CLINICAL ORTHOPAEDICS AND RELATED RESEARCH
Number 397, pp. 248–258

GIANT CELL TUMOR OF BONE

Giant Cell Tumor of Long Bone: A Canadian Sarcoma Group Study

Robert E. Turcotte, MD,** Jay S. Wunder, MD†‡; Marc H. Isler, MD*; Robert S. Bell, MD†; Norman Schachar, MD§; Bassam A. Masri, MD***; Guy Moreau‡; and Aileen M. Davis, PhD‡‡*

A multicentric retrospective study of giant cell tumor of bone was conducted among Canadian surgeons. The hypothesis was that no differences would be found in health status, function, or recurrence rate irrespective to the nature of filling material or adjuvant used in patients treated with curettage. One hundred eighty-six cases were collected. There were 96 females and 90 males. The mean age of the patients was 36 years (range, 14–72 years), the minimum followup was 24 months, and the median followup was 60 months. Sixty-two percent of the tumors involved the knee region. One hundred fifty-eight were primary tumors and 28 were recurrences. Campanacci grading was as follows: Grade 1, seven patients; Grade 2, 100 patients; Grade 3, 76 patients; and unknown in three patients. Fifty-six patients had a pathologic fracture. Resection was done in 38 patients and 148 patients had curettage. The latter was supplemented with high speed burring in 135 patients, cement in 64 patients, various combinations of autograft or allograft bone in 61 patients, phenol in 37 patients, and liquid nitrogen in 10 patients. Structural allografts were used in 25 patients. The overall recurrence rate was 17%, 18% after curettage, and 16% after resection. Patients with primary tumors treated with curettage had a 10% recurrence rate. For recurrent lesions treated by curettage, the recurrence rate was 35%. The nature of the filling material used or the type of adjuvant method used or any combination of both failed to show any statistical impact on the recurrence risk. The results from the Musculoskeletal Tumor Society rating from 1987 were significantly lower in patients who sustained a displaced fracture. Results from the bodily pain section of the Short Form-36 also were found to be lower when a pathologic fracture was present. Results from the Musculoskeletal Tumor Society Rating 1987, the Short Form-36, and the Toronto Extremity Salvage Score did not show differences when either cement or bone graft were used after curettage.

From the *University of Montreal, and **McGill University, Montreal, Quebec, Canada; the †University of Toronto, ‡Mount Sinai Hospital, and ‡‡Toronto Rehabilitation Institute, Toronto, Ontario, Canada; the §University of Calgary, Calgary, Alberta, Canada; the ***University of British Columbia, Vancouver, BC, Canada; and the ††University of Ottawa, Ottawa, Ontario, Canada.

Reprints requests to Robert E. Turcotte, MD, University of Montreal, 5345 Boul. De L`Assomption, Suite 055, Montreal, Quebec, Canada, H1T 4B3.

Giant cell tumor of bone is an uncommon disease but comprises 20% of biopsy-analyzed

benign bone tumors.[15,57] It typically affects young adults between the ages of 20 and 40 years, and several authors have reported a slight predominance of women over men.[6,57] Histologically, it is characterized by numerous giant cells scattered evenly among mononuclear stromal cells. Giant cells may contain as many as 100 nuclei.[6,15,57]

Giant cell tumor is characterized by its typical location in the epiphysis of long bone. Rarely, when it occurs in teenagers with an open physis, the metaphyseal area may be involved first.[27,45] This tumor also is well known for its potential to recur after treatment such as curettage or incomplete resection, which leaves microscopic residual.[30,41] Historically, the rate of local recurrence after curettage and bone grafting has been reported to range between 25% and 50%.[6,15,16,21,26,30,43,48,52,54,56,57] This has led surgeons to enhance their surgical procedure with adjuvants such as liquid nitrogen,[31,34] acrylic cement,[2,3,6,39,43] phenol,[6,20,41,46] hydrogen peroxide,[40] locally delivered chemotherapy,[62] or radiation therapy. The latter has been associated with malignant transformation in the past[5,6,50] but the risk of this complication recently has been challenged and may be different with modern radiotherapy modalities.[13,32,38] Wide resection is associated with much better local control, but it often impairs limb function because it implies the sacrifice of a significant segment of bone.[30,43,61]

Occasionally, giant cell tumor of bone can have malignant behavior despite typical, benign histologic features. Lung metastases occur in as many as 3% of patients.[1,2,6,14,33,48,49,53] Because most giant cell tumors are benign[50] and are located near a joint in young adults, several authors favor an intralesional approach that preserves anatomy of bone in lieu of resection.[7,8,12,19,36] In a more expendable location such as the fibular head, resection is preferred.

Adjuvant liquid nitrogen has been reported to provide the best local control but its use has not gained popularity because handling the product is difficult and pathologic fractures have been frequent.[31,34] Although acrylic cement initially seemed to enhance local control[3,43] this has been challenged.[4,42] Comparably low local recurrence rates have been reported using modern surgical techniques without the addition of adjuvant.[4] Compared with other filler material such as autograft or allograft bone, cement is easy and inexpensive to use, provides immediate stability allowing early weightbearing, may avoid the necessity of internal fixation, and allows for early detection of recurrence as a lytic defect at the bone-cement interface.[44,47] Cement also can be used when a fracture is present.[19] The risk of joint degeneration after cementation seems to be minimal[23,24,29,51] although some authors prefer to interpose bone chips between cartilage or subchondral area and cement in an attempt to prevent joint degeneration.[8]

When feasible, local recurrences generally are treated in the same manner as if the tumor was seen primarily. This is achieved by making a large window in bone, or cement, or both, to access the recurrence, then curette and burr the lesion and fill again the cavity with cement or bone graft.

