Cryosurgery in the Treatment of Giant Cell Tumors of Bone

A Report of 52 Consecutive Cases

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Cryosurgery for the treatment of localized primary and metastatic bone tumors has been employed at Memorial Hospital for Cancer and Allied Diseases and the Hospital for Joint Diseases since its introduction as a therapeutic modality in 1964. Its usefulness and effectiveness in our hands as an adjunctive surgical procedure for locally aggressive and recurrent benign bone tumors, for low grade malignancies and for localized metastatic disease has now been well documented[1, 11–15] and has been used in over 600 cases. The promising results with this technique in an initial series of 25 giant cell tumors of bone has already been reported.[11] Since that first report, further refinement in surgical technique by wider incision, more thorough curettage and repetitive exposure of a larger bony area to temperatures of at least −20° has produced significant improvement in the rate of local tumor recurrence and marked reduction in the incidence of associated complications. We are now convinced that the use of cryosurgery as a supplement to completely adequate curettage, has a substantial benefit to offer in reliably reducing the incidence of local recurrence and preserving joint function. The present study updates our previous experience with cryosurgery in the management of giant cell tumors of bone and further evaluates this modality of treatment. Our fully malignant rate of one out of 52 cases (1.9%) is significantly less than the previously reported Memorial Hospital series (16%). Many of these Memorial Hospital cases, of course, did[7] and still do represent cases with multiple prior recurrences (some even had radiotherapy). Jaffe also noted a 15% metastatic rate.[5]

MATERIALS AND METHODS

Fifty-two consecutive cases of benign giant cell tumor of bone treated between 1965 and 1977 at the Memorial Hospital for Cancer and Allied Diseases, the New York Hospital-Cornell Medical Center and the Hospital for Joint Diseases have been included in this study. All of the patients in this series were treated by thorough curettage of the tumor followed by instillation of liquid nitrogen—the rationale being to destroy any residual tumor at the margins of curettage by a process of repetitive rapid freezing and thawing. The mode of action and factors influencing such therapy[2–5, 11] as well as further technical details of the procedure[11] have been documented and discussed in our previous report.[11]

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FIG. 1. Illustration of cryosurgery (intraoperative view) with skin retracted, and a funnel sealed to the bone using moist gelfoam. Water vapor seen as liquid nitrogen flows through the funnel and gelfoam openings into the osseous lesion.

In our initial experience a double lumen probe with circulating liquid nitrogen was employed; however, the procedure now used is to pour liquid nitrogen through a funnel directly into the tumor cavity after a thorough curettage. This is the preferred method, for it allows a more complete contact of the irregularly shaped residual cavity with liquid nitrogen, thus producing a more extensive freezing of any residual tumor cells in the cavity wall (Fig. 1).

In the initial cases of this series the resulting cavity after curettage and cryosurgery was most frequently filled with homogenous (bank) or autogenous (iliac crest) bone graft but occasionally left to heal spontaneously. Later fibular strut grafts were used to provide additional structural support when needed and to prevent fracture or displacement but currently methylmethacrylate is being used along with corticocancellous onlay graft until peripheral bone regeneration occurs. This has provided increased bone stability and prevented pathological fractures immediately following cryosurgery. A long leg ischial weight bearing brace is used for additional support while bone healing is taking place.

During freezing, the surrounding skin, soft tissues and neurovascular structures must be protected by adequate immobilization, wide retraction and continuous bathing with lukewarm water. The use of gelfoam to seal the funnel to the bone cavity and form a liquid tight space has been described in a previous paper[11] and facilitates the procedure. A pneumatic tourniquet is used during the procedure where possible to decrease local bone bleeding and prevent blood from acting as a barrier to achieve sufficient depth of freeze. To further facilitate the procedure, blood must be suctioned from the cavity as completely as possible before each freeze to avoid blocking off portions of the space from contact with liquid nitrogen. We have found that these finer details of technique are probably responsible to achieve optimum freezing and improve the rate of tumor eradication. A more thorough curettage is especially helpful for a better nitrogen contact.

