	—	7	4
O'Donnell et al[54]	19	8	24	4	—	—	—	—
Kattapuram et al[30]	7	3	—	—	—	—	—	—
Yip[69]	—	—	29	2	15	0	—	—
Total	648	265	175	16	339	44	91	20
Percent		40.8		9.1		12.9		21.9

Present study	n	LR (%)
Patients with giant cell tumor, treated primarily with cryosurgery	*86*	*2 (2.3)*
Patients with already recurrent giant cell tumor, treated with cryosurgery	*16*	*6 (37.5)*
Total	*102*	*8 (7.9)*

n = number of treated patients; LR = number of patients with recurrent disease.

adequate curettage. It has to be elliptical with its axis parallel to the long axis of bone to reduce the stress rising effect (Fig 2). The tumor was approached through the retained thinned or destroyed cortex to minimize additional bone loss. All gross tumor was removed with hand curettes. This was followed by high speed burr drilling with Midas Rex® (Midas Rex, Forth Worth, TX) or Black Max® (Anspach, Lake Park, FL) of the inner reactive shell (Fig 3). Before introduction of the liquid nitrogen, bony perforations were identified and sealed, and the surrounding skin, soft tissues, and neurovascular bundle were protected by mobilization and shielding with Gelfoam® (Upjohn, Kalamazoo, MI). Large skin flaps were retracted to protect them from any possible spillage of the liquid nitrogen (Fig 4).

The direct pour (open) technique as described by Marcove et al [42] was used; liquid nitrogen (-196° C) was poured through a stainless steel funnel into the tumor cavity, and care was taken to fill the entire cavity. A thermocouple was used to monitor the freeze within the cavity, cavity wall, adjacent soft tissue, and the area 1 to 2

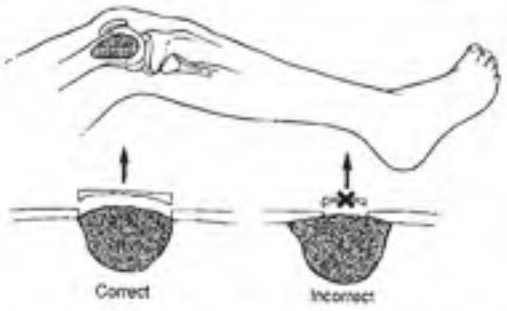

Fig 2. A large cortical window is essential to expose the entire tumor and avoid inadequate curettage.

mm from the periphery of the cavity. The surrounding soft tissues were irrigated with warm saline solution to decrease the possibility of thermal injury. Two freeze and thaw cycles were administered. In each cycle, liquid nitrogen was left in the cavity until it had evaporated completely. Each cycle lasted for 1 to 2 minutes and was proportional to the volume of poured liquid nitrogen. Spontaneous thaw was allowed to occur for 3 to 5 minutes. The temperature of the cavity was monitored with a thermocouple; once it rose above 0° C, the cycle was considered complete. After evaporation, the cavity was irrigated with saline.

Reconstruction then was performed. Three types of reconstructions were used depending on the site and size of the cavity. These were classified as Type 1, no reconstruction, usually for small cavities of less than 2 cm in nonweightbearing areas; Type 2, polymethylmethacrylate plus or minus bone graft, before the routine use of internal fixation; and Type 3, polymethylmethacrylate plus or minus bone graft plus internal fixation with intramedullary hardware (Figs 5–7). Proximal femur

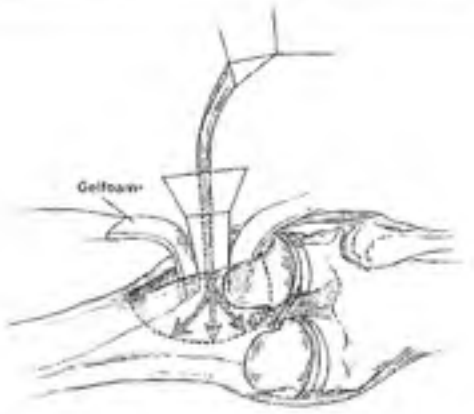

Fig 4. Liquid nitrogen is poured through a stainless steel funnel. Temperature within the cavity, and in the surrounding bone and soft tissues is monitored with thermocouples. Tissues are irrigated continuously with warm saline solution.

lesions were reconstructed with a side plate and compression screw (Fig 8). The subchondral surfaces were reconstructed with autologous bone graft before cementation. There were nine Type 1, 20 Type 2, and 73 Type 3 reconstructions.