Goals of the Study

This study reviewed the treatment and outcome of patients with giant cell tumor of long bone in a large multicenter study in which patients were treated using contemporary techniques (that included computed tomography [CT] scanning or magnetic resonance imaging [MRI], high speed burring, and the use of adjuvant). The primary hypothesis was that the use of any one or a combination of adjuvants would not provide better local control, function, or quality of life.

MATERIALS AND METHODS

Participating surgeons were all orthopaedic surgeons trained in orthopaedic oncology and members of the Canadian Sarcoma Group. Patients were eligible for the study if they had: histologically proven benign giant cell tumor of bone, involvement of long bones of the appendicular skeleton, excluding flat bones (scapula, ribs, and pelvis), spine, and small bones of the hands and feet; and a minimum followup of 2 years after treatment.

In addition to the usual demographic data, Campanacci staging,[6] treatment and disease end-result data, when feasible, the functional results as assessed by the Musculoskeletal Tumor Society Score[22] and the Toronto Extremity Salvage Score as reported by Davis et al[17,18] were included. Health status was assessed by the Short Form-36 questionnaire.[58–60] These patients were evaluated after informed consent was obtained.

Patients were followed up at 3- to 4-month intervals for the first 2 years, every 6 months for Years 3 to 5, and yearly thereafter until Year 10. At each visit, plain radiographs of the affected area were obtained. Computed tomography scans and MRI studies were done frequently, but not routinely, for the first 2 years after surgery or when recurrence was suspected.

The Musculoskeletal Tumor Society system developed by Enneking[22] is a clinically based and standardized evaluation system proposed to measure functional outcome in patients with musculoskeletal tumors. It is completed by the physician. The Musculoskeletal Tumor Society 1987 version[22] evaluates seven parameters, mostly clinical, including pain, range of motion (ROM), stability of the joint, strength, deformity, general functional activity, and emotional acceptance of the procedure by the patient. Each parameter is rated excellent, good, fair, or poor according to specific guidelines and each is given a maximum of five points. The overall result is expressed by combining the individual rating on each parameter for a maximum of 35 points. The Toronto Extremity Salvage Score is a validated measure developed by Davis et al[17,18] to evaluate physical disability in patients treated for tumors of the extremity from the patient's perspective. It includes 30 items on activity limitations in daily life such as restrictions in body movement, mobility, self-care, and performance of daily tasks and routine. Irrelevant items can be omitted by patients. Each item is scored from 0 to 5 points. The raw score is converted to a score of 100 points with the higher scores indicating less disability. The Short Form-36 is a validated generic tool. It is self-administered and evaluates eight health concepts: physical functioning, role limitations because of physical problems, bodily pain, general health, vitality, social functioning, role limitations because of emotional problems, and mental health. Each health profile is scored on a 100-point scale; a higher score means a lesser disability. These eight subscales also can be combined to create a physical component score and a mental component score.[58–60]

RESULTS

One hundred eighty-six patients satisfied the inclusion criteria. Participating centers and numbers of patients entered for each are shown in Table 1. There were 96 females and 90 males. The mean age of the patients was 36 years (range, 14–72 years). One hundred fifty-six patients had primary tumors and 28 had a recurrence when initially seen by authors (the presenting status was unknown for two patients). The distal femur (66 patients) and the proximal tibia (49 patients) accounted for 62% of all locations (Table 2).

The followup ranged from 24 to 192 months, averaging 57 months (median, 50 months). Campanacci's radiologic grading was available in 183 patients and unknown in three patients. Seven patients had Grade 1 lesions, 100 patients had Grade 2 lesions (Fig 1), and 76 patients had Grade 3 lesions (Fig 2A). Fifty-six (30%) patients had a pathologic fracture at

TABLE 1. Distribution of Patients From Participating Centers

Centers	Period*	Curettage Group	Resection Group	Total
Calgary	1983–1998	13	3	16
Montreal	1989–1998	29	6	35
Ottawa	1994–1998	7	1	8
Toronto	1986–1998	89	25	114
Vancouver	1991–1998	10	3	13
Total		148	38	186

*Reflects the years participating surgeons initially treated patients with giant cell tumors.

TABLE 2. Anatomic Location of 186 Giant Cell Tumors of Long Bone

Site	Number of Patients
Proximal humerus	7
Distal humerus	1
Distal radius	19
Proximal femur	14
Distal femur	70
Proximal tibia	52
Distal tibia	9
Proximal fibula	14
Total	186

presentation of which only 17 (30%) were displaced. One hundred forty-eight patients were treated by curettage. Tumors were Campanacci's Grade 1 in seven patients (5%), Grade 2 in 89 patients (62%), and Grade 3 in 49 patients (33%). Three tumors were not graded. After curettage, a high speed burr was used in 131 patients and phenol was used in 37 patients. Liquid nitrogen only was used in 10 patients. After curettage, the cavity was filled with autograft only in 18 patients, a mix of autograft and allograft in 43 patients, cement in 52 patients (Fig 2B), and cement and autograft underneath the exposed articular cartilage in 10 patients. In 25 patients, structural allograft was used in conjunction with autograft, and morselized allograft, or both.