The concept of rebiopsy following cryosurgery (second look procedure) to determine the efficacy of treatment was propounded in our earlier paper[11] and has been continued as a matter of routine in this series. A rebiopsy was performed 3–6 months after the original cryosurgical procedure and provides a check on the thoroughness of the original procedure as well as permitting early treatment of residual or recurrent tumor by repeat cryosurgery before its obvious destructive roentgenographic or clinical manifestations.

Clinical Data

Between the years 1965–1977, 52 consecutive patients with benign giant cell tumors of bone were treated with cryosurgery. Most of the patients in this series were referral cases because of particular difficulty in the treatment or previous unsuccessful therapy. Thus the clinical presentation of this series may not be entirely typical, our cases being particularly large and difficult to treat. Thirty-four patients were female, 18 male. The age of the patients ranged from 9 to 66 years, with a mean age of 30 years (Fig. 3). The postoperative follow-up ranged from 3 months to 10 years and 3 months with 33 patients being followed over 3 years and an average follow-up of 43 months since last evidence of disease (66 months for the initial group of 25 cases and 22 months for our second series of 27 patients). Seventy per cent of the cases were located about the knee joint, 21 in the distal femur and 14 in the proximal tibia (Fig. 4). Twenty-six patients had previous operative attempts at treatment prior to cryosurgery (usually curettage and bone grafting), 9 of which had undergone multiple procedures. Following cryosurgery 9 of the initial 25 cases reported in our earlier study had viable tumor present at rebiopsy. Only 3 patients in the second series of 27 cases showed positive rebiopsy, but no recurrences were in the area originally treated and the details will be discussed below. All of the patients studied in this report are free of disease at the present time.

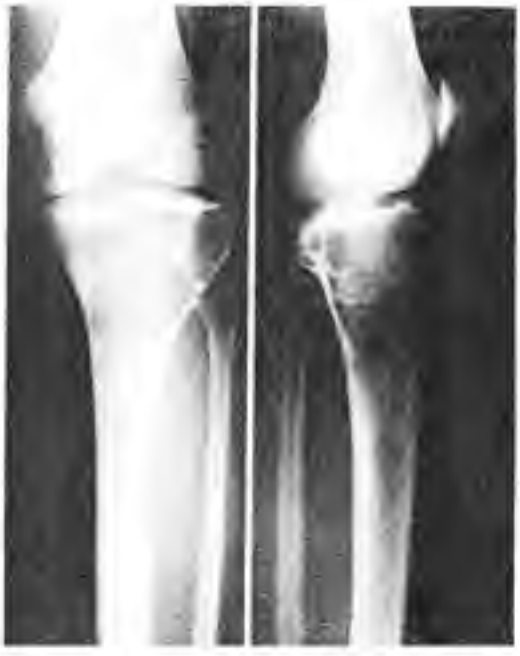
Pathological Data

The pathology observed in our additional group of 27 cases did not differ substantially from that reported in the initial 25 cases[11] either at the time of cryosurgery or following second look procedure.

An analysis of the histopathology from all 52 cases in this series is summarized in Table 1. There were 34 (65.5%) typically "benign" giant cell tumors having completely benign mononuclear stroma and abundant numbers of giant cells which were designated grade I. Eighteen (34.5%) cases showed sufficient stromal atypia with interspersed areas of spindle cells, increased mitotic rate and decreased numbers of giant cells that they were felt to be "focally malignant"[7] or grade II. A prominent telangiectatic or sinusoidal vascular pattern was present in 11 (32%) grade I cases, and one (5.5%) grade II cases to be considered as aneurysmal components or secondary aneurysmal bone cysts (23% overall). Scattered small areas of minimal osteoid production were of note in 7 (20%) grade I lesions and 3 (16.5%) grade II lesions or 19% for the entire series. Local recurrences occurred in 9 (17%) grade I lesions and 3 (17.5%) grade II lesions which represents no significant difference from the relative per cent of the entire series represented by each grade. There was no correlation of either local recurrence or malignant transformation with the presence of aneurysmal changes or minimal osteoid formation, though the one case showing tumor invading veins did recur locally. In this relatively small series therefore it has not been possible to usefully predict tumor behavior from histological grading of grade I and II lesions. Two of the lesions initially felt to be "benign" eventually behaved in an aggressive manner, one producing pulmonary metastases still retaining the same histology of a "benign" giant cell tumor and one transforming into an osteogenic sarcoma 2" proximal to the area previously treated by cryosurgery.