Postoperative Management

Routine perioperative prophylactic antibiotics were administered for 3 to 5 days. The wounds were examined on the third day after surgery. If the skin was intact, passive and active motion of the adjunct joint was begun. Patients with lesions of the lower extremities were kept nonweightbearing for 6 weeks. Radiographs were obtained 6 weeks postoperatively to rule out fracture and to establish bone graft incorporation. If healing had progressed satisfactorily, weightbearing was

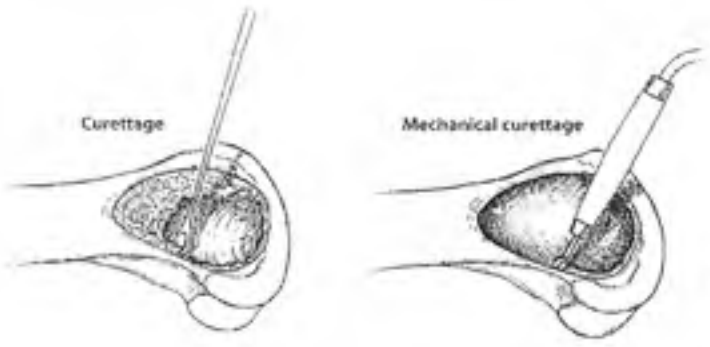

Fig 3. To remove all macroscopic tumor, curettage has to be followed by meticulous burr drilling.

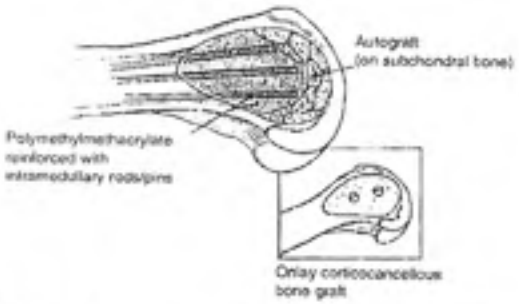

Fig 5. Type 3 reconstruction with intramedullary hardware and reinforcement with polymethylmethacrylate and corticocancellous bone graft.

allowed. For the first 2 years after surgery, patients were observed in the outpatient clinic every 3 months. On each visit, physical examination and radiographs were performed. Patients were examined semiannually for an additional 3 years and annually thereafter.

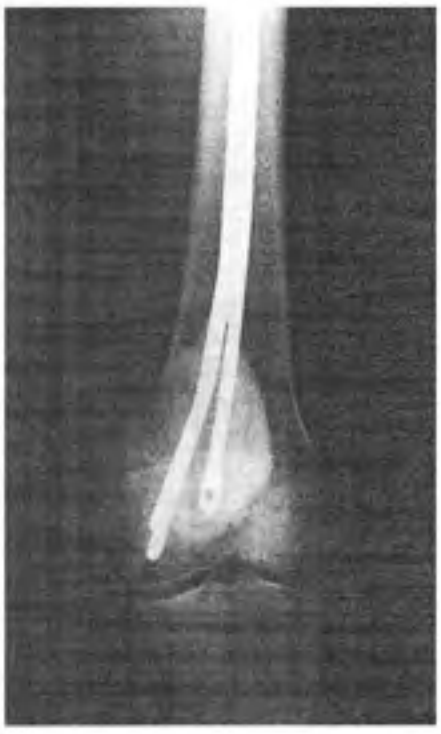

Fig 6. Plain radiograph of Type 3 reconstruction of the distal femur.