Resection was done for 38 patients with giant cell tumors of whom only five presented with local recurrence. Of these patients, 11 (29%) had Campanacci Grade 2 tumors and 27 patients (71%) had Grade 3 tumors (Figs 2A, 3A). Eleven patients had a fracture of which two were displaced. All 14 lesions involving the proximal fibula and eight of the 20 lesions at the distal radius were resected. Other locations included distal femur (eight patients), proximal tibia (six patients), proximal humerus (one patient), and distal humerus (one patient).

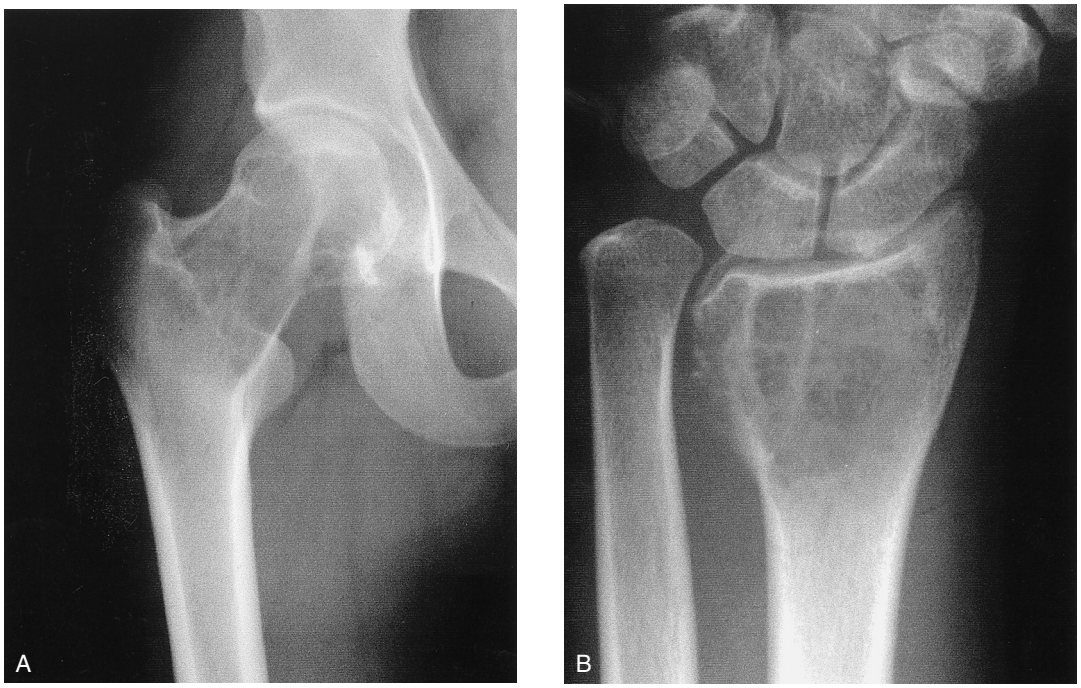

Fig 1A–B. (A) This radiograph shows a Stage 2 giant cell tumor involving the right femoral head and neck in a 24-year-old man. (B) A radiograph shows a Stage 2 giant cell tumor involving the distal radius in a 30-year-old woman.

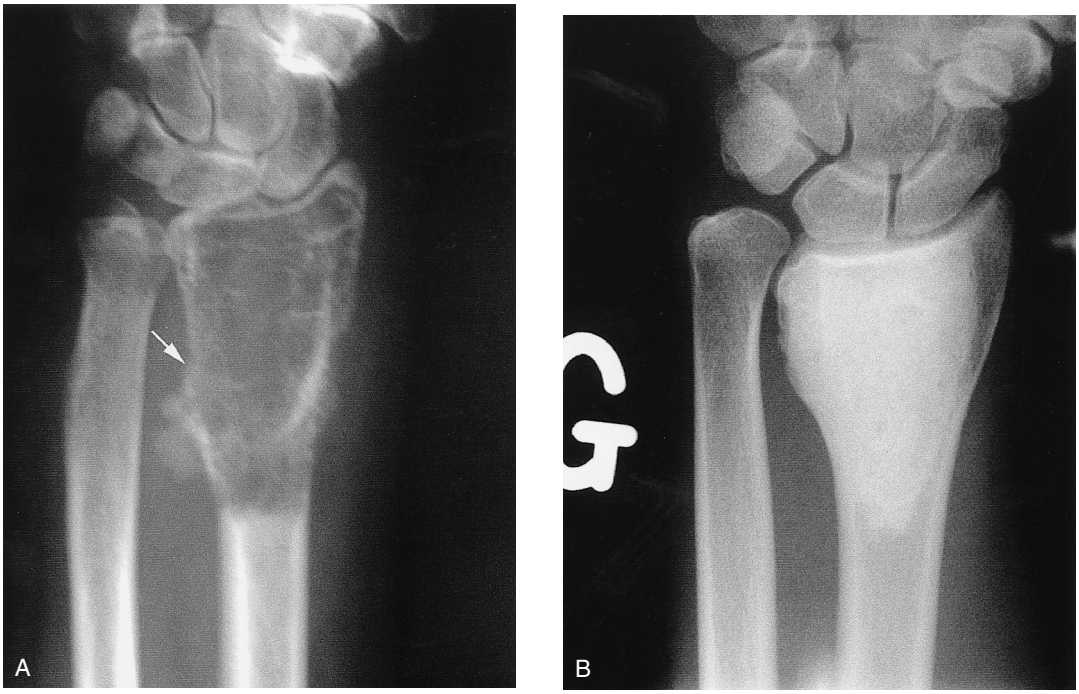

Fig 2A–B. (A) A radiograph of a Stage 3 giant cell tumor in a 67-year-old woman with a pathologic fracture (arrow) is shown. (B) A radiograph shows the result 5 years after curettage, phenol, and cement. No significant joint narrowing can be seen.