RESULTS, COMPLICATIONS AND THEIR MANAGEMENT (Table 1)

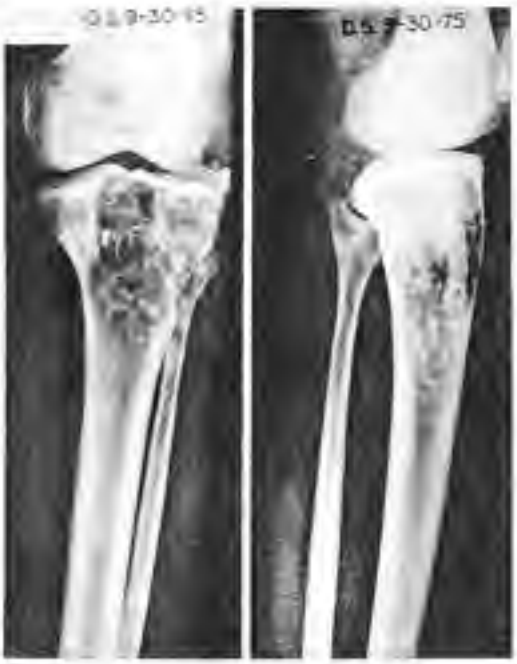
Since our report on the first 25 cases of giant cell tumor treated by cryosurgery[11] an additional 27 patients have undergone this treatment. In this second group, the effectiveness of initial treatment and control of the local tumor has been significantly improved and the incidence of complications markedly reduced.



Figs. 2A and B. Case #41, age 48. Pain in left knee of 2 year duration. Lesion first seen July 30, 1975.

Residua and Recurrences

Our previous paper reviewed the first 25 cases of this study in which there were 9 instances of residual tumor foci demonstrated on second look biopsy. These were usually otherwise nondetectable, nonclinical microscopic residua. In the subsequent 27 cases, 25 have undergone rebiopsy and 3 have shown presence of viable tumor, but none at the site of original involvement: one case produced a malignant transformation upon recurrence at a site proximal to the original lesion which necessitated amputation for adequate treatment (he has remained well); a second case demonstrated a soft tissue recurrence separate from the original site of curettage and was probably secondary to accidental surgical spill; in the third case, a separate bone focus of tumor developed which was not seen at the time of initial X-ray examination or surgical curettage and was responsible for the only bone local recurrence. This tumor cavity did not com-



FIGS. 2C and D. Postoperative view, one month after curettage, cryosurgery and insertion of iliac crest graft. Slight depression of lateral condyle is seen.

municate with the original area treated when flushed with irrigating solution after treatment. Both of these latter 2 cases were successfully treated with reapplication of cryosurgery and presently are disease free.

Infections

The incidence of postoperative infection experienced a sharp decline in our second series of cases where we have had only one serious deep wound infection which responded readily to antibiotic therapy. This contrasts sharply with 4 minor postoperative infections in the earlier series and 3 serious ones which necessitated local en bloc resection and one amputation to effect control. We feel this improvement in our later series has resulted from additional refinements of surgical technique which have emphasized the avoidance of skin injury from the freezing process by adequate mobilization, wide retention, and also continuous irrigation of the surrounding tissues. Prophylactic antibiotics have been used.