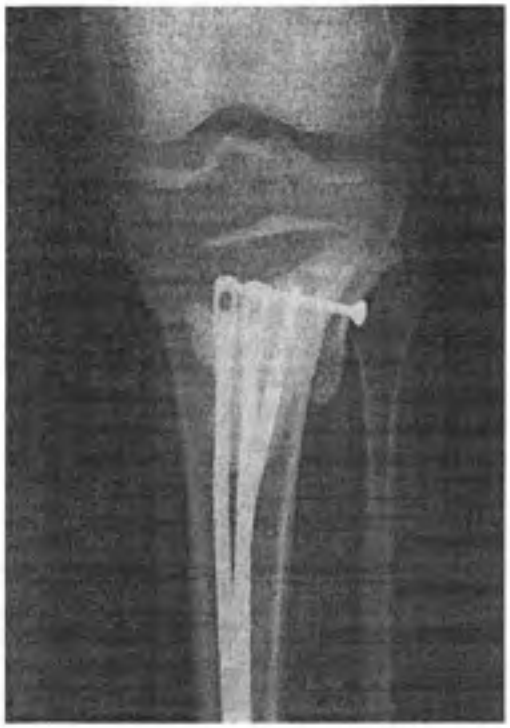

Fig 7. Plain radiograph of Type 3 reconstruction of the proximal tibia.

Data Analysis

All clinical records and imaging studies were analyzed for each patient by an orthopaedic oncologist and musculoskeletal radiologist. The site and stage of each lesion was observed on radiographs. The rates of local recurrence, fracture, neurapraxia, wound complications, and degenerative changes were determined. Functional evaluation was done according to the American Musculoskeletal Tumor Society system, [18] and was determined by the orthopaedic oncologist at each patient's most recent followup.

RESULTS

One hundred two patients with giant cell tumor of bone were treated with curettage, burr drilling, and cryosurgery with either Type 1, Type 2, or Type 3 reconstruction. The average followup was 6.5 years with a minimum of 4 years.

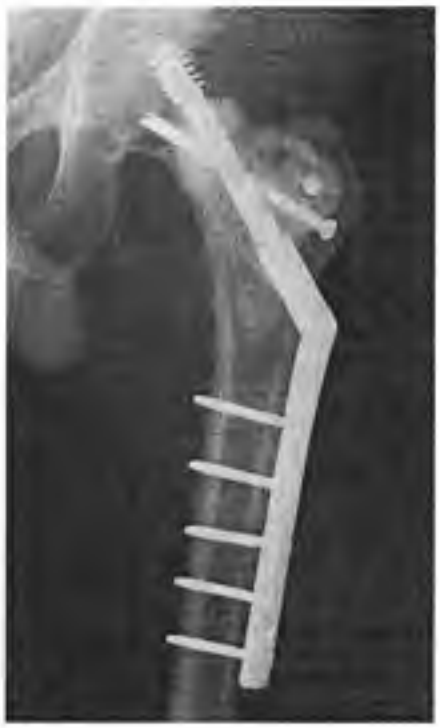

Fig 8. Plain radiograph of Type 3 reconstruction of the proximal femur.

Local Recurrence

Local recurrence developed in eight patients (7.9%), of which seven were located in bone and one in the soft tissues. The rate of local recurrence among the 86 patients with no prior treatment was 2.3% (two patients), whereas the recurrence rate among the 16 patients who were referred with local recurrence was 37.5% (six patients). After cryosurgery, none of the three patients who presented with a pathologic fracture had a local recurrence.

Local recurrences appeared 9 to 48 months after surgery (average, 16 months). Six of the eight patients with local recurrences were treated by recurettage and cryosurgery; the two other patients underwent resection surgery. One of these patients had an endoprosthetic replacement and the second underwent resection arthrodesis (radiocarpal fusion). One hundred of 102 patients in the present series were cured with cryosurgery. All of the patients were disease free at their most recent followup.