Reconstruction was done in 21 patients and was justified when joint stability or weightbearing was impaired (Fig 3B–C). Metallic hardware, including pins and staples, was used in 105 of the 186 patients in this series (Fig 4). In the patients who had curettage (147 patients), internal fixation was used more frequently when bone graft was selected as the filler (74 of 95 patients or 78%) instead of cement (12 of 52 patients or 23%) ($p > 0.05$). Local recurrence occurred in 32 of the 186 patients (17%). The average recurrence occurred at 36 months (range, 6–47 months). The local recurrence rate was 16% for the patients who had resection and 18% for the patients who had curettage. In the latter group, no significant statistical effect on local recurrence rate could be identified for gender, tumor location, Campanacci's grading, the existence of a fracture, the use of high speed burr, phenol, or cement. The average followup did not differ between patients who had a recurrence (69.5 months; standard deviation, 41.2) and patients who did not have a recurrence (54 months; standard deviation, 29.8) ($p = 0.08$).

None of the 10 patients treated with liquid nitrogen had a recurrence but the numbers were too small to show any valid statistical difference. The combination of adjuvants, including phenol plus cement, was not associated with a significantly reduced local recurrence rate (Table 3). The group that received curettage was analyzed to determine whether patients who received cement had recurrences less often than patients who received grafts. No statistical difference in the recurrence rate could be found but it was found that cement was used more often in patients with lower Campanacci grade tumors ($p = .008$) and less often when a fracture was present ($p = .003$).

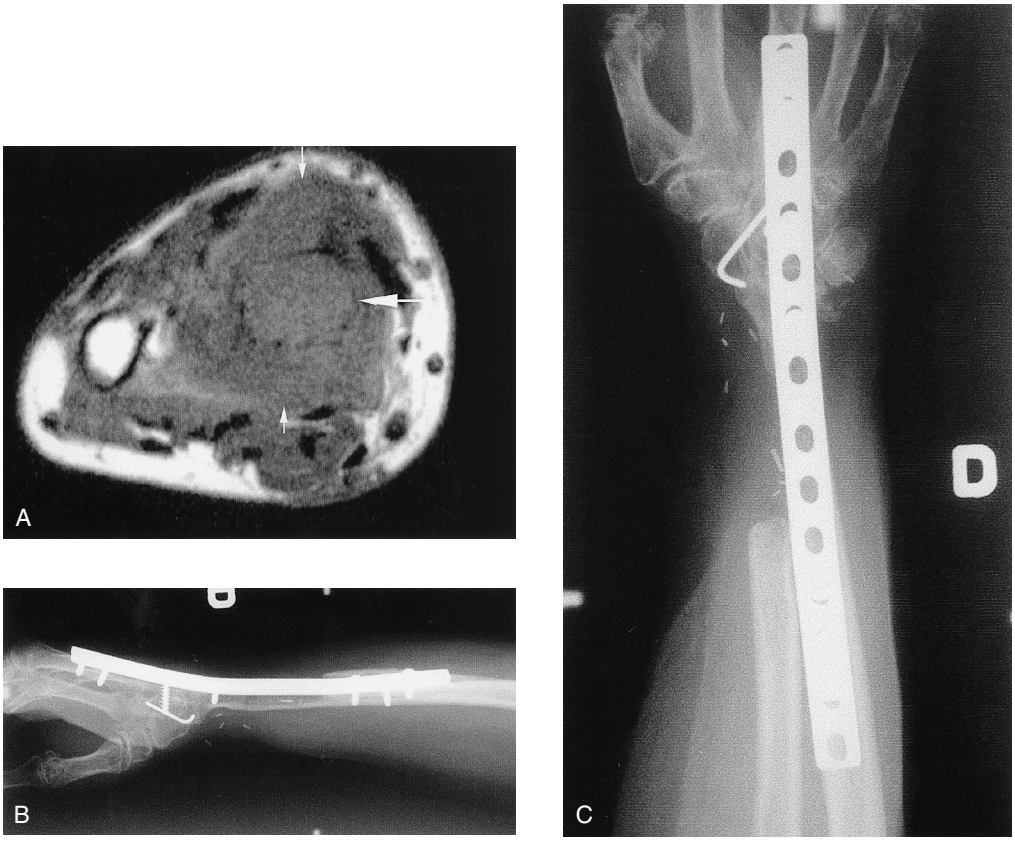

Fig 3A–C. (A) A magnetic resonance imaging scan shows extensive soft tissue involvement (thin arrows) that extends outside the vestigial cortex (thick arrow). (B) Anteroposterior and (C) lateral radiographs of the distal forearm were obtained 2 years after resection of the distal half of the radius and the distal extremity of the ulna. Wrist arthrodesis was done with a plate and a sliding graft of the ulna (one-bone forearm).

Patients presenting with a local recurrence had a significantly higher risk of having another recurrence with a rate of 35% ($p < 0.05$).

The Musculoskeletal Tumor Society 1987 scoring system was available for 121 patients (65%). These scores were reduced significantly in patients with a fracture ($p = 0.001$) with post hoc analysis showing that this difference was related to the existence of a displaced fracture. In comparing patients who received cement with patients receiving other types of filler after curettage, there was no significant difference in the Musculoskeletal Tumor Society scores (Table 4). The type of filler used in the patients who had curettage also did not result in any statistical difference for the Toronto Extremity Salvage Scores. The Short-Form 36 questionnaire was completed by 115 patients (62%). Subset analysis revealed that Short Form-36 scores were significantly lower in the bodily pain section when patients had sustained a fracture ($p < 0.05$). This group of patients also scored lower in the physical section at a level close to statistical significance ($p = 0.057$). The type of filler used in the patients who had curettage did not result in any statistical differences for Short Form-36 subscales.