Skin Problems

The incidence of skin blistering and necrosis has likewise been reduced from the 4 cases reported in our initial group of patients. There was only one significant case of local skin necrosis which delayed wound healing and necessitated further treatment in the current series. That occurred with a distal tibial lesion where adequate soft tissue mobilization about the medial malleolus was quite difficult. We feel that the same factors which have influenced the rate of infection here are also related to the reduced incidence of skin problems.

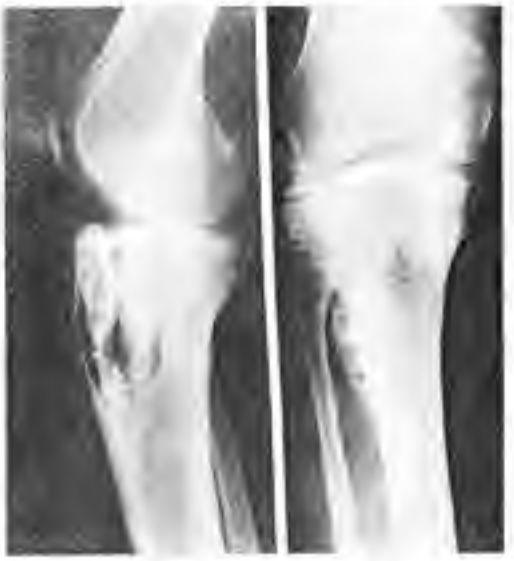
Nerve Problems

Neuropraxias following cryosurgery occur from proximity of the nerve to an area of bone being treated. The 3 patients that encountered nerve palsies in our first series have all shown complete resolution and return of function. In the last 27 cases we have had only one patient with neuropraxia. That was a sciatic nerve palsy following the freezing of a large giant cell tumor of the ilium and since this patient has had only a few months follow-up, we cannot comment at this point on the ultimate return of function. From previous experience with neuropraxia secondary to freezing however, we anticipate complete return of this palsy.

Malignancy

All tumors treated by cryosurgery were considered histologically benign on previous biopsy. Amputation was advised for any tumor with fully malignant histologic appearance. Among the initial 25 cases, a single tumor did metastasize as a solitary nodule in the lung 18 months after cryosurgery. A pulmonary wedge resection was performed and the patient is now free of disease 6 years and 9 months following treatment. This was

the patient who had residual tumor at a separate local focus, subsequent infection and was amputated. The histological grading of both the primary tumor and the metastatic nodule in this case was felt to be grade I benign despite its aggressive behavior. One case in the second series showed fully malignant histologic transformation to osteogenic sarcoma and subsequently required amputation. As mentioned before this lesion appeared above the previously frozen area. One other patient in our earlier group developed a reticulum cell sarcoma in nearby lymph nodes 8 years prior to her giant cell tumor, treated successfully with 3100 R. She is now over 10 years since cryosurgery for her giant cell tumor and walks normally with a full, pain free range of motion of the knee.



FIGS. 2E and F. Nineteen months post-cryosurgery and 15 months postnegative rebiopsy showing marginal sclerosis. Knee range of motion is 90°.

FRACTURES

While none of the patients in our most recent series of cases incurred pathologic fractures preoperatively, 3 of the patients in the original group did need treatment for this problem. Two of these eventually required knee fusion for persistent malunion after cryosurgical eradication of the tumor and the other patient required an ischial weight bearing brace for 2 years before fracture healing occurred. The postoperative fractures in the initial 25 patients have been previously reported (8 patients incurred fractures following cryosurgery: 3 healed uneventfully, 3 required prosthetic joint replacement, one necessitated bone grafting and one, an infected pathologic fracture, required bloc resection and knee fusion as previously reported). Five patients of the current 27 cases had postoperative fractures: one healed spontaneously with closed treatment, 2 required bone grafting of which one also needed internal fixation, one required prosthetic replacement and one infected pathologic fracture required bloc resection and knee fusion. All of these cases occurred prior to our use of methyl methacrylate combined with onlay grafts to support the tumor cavity and articular surface and reconstitute the surrounding bone cortex. Since then we have had no such fractures when using this regimen in combination with routine and prolonged use of ischial weight bearing long leg braces postoperatively. Although the lack of methyl methacrylate shear strength is well known, so far the postoperative fixation has been quite successful, (especially when supplemented by use of the ischial weight bearing brace) until peripheral bone healing has occurred.