Fracture

Postoperative fracture occurred in six patients (5.9%), none of whom had undergone internal fixation. Therefore, the fracture rate among patients treated by internal fixation (Type 3 reconstruction) is 0% (0 of 73 patients) and 21% (six of 29 patients) among patients who were not treated with internal fixation (Type 1 or Type 2 reconstruction). All fractures occurred during the first 2 years after the operation, all around the knee joint (distal femur, four; proximal tibia, two), and often after minor trauma to the extremity. Five fractures eventually united after conservative treatment by means of closed reduction and external immobilization with cast or braces for an average of 9 months. The one remaining patient required surgery for an asymptomatic nonunion of the tibia.

Wound, Soft Tissue Injury

There were no cases of early or late bone or soft tissue infection, wound dehiscence, or full thickness skin necrosis. Three patients (2.9%) sustained partial skin necrosis. This damage resulted from contact with leaking liquid nitrogen and was managed satisfactorily by nonsurgical treatment. A peroneal nerve palsy was observed in one patient and recovered spontaneously after 6 months. No venous or arterial thromboses were observed. No neurologic deficits were observed in the one patient who was treated for giant cell tumor of the sacrum. In that case, as in any other anatomic location, nerves were retracted and protected with Gelfoam.®

Degenerative Changes

Radiographic and clinical evidence of degenerative changes around the knee joint developed in two patients. One had mild symptoms that were managed with conservative treatment and the other required a total knee replacement.

Function

Function was estimated to be good or excellent in 94 patients (92.2%), moderate in seven patients (6.9%), and poor in one patient (0.9%).

DISCUSSION

The purpose of this study was to determine the efficacy of cryosurgery in the treatment of giant cell tumor of bone. One hundred two consecutive patients with giant cell tumor of bone were treated with cryosurgery with a long term followup. This is the largest report to date of giant cell tumors treated by cryosurgery.

Giant cell tumor is a benign aggressive lesion. For that reason, absence of local recurrence, rather than patient survival, is the major criterion used to assess adequacy of surgical treatment. Adequacy of the surgical margin, rather than the radiologic stage of the tumor, is the major determinant of local tumor control.[6,46]

Treatment Strategies

During the past several decades, surgeons have used various modalities in the treatment of giant cell tumors of bone: (1) curettage,[6,12,22,27,28,32,45,48,51,54,60,63,69] (2) curettage and cytotoxic agents such as phenol,[12,14,15,21,54,63] zinc chloride,[48] alcohol,[15,63] and H_2O_2,[55,56] (3) curettage and a physical adjuvant (polymethylmethacrylate[3,54–56] and cryosurgery[25,36,37,39,42]), (4) primary resection,[6,12,19,21,24,27,46,48,51,60,63,69] (5) radiation therapy,[6,27,51,62] and (6) embolization, which is practiced in unresectable tumors.[8] In a classic study from the Memorial Sloan-Kettering Hospital, Hutter et al[24] reported that recurrence rates in giant cell tumors treated by curettage alone were higher than those in tumors treated by resection or curettage in combination with physical adjuvants. Table 2 summarizes a large combined clinical experience of 648 patients with giant cell tumor treated by curettage with an average local recurrence rate of 40.8% (265 patients).

After the neoplastic tissue is curetted away from the inner wall of the lesion, the reactive shell consistently reveals an irregular contour. This irregularity makes it virtually impossible to remove all the tissue with a curette.[16] When curettage is followed by burr drilling, the rate of local recurrence seems to decrease significantly; however, although burr drilling is a basic step in most nonresection surgeries of giant cell tumors, there are only a few series of patients treated with curettage and burr drilling alone (Table 2).

The difficulties with local control led some investigators to recommend en bloc resections for persistent cases of giant cell tumor. An analysis of 14 studies involving 339 patients treated with resection surgery yielded an average recurrence rate of 12.9% (Table 2). Although this group of patients has one of the lowest recurrence rates, joint function was limited because most tumors are epiphyseometaphyseal and, therefore, necessitate intraarticular resection.[6,16,21,63] Wide excision and replacement with an allograft or a prosthesis is considered too extensive surgery to obtain local control, and curettage plus an adjuvant modality is the main technique used in the treatment of most giant cell tumors of bone.