DISCUSSION

This large study of giant cell tumors of long bone included all patients with long bone in-

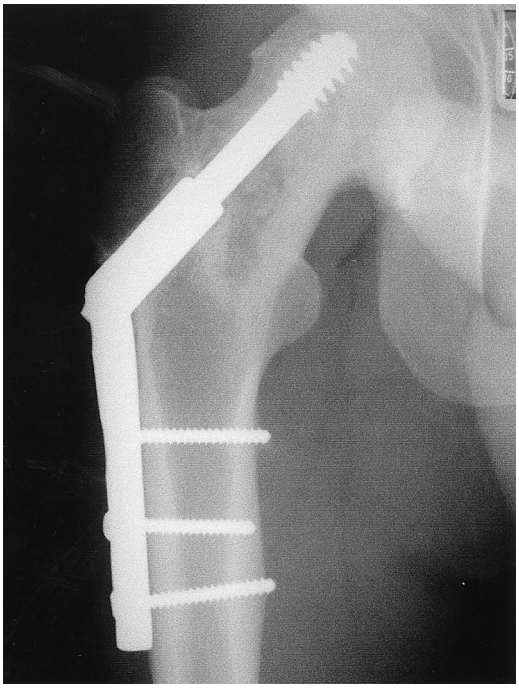

Fig 4. A radiograph was obtained 4 years after curettage, phenol, allograft, and internal fixation of a giant cell tumor in the patient shown in Figure 1A.

volvement treated by the authors with a minimum followup of 2 years. Although retrospective, it is multicentric and more likely reflects the reality than a one-institution study. Patients with tumors in difficult locations such as the distal radius were included. These patients require a more aggressive treatment approach according to some authors.[4,25,28,42]

The current report suggests an improvement in the local control rate of these tumors with modern curettage techniques. Historically, the reported local recurrence rate ranged from 20% to 50% averaging 33%.[6,9,21,26,35] An overall recurrence rate of 17% was reported in the current multicentered study. If the patients with recurrent disease who were referred to the current authors were excluded, a 10% failure rate was obtained, which can be considered very low. The local recurrence rates also were similar among the different participating institutions and other recent series have reported similar results.[4,31,42] The only significant risk factor for increased local recurrence was referral for recurrent tumor. In this subset of patients, the local recurrence rate was 35%. This is compared with a study by Tomeno and

TABLE 3. Giant Cell Tumor of Long Bone Treated by Curettage: Factors Versus Local Recurrence

Criteria	Value	Number of Patients	No Recurrence	Local Recurrence	p Value
Campanacci grade	1	7	7 (100%)	0 (0%)	
	2	89	76 (85%)	13 (15%)	N.S.
	3	49	36 (73%)	13 (27%)	
Fracture	No	103	84 (82%)	18 (18%)	
	Yes	45	38 (84%)	7 (16%)	N.S.
Local recurrence	No	120	105 (88%)	15 (12%)	
	Yes	23	15 (65%)	8 (35%)	$p < 0.05$
Cement	No	85	71 (84%)	14 (16%)	
	Yes	62	50 (81%)	12 (19%)	N.S.
High speed burr	No	15	12 (80%)	3 (20%)	
	Yes	131	109 (83%)	22 (17%)	N.S.
Phenol	No	110	92 (84%)	18 (16%)	
	Yes	37	30 (81%)	7 (19%)	N.S.
Liquid nitrogen	No	138	112 (81%)	26 (19%)	
	Yes	10	10 (100%)	0 (0%)	N.S.
Any adjuvant	No	8	5 (63%)	3 (37%)	
	Yes	140	117 (84%)	23 (16%)	N.S.

N.S.: Not significant

TABLE 4. Quality of Life and Functional Assessment Scores for Giant Cell Tumor of Long Bone According to Treatment

Tests (number of patients)		Curettage		Excision	
		Mean	*(standard deviation)*	*Mean*	*(standard deviation)*
Short Form-36	Physical function	77	(23)	73	(27)
	Role physical	81	(35)	83	(34)
(curettage, 115)	Bodily pain	77	(24)	78	(23)
(excision, 25)	General health	79	(18)	78	(24)
	Vitality	66	(20)	69	(19)
	Social	89	(20)	87	(18)
	Role emotional	85	(33)	83	(32)
	Mental health	76	(18)	77	(14)
MSTS 1987*	Pain	4.29	(1.05)	4.41	(.98)
(curettage, 123)	Range of motion	4.63	(1.02)	4.59	(.82)
(excision, 29)	Strength	4.41	(1.19)	4.38	(1.21)
	Stability	4.92	(.40)	5.00	(.27)
	Deformity	4.69	(.96)	4.59	(1.24)
	Function	4.00	(1.21)	3.90	(1.14)
	Emotional acceptance	4.72	(.89)	4.52	(1.02)
	Total score	32.1	(3.7)	29.4	(5.6)
TESS**	Total score	90	(13)	87	(15)
(curettage, 117)					
(excision, 25)					

*MSTS 1987: Musculoskeletal Tumor Society functional assessment, 1987 version

**TESS: Toronto Extremity Salvage Score

Ochoa[55] who reported a 13% failure rate after repeated curettage for recurrent tumors.