JOINT MOTION

Of our first 25 cases, 20 major weight bearing joints of the lower extremities were involved. In 13 of those (65%), the original joint was salvaged by curettage and cryosurgery, 3 of these requiring supplementary bone grafting. The follow-up of the remaining patients has been previously reported and remains unchanged. In our later series, 21 major weight bearing joints of the lower extremities were treated. Of these, 17 cases (81%) have thus far been salvaged without requiring ar-

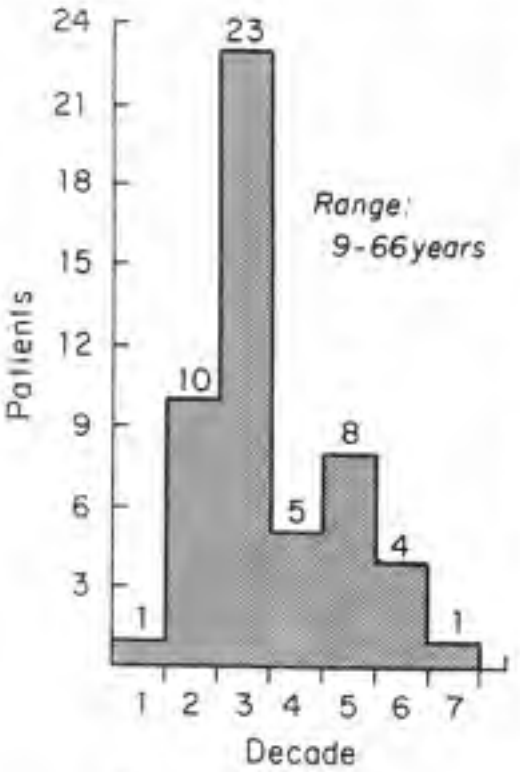


FIG. 3. Age distribution.

throdesis or prosthetic arthroplasty, though 6 cases did necessitate additional bone grafting. The other 4 cases consisted of: one requiring femoral head replacement by endoprosthesis, one total knee arthroplasty for pathologic fracture, one distal tibial endoprosthesis due to joint deformity, and one en bloc resection and knee fusion for pathologic fracture with malignant degeneration 2" above the cryosurgery zone which eventually required the only amputation in this group. This latter patient has remained well and disease free as has the patient who underwent pulmonary resections in the initial series.

DISCUSSION

Giant cell tumors which typically present with large areas of bone destruction produce a particularly difficult therapeutic problem for the orthopedic surgeon. Although almost always benign, these tumors are "locally aggressive" and tend to have a high recurrence rate (probably 60% or greater)[3,7,9] (Fig. 5) after treatment by curettage and bone grafting. Malignant transformation is well known to be 6–15%. The large areas of bone destruction they produce typically erode the subchondral bone plate and undermine support of the adjacent articular surface in such a way as to compromise attempts at both tumor removal by curettage and reconstruction. Anatomic localization of these lesions is most frequent about the knee joint (34–54% of the cases in the distal femur or proximal tibia[5,9,16]) which must be able to withstand major weight bearing forces following treatment (in our series 70% of the cases were localized about the knee). And finally, these tumors occur typically in young adults whose normal life expectancy and active life style necessitate a reliable and durable surgical remedy for eradicating the tumor and preserving joint function.