Phenol, which coagulates all proteinaceous substances, may remove microscopic tumor residua that remains after curettage.[14,15,63] Because the number of reported patients treated with only curettage and phenol is quite small and the recurrence rate is extremely variable (5% to 66%),[12,15,21,54,63] the efficacy of phenol as an adjuvant to curettage is questionable. O'Donnell et al[54] compared two groups of patients treated with burr drilling and either phenol or no adjuvant and found exactly the same recurrence rate (16.6%).

The two most commonly used physical adjuvants are polymethylmethacrylate and cryosurgery. Originally, polymethylmethacrylate was used when simple filling with autologous bone was insufficient and arthrodesis was in question.[56] Because the cement filled defect is stable mechanically, patients can bear weight

immediately and rehabilitate quickly.[3,56] It was hypothesized that the heat of polymerization of the polymethylmethacrylate could induce tumor necrosis and advance the excision margin after curettage. Moreover, the monomer has a direct toxic effect that results in hypoxia.[50] Experimental data showed that the heat of polymerization drops sharply between the center of the polymethylmethacrylate and the interface with the adjacent bone.[58] Wilkins et al,[67] who reviewed the effect of heat in a dog model, reported that bone marrow necrosis occurs at 60° C, variable and time dependent necrosis occurs between 50° C and 60° C, and no necrosis occurs below 48° C. They concluded that necrosis of tumor cells was questionable under surgical conditions because the maximum temperature at the cancellous bone interface in their dog model, using a lateral condyle filled with polymethylmethacrylate, never exceeded 46° C.[67] Malawer et al[34] using a skeletally mature mongrel dog in a tumor model of the distal femur, compared whole mount sections with plain radiographs, hematoxylin and eosin sections, and tetracycline fluorescence. No evidence of adjacent bony necrosis was seen when the cavity was filled with polymethylmethacrylate alone. The main role of polymethylmethacrylate is to provide mechanical stability. Structural reconstruction, using polymethylmethacrylate and internal fixation (Type 3 reconstruction in this study), is essential to provide mechanical support and prevent fractures through the large curetted, frozen bone cavity. In addition, immediate fixation allows early rehabilitation of the adjacent joint. A proven benefit of polymethylmethacrylate is that recurrences are readily discernible at the bone-cement interface.[56]

The use of polymethylmethacrylate to fill defects has been criticized because of concern that its stiffness would lead to early degenerative changes when used to support a subchondral defect.[56] Wilkins et al[67] disputed this theory and suggested that the stiffness of the polymethylmethacrylate is not a significant cause of secondary osteoarthritis. However, it has been shown that the incidence of degenerative joint changes after the use of polymethylmethacrylate alone to fill large subchondral bone defects is related to the proximity of the cavity to the articular cartilage.[7] When the distance of the tumor from the articular cartilage was less than 1 cm, the incidence of degenerative changes was 2.5 times greater than when the distance was greater than 1 cm.[7] The use of subchondral bone graft, as advocated by Campanacci et al[7] and routinely used in the present series, may decrease the likelihood of degenerative changes by forming a thicker bony interface between the polymethylmethacrylate and the articular cartilage. In the present series there were two patients with degenerative joint changes after cryosurgery. The clinical and radiologic findings were no different than for any other patient with noninflammatory arthritides, but the fact that these changes occurred in the same compartment in which the surgery was performed suggests that they might be related to it. In the one patient who underwent total knee replacement, surgical specimen was not sent for pathologic evaluation.

Marcove et al [36,37,39,42] reported their results with treating giant cell tumor by curettage, cryosurgery, and bone grafting or packing the cavity with polymethylmethacrylate. They summarized the experience with two patient groups.[42] A 36% recurrence rate was observed in the first group (25 patients). That recurrence rate, although high, is lower than the 50% rate after curettage that was the standard in that time (Table 2). After Marcove refined the surgical technique to include a wider exposure and more careful curettage, the rate of recurrence dropped to 12% in the second group (27 patients).[42] In the present study, the recurrence rate after minimum followup of 4 years was 2.3% among the 86 patients who were treated primarily by cryosurgery and 7.9% in the entire group of 102 patients that included 16 patients with recurrent tumor. This is among the lowest reported recurrence rates after any surgical intervention for giant cell tumor of bone. Moreover, because 84% to 97% of lo-

cal recurrences appear within 2 years,[22] and all recurrences were manifest within 3 years in the series of Campanacci et al,[6] it is unlikely that a longer followup period significantly would change these results.