As reported previously,[2,35] no correlation could be found between Campanacci's radiographic classification and the risk of recurrence. High speed mechanical burring was done in 90% of patients with curettage (Table 3) because it is thought to provide for a deeper and more thorough curettage and is part of what is considered a modern curettage technique. The recurrence rate without burring was not higher but because of the small number of patients who did not have burring, a valid statistical analysis could not be done.

In addition to the improved access afforded by a large bone window and the more aggressive curettage achieved with power tools, important advances in imaging modalities allowing better delineation of the tumor also may have improved local control (Fig 3A). Although giant cell tumor most often recurs within 3 years, the current series showed that some tumors recur as late as 4 years after treatment. As the followup period increases, the final recurrence rate might increase.

Acrylic cement initially was reported to have an adjuvant role in the treatment of giant cell tumor of bone.[6,10] Proposed mechanisms involved either the toxicity of the acrylic monomer or thermal necrosis induced by cement polymerization.[37,39] O'Donnel et al[42] challenged this idea when they reported a series of patients with giant cell tumors treated with cement compared with other filling materials and found no difference in local recurrence. The current authors did not observe the significant decrease in the recurrence rate that was reported by Campanna et al[10] with the combination of phenol and cement, nor was a difference seen with any single or combination of adjuvant. The only eight patients who did not have any kind of adjuvant had a recurrence rate of 37% compared with 16% if any adjuvant was used (Table 3). This finding is to

be taken cautiously because the number of patients in the first group was too small to allow for any statistical study. It suggests that adjuvant might have a positive role in giant cell tumor of bone although the current authors were unable to prove it. It also failed to show superiority of any combination of adjuvant. The authors recognize the intrinsic limitations of a retrospective study, and think there is a need for a prospective randomized trial that would compare treatment methods. From the current study, it seems reasonable to choose either bone graft or cement according to the surgeon's preference, the nature of the defect, and its location. Long-term studies comparing outcome and cost-benefit ratios might provide useful data for selection of the best filling material.

Resection for giant cell tumor has been indicated when bone destruction was extensive with large soft tissue mass, when the joint could not be preserved, when the surgeon thought that the tumor could not be addressed safely by curettage, or when sacrifice of the bone would provide the best tumor control and minimal functional impairment such as tumors located at the fibular head. Patients who had resection of the diseased segment of bone had a local recurrence rate of 16%, which seems higher than numbers reported previously[25,61] and similar to the results of curettage in the current series. Radiographic Grade 3 tumors (that have a more aggressive appearance and more bone destruction on plain radiographs) were more frequent in the patients who had resection (71% versus 30%) but this failure rate could not be related to radiographic graded on a statistical level, possibly because of the small number of total recurrences (six), three of which occurred in the 27 patients with Grade 3 tumors and three of which occurred in the 11 patients with Grade 2 tumors. In the current series, margins were not assessed for patients who had resection, but tumor contamination may explain these results. Positive margins are a known factor for recurrence of giant cell tumors.[25,30]

In the past, there was a tendency to use a more aggressive surgical approach toward giant cell tumors, similar to that used in malignant tumors, to achieve negative resection margins. This resulted in better control at the expense of greater functional deficit in patients who usually were young and healthy.[11,25,28,30] Currently, wide resection usually is limited to patients with severe Grade 3 tumors, displaced pathologic fractures with poor bone stock not allowing for internal fixation even with cement, or in patients with joint destruction. Resection is advised for giant cell tumors involving expendable bone such as the proximal fibula because the functional deficit is minimal. Although not always desirable in certain locations or achievable in patients who have major soft tissue extension, wide margins are the goal when resections are done. Achievement of such a wide margin with resection should be counterweighted by the functional deficit expected with a wide margin, as the current series reported a low recurrence rate, similar to curettage, when resection without a wide margin was done.

Function was good after curettage and filling of giant cell tumors as shown by a Musculoskeletal Tumor Society 1987 score of 31 of a maximum of 35 points. Similarly, patients scored themselves at 90% on the Toronto Extremity Salvage Score. Although acceptable, these scores show that some sequelae remained after treatment by curettage. Pathologic fractures were associated with worse function as measured by the 1987 version of the Musculoskeletal Tumor Society and the bodily pain section of the Short Form-36. A more extensive surgical approach, arthrotomy, and the use of hardware all are possible reasons to explain the higher incidence of pain and joint problems, especially in patients with displaced fractures.

With modern surgical techniques and imaging modalities, the recurrence rate after curettage of giant cell tumor of bone is lower than historically reported. No benefit from adjuvants could be identified although the current authors could not report on liquid nitrogen because it rarely was used in this series. Cement seemed to work well as a filler but not as an adjuvant in reducing tumor recurrence.