Cryosurgery as developed over the past 12 years on the bone service of Memorial Hospital for Cancer and Allied Disease[1,11–15] has emerged as a most valuable technique for the orthopedic surgeon and one with distinct advantages for treating giant cell tumors[11] especially where preservation of joint motion is desired. Cryosurgery is able to enhance curettage with regard to a more complete elimination of tumor at the margins and it avoids a sacrifice of surrounding tissues needed for subsequent reconstruction and joint function. The residual gait is far superior as compared with knee fusion or prosthesis. This is easily documented by videotape gait analysis. By performing cryosurgery after curettage, one can cause necrosis of residual tumor cells usually as far as one to 2 cm from the residual cavity wall. The frozen marginal bone of the curetted cavity is left as an autograft in continuity *in situ*. Repeated biopsies have shown that eventual restoration of bone occurs by creeping substitution. In most frac-

tures, healing will occur but if fracture and instability do presist after cryosurgery, a massive resection of the area is not necessary so as to prevent local recurrence and therefore facilitates arthrodesis or secondary insertion of a prosthesis.

Hutter *et al.*[7] have emphasized the usual rapid recurrence of a giant cell tumor unsuccessfully treated. Of the 52 patients treated with cryosurgery in this series, 8 have been followed for less than one year, 33 for over 3 years; although the average follow-up in this series is 43 months, it certainly covers the period within which 90%[4,7,9] of all clinical recurrences will occur. Our initial group of 25 cases produced 9 preclinical recurrences following cryosurgery (36% recurrence rate). But early detection of residual tumor by employing second look biopsies combined with repeat cryosurgery has resulted in a 90% cure rate in those 25 patients. With further refinement of the surgical technique by a more careful curettage and wider exposure, our second series of 27 cases have shown only 3 local recurrences (12% recurrence rate), none of which occurred in the exact same area of the original lytic lesion. Except for a single instance of malignant transformation proximal to the treated area which necessitated amputation, the "cure rate" at this time following repeat cryosurgery in this group is otherwise 100%! These results certainly compare strikingly with those in the literature showing roughly 60% for recurrence even with en bloc resection.[5] In addition there is the obvious advantage of the preservation of the original joint involved without total arthroplasty or arthodesis in nearly ¾ of our 52 patients (73%) and in over 80% of the most recent 27 cases. The poor klunky gait of a knee arthroplasty without a brace and the difficulty sitting and dressing with an arthodesis is far less desirable.

It is worthy of re-emphasis at this time that the way we have used the terms re-

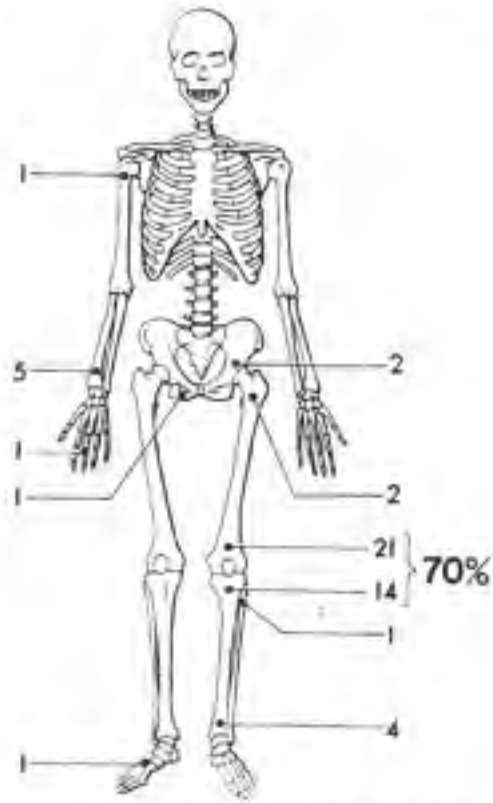


FIG. 4. Distribution of lesions (70% around knee).

currence and residual tumor with regard to our second look specimens is not the same as when these terms are applied to situations in which the evidence for recurrence is based only on clinical or roentgenographic manifestations. No other series in the literature has documented results with repeat biopsies, without which actual recurrence rates remain unknown. The rebiopsy procedures most likely produce a higher yield for minimal residual tumor than by waiting for the rather unpredictable biologic behavior of this tumor to show up clinically. Giant cell tumors recurring up to 12 years after curettage are well known even though most recur early. When a positive second look specimen is obtained, it must be realized that one cannot make assumptions about the clinical activity of that

TABLE 1.