Postoperative fracture is the most common and serious complication associated with cryosurgery.[25,42] Fracture is an inherent risk after reconstruction of any large bone defect, and especially after cryosurgery near a weightbearing joint. After cryosurgery, bone necrosis and disruption of osteoid extend the period through which reossification occurs and delay bone healing.[34] Vigorous freezing increases the likelihood of cure at the cost of higher rate of pathologic fractures, whereas inadequate freezing of bone surrounding the tumor may predispose to local recurrence. Marcove et al[42] made only a minimal attempt to reconstruct these defects and reported a 25% fracture rate that is similar to the fracture rate of the current series when internal fixation was not used. The fractures they reported occurred before the use of polymethylmethacrylate combined with internal fixation. In the present series there were six postoperative fractures and all occurred in patients who had not undergone internal fixation (six of 29 cases). As a result, the use of internal fixation is recommended in all patients with giant cell tumors who are undergoing cryosurgery.

Wide exposure and adequate mobilization of skin flaps and adjacent neurovascular bundle, along with continuous irrigation of tissues with warm saline solution, reduces the incidence of skin necrosis. Three patients in the present series had a superficial skin necrosis that healed with conservative local care. That low rate of skin necrosis (< 3%) compared favorably with the 8% rate reported by Marcove et al.[42] No patients in this study had a postoperative infection. It probably is the result of the protective measures used, including perioperative antibiotics, protection of the skin edges during the procedure, and postoperative elevation of the extremity to reduce venous stasis and edema of the flap.

Joint function, evaluated by the American Musculoskeletal Tumor Society system was well preserved (good to excellent function) in 92% of the patients in the current series. This rate is similar to the rate reported by Jacobs and Clemency, [25] who reported preservation of joint function in 10 of 12 patients treated by cryosurgery. It also compares favorably with results among the patients treated by resection. As recommended by Cowell and Curtiss[11] the followup in the present study is greater than 2 years, as that period being the minimum period of time required in reporting functional outcome in patients who have had a reconstructive surgical procedure.

To perform a controlled study to evaluate the efficacy of cryosurgery in local control over giant cell tumor of bone, one has to randomize patients to two treatment groups. The first group would be treated with curettage, burr drilling, and cryosurgery, and the second with curettage and burr drilling alone. This study was not performed in this fashion. Given the local aggressiveness of this tumor that could result in loss of the adjacent joint and the increased risk of malignant transformation after local recurrence, the authors thought that it would be unethical not to use a physical adjuvant to curettage and burr drilling. As recommended by Rudicel and Esdaile,[39] it is valid statistically and ethically preferable to randomize surgical procedures to different institutions, each skilled and experienced in a specific procedure. This eliminates any bias that results from asking one surgeon to perform two or more different procedures with the same skill for a given disease process and, therefore, results of that study were compared with contemporary published results of alternative treatment modalities.

Cryosurgery is recommended as a physical adjuvant to curettage in the treatment of giant cell tumor of bone. It extends the margin of a simple curettage or resection curettage and makes it biologically equivalent to that of a wide resection. Compared with other techniques, cryosurgery with composite fixation not only preserves joint function

but also significantly decreases the rate of local tumor recurrence. The routine use of internal fixation with polymethylmethacrylate and bone graft is recommended. Careful attention to soft tissue protection and surgical reconstruction significantly decreases the previously published reports of high rates of fracture and infection. Resection surgery is reserved for malignant giant cell tumor of bone or for either primary or recurrent giant cell tumor with an extensive bone destruction and soft tissue component that represent less than 5% of the cases in experience. Most primary giant cell tumors of bone can be treated successfully with curettage, burr drilling, and cryosurgery, thus avoiding the need for resection and joint reconstruction.

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