References

1. Bertolini F, Present D, Enneking WF: Giant cell tumor of bone with pulmonary metastases. J Bone Joint Surg 67A:890–900, 1985.
2. Bertoni F, Present D, Sudanese A, et al: Giant-cell tumor of bone with pulmonary metastases: Six case reports and a review of the literature. Clin Orthop 237:275–285, 1988.
3. Bini SA, Gill K, O Johnston JO: Giant cell tumor of bone: Curettage and cement reconstruction. Clin Orthop 321:245–250, 1995.
4. Blackley HH, Wunder JS, Davis AM, et al: Treatment of giant-cell tumors of long bone with curettage and bone-grafting. J Bone Joint Surg 81A:811–820, 1999.
5. Boriani S, Sudanese A, Baldani N, Picci P: Sarcomatous degeneration of giant cell tumors. Ital J Orthop Trauma 12:191–199, 1986.
6. Campanacci M: Giant Cell Tumor. In Gaggi A (ed). Bone and Soft-Tissue Tumors. Bologna, Springer-Verlag 117–153, 1990.
7. Campanacci M, Baldini N, Boriani S, Sudanese A: Giant-cell tumor of bone. J Bone Joint Surg 69A:106–114, 1987.
8. Campanacci M, Campanna R, Fabbri N, Bettelli G: Curettage of giant cell tumor of bone: Reconstruction with subchondral grafts and cement. Chir Organi Mov 75 (Suppl 1):212–213, 1990.
9. Campanacci M, Giunti A, Olmi R: Giant-cell tumors of bone: A study of 209 cases with long-term follow-up in 130. Ital J Orthop Trauma 1:153–180, 1975.
10. Campanna R, Fabbri N, Bettelli G: Curettage of giant cell tumor of bone: The effect of surgical technique and adjuvants on local recurrence rate. Chir Organi Mov 75 (Suppl 1):206, 1990.
11. Campbell CJ, Akbarnia NA: Giant cell tumor of the radius treated by massive resection and tibial bone graft. J Bone Joint Surg 57A:982–986, 1995.
12. Carrasco CH, Murray JA: Giant cell tumors. Orthop Clin North Am 20:395405, 1989.
13. Chakravarti A, Spiro IJ, Hug EB, et al: Megavoltage radiation therapy for axial and inoperable giant-cell tumor of bone. J Bone Joint Surg 81A:1566–1573, 1999.
14. Connell D, Munk PL, Lee MJ, et al: Giant cell tumor of bone with selective metastases to mediastinal lymph nodes. Skeletal Radiol 27:341–345, 1998.
15. Dahlin DC: Bone Tumours, General Aspects and Data on 6,221 Cases. Ed 3. Spring field, IL, Charles C Thomas 1978.
16. Dahlin DC, Cupps R, Johnson EW: Giant cell tumor: A study of 195 cases. Cancer 25:1061–1070, 1980.
17. Davis AM, Bell RS, Badley EM, Yoshida K, Williams JI: Evaluating functional outcome in patients with lower extremity sarcoma. Clin Orthop 358:90100, 1999.
18. Davis AM, Wright JG, Williams JI, et al: Development of a measure of physical function for patients with bone and soft tissue sarcoma. Qual Life Res 5:508516, 1996.
19. Dreinhofer KE, Rydholm A, Bauer HC, Kreicberg A: Giant cell tumours with fracture at diagnosis: Curettage and acrylic cementing in 10 cases. J Bone Joint Surg 77B:189–193, 1995.
20. Durr HR, Maier M, Jansson V, Baur A, Refior HJ: Phenol as an adjuvant for local control in the treatment of giant cell tumour of the bone. Eur J Surg Oncol 25:608610, 1999.
21. Eckardt JJ, Grogan TJ: Giant cell tumor of bone. Clin Orthop 204:45–58, 1986.
22. Enneking WF: Modification of the System for Functional Evaluation in the Surgical Management of Musculoskeletal Tumors. In Enneking WF (eds). Limb Salvage in Musculoskeletal Oncology. New York, Churchill Livingstone 626–639, 1987.
23. Frassica FJ, Gorski JP, Sim FH, Pritchard DJ, Chao EY: A comparative analysis of subchondral replacement with polymethylmethacrylate or autogenous bone grafts in dogs. Clin Orthop 293:378–390, 1993.
24. Frassica FJ, Sim FH, Pritchard DJ, Chao EY: Subchondral replacement: A comparative analysis of reconstruction with methylmethacrylate or autogenous bone graft. Chir Organi Mov 75 (Suppl 1):189–190, 1990.
25. Gitelis S, Mallin BA, Piasecki P, et al: Intralesional excision compared with en bloc resection for giant-cell tumors of bone. J Bone Joint Surg 75A:1648–1655, 1993.
26. Goldenberg R, Campbell CJ, Bonfiglio M: Giant cell tumor of bone: An analysis of two-hundred and eighteen cases. J Bone Joint Surg 52A:619–664, 1970.
27. Hoeffel JC, Galloy MA, Grignon Y, et al: Giant-cell tumor of bone in children and adolescents. Rev Rhum 63:618–623, 1996.
28. Lackman RD, McDonald DJ, Beckenbaugh RD, Sim FH: Fibular reconstruction for giant cell tumor of the distal radius. Clin Orthop 218:232–238, 1987.
29. Lavoie S, Turcotte RE, Berthiaume MJ, Doyon J: The arthrogenic effect of cementation for the treatment of giant cell tumor of the knee. J Bone Joint Surg 90B (Suppl 1):14, 1998.
30. Liu HS, Wang JW: Treatment of giant cell tumor of bone: A comparison of local curettage and wide resection. Chang Keng I Hsuey 21:37–43, 1998.
31. Malawer MM, Bickels J, Meller I, et al: Cryosurgery in the treatment of giant cell tumor: A long term follow-up study. Clin Orthop 359:176–188, 1999.
32. Malone S, O'Sullivan B, Catton C, et al: Long term follow-up of efficacy and safety of megavoltage radiotherapy in high-risk giant cell tumour of bone. Int J Radiat Oncol Biol Phys 33:689–694, 1995.
33. Maloney WG, Vaughan LM, Jones HH, Ross J: Benign metastasizing giant-cell tumor of bone: Report of three cases and review of the literature. Clin Orthop 243:208–215, 1983.
34. Marcove RC, Weis LD, Vaghaiwalla MR, Person R, Huvos AG: Cryo-surgery in the treatment of giant cell tumors of bone: A report of 52 consecutive cases. Cancer 41:957–969, 1978.
35. McDonald DJ, Sim FH, McLeod RA, Dahlin DC: Giant cell tumor of bone. J Bone Joint Surg 68A:235–242, 1986.
36. Miller G, Bettelli G, Fabbri N, Campanna R: Curettage of giant cell tumor of bone: Introduction, material and method. Chir Organi Mov 75 (Suppl 1):203, 1990.
37. Mjoberg B, Pettersson H, Rosenqvist R, Rhydolm A: Bone cement, thermal injury and the radiolucent zone. Acta Orthop Scand 55:597600, 1984.

38. Nair MK, Jyothirmayi R: Radiation therapy in the treatment of giant cell tumor of bone. Int J Radiat Oncol Biol Phys 43:1065–1069, 1999.
39. Nelson DA, Barker ME, Hamlin BH: Thermal effect of acrylic cementation at bone tumour sites. Int J Hyperthermia 13:287–306, 1997.
40. Nicholson NC, Ramp WK, Kneisl JS, Kaysinger KK: Hydrogen peroxide inhibits giant cell tumor and osteoblast metabolism in vitro. Clin Orthop 347:250–260, 1998.
41. Oda Y, Tsuneyoshi M, Iwamoto Y: Giant cell tumour of bone: Oncological and functional results of long term follow-up. Jpn J Clin Oncol 28:323–328, 1998.
42. O'Donnell RJ, Springfield DS, Motwani HK, et al: Recurrence of giant cell tumors after curettage and packing with cement. J Bone Joint Surg 76A:1827–1833, 1994.
43. Persson BM, Ekelund L, Lövdahl R, Gunterberg B: Favorable results of acrylic cementation for giant cell tumors. Acta Orthop Scand 55:209–214, 1984.
44. Pettersson H, Rydholm MA, Persson B: Early detection of local recurrence after curettage and acrylic cementation of giant cell tumors. Eur J Radiol 6:1–4, 1986.
45. Picci P, Manfrini M, Zucchi V, et al: Giant cell tumor of bone in skeletaly immature patients. J Bone Joint Surg 65A:486–490, 1983.
46. Quint U, Mueller RT, Muller G: Characteristic of phenol: Instillation in intralesional tumor excision of chondroblastoma. osteoclastoma and enchondroma. Arch Orthop Trauma Surg 117:p. 43–46, 1998.
47. Remedios D, Saifuddin A, Pringle J: Radiological and clinical recurrence of giant-cell tumour of bone after the use of cement. J Bone Joint Surg 79B:26–30, 1997.
48. Rock MG: Curettage of giant-cell tumor of bone: Factors influencing local recurrences and metastasis. Chir Organi Mov 75 (Suppl 1):204–205, 1990.
49. Rock MG, Sim FH, Unni KK: Metastases from histologically benign giant-cell tumor of bone. J Bone Joint Surg 66A:269–274, 1984.
50. Rock MG, Sim FH, Unni KK, et al: Secondary malignant giant cell tumor of bone: Clinicopathological assessment of nineteen patients. J Bone Joint Surg 68A:1073–1079, 1986.
51. Segura J, Albareda J, Bueno AL, et al: The treatment of giant cell tumors by curettage and filling with acrylic cement: Long term functional results. Chir Organi Mov 82:373–380, 1997.
52. Shih HN, Hsu RW, Sim FH: Excision curettage and allografting of giant cell tumours. World J Surg 22:432–437, 1998.
53. Siebenrock KA, Unni KK, Rock MG: Giant-cell tumor of bone metastasizing to the lung: A long term follow-up. J Bone Joint Surg 80B:43–47, 1998.
54. Sung HW, Kuo DP, Shu WP, et al: Giant cell tumor of bone: Analysis of two hundred and eight cases in Chinese patients. J Bone Joint Surg 64A:755–761, 1982.
55. Tomeno B, Ochoa S: Curettage of giant cell tumor of bone: Treatment of local recurrence. Chir Organi Mov 75 (Suppl 1):207–208, 1990.
56. Trieb K. Bitzan P, Dominkus M, Kotz R: Giant-cell tumors of long bone. J Bone Joint Surg 82A:1360–1361, 2000.
57. Unni KK: Dahlin's Bone Tumors: General Aspect and Data on 11087 Cases, Ed 5. Philadelphia, Lippincott-Raven 1998.
58. Ware Jr JE: SF-36 Health Survey: Manual and Interpretation Guide. Boston, Nimrod Press 1993.
59. Ware JE, Kosinski M, Keller SD: SF-36 Physical and Mental Health Summary Scales: A User's Manual. Boston, The Health Institute, New England Medical Center 1994.
60. Ware Jr JE, Sherbourne CD: The MOS 36-Item Short Form Health Survey (SF-36). I: Conceptual framework and item selection. Med Care 30:473–483, 1992.
61. Yip KM, Leung PC, Kumta SM: Giant cell tumor bone. Clin Orthop 323:60–64, 1996.
62. Zhang Y, Hou C, Chen A: A preliminary observation of giant cell tumor of bone treated by adriamycin-loaded chitosan drug delivery system. Chung Kuo Hsiu Fu Chung Chien Wai Ko Tsa Chih 12:280–282, 1998