Case	Age Sex	Site	Grade	Previous Therapy	First Cryosurgery	Bone Graft	Rebiopsy Results	Repeat Cryosurgery	Fracture
1.	18 F	R distal femur	I	None	10/65		6/68 (+)		6/68 distal femur
2	30 F	R prox tibia	I	5/65 2400 rads 6/65 curet., bone graft	2/66				
3	55 M	R distal femur	I	10/53 curet., bone graft	7/66	Bank			
4	16 F	L prox tibia	I	None	7/67	Bank			
5	21 F	Base of 3rd middle phalanx	I	12/67 curet.	2/68		1/71 (−)		3/68 base of middle phalanx postop
6	66 F	R prox tibia	II	6/65 curet., bone graft 1/66 repeat 4/67 repeat	3/68		5/68 (−)		
7	23 F	L distal femur	II	4/68 splinting for path. fracture	5/68	Iliac crest	6/68 (−)		
8	26 M	R prox tibia	I	5/68 curet.	6/68		9/68 (+) 10/68 (+) 1/70 (+)	9/68	9/68 prox. tibia
9	59 F	R distal femur	II aneurysmal areas	None	8/68		11/68 (−)		11/68 distal femur postop
10	55 F	R prox tibia	II	63 curet.	11/68	Bank	2/69 (−) 4/69 (−)		
11	26 M	R prox tibia	II	None	12/68	Bank	2/69 (+) 3/69 (−)	2/69	
12	28 M	L distal femur	I	12/68 curet., splint for path. fx.	2/69		3/69 (+) 5/69 (+) 8/69 (−)	3/69 5/69	
13	22 F	R distal femur	I	7/68 curet., bone graft	3/69		6/69 (−)		
14	26 M	R ilium	II	9/69 curet.	10/69		1/70 (+) 6/70 (−)	1/70	
15	18 F	R distal femur	I	None	11/69	Fibula Strut	2/70 (−)		3/70 distal femur postop
16	21 M	L prox tibia	I aneurysmal areas benign osteoid	None	9/70		2/71 (+)	3/71	

Complications		*Other Treatment*		*Follow-up*	
Infection	*Others*	*Surgery*	*Other*	*Months Ned*	*Comment*
		6/69 total knee arthroplasty 11/69 knee fusion 2/71 left femur shortening		56	Lost to follow-up after 1973
	1953—R. inquinal reticulum cell sarcoma-radiation therapy. NED			136	Reticulum Cell Sarcoma treated with 3100 rads locally in 1953
	minor skin necrosis			126	
	minor skin necrosis			113	
				106	
5/68	knee joint instability	3/70 knee fusion	long leg brace	105	
5/68	fracture non-union	4/69 knee fusion 11/70 knee fusion	long leg brace	107	
9/68		11/68 knee fusion 1/70 Lung resection en bloc excision, proximal tibia 7/70 Above knee amputation	(Grade I)	86	Amputation for chronic infection
		4/69 total knee arthroplasty 6/69 tibial osteotomy		48	Lost to follow-up after 1972
2/69		4/69 wound debridement	long leg brace	45	10/75 persistent minor wound drainage
2/69		3/69 wound debridement 2/71 en bloc excision prox. tibia, knee fusion 11/71 pseudoarthrosis repair		93	
			long leg brace	24	
6/69 distal femur postop	minor skin necrosis transient nerve palsy	6/69 iliac bone graft to fx. site	spica cast long leg brace	66	
		1/70 fibula strut graft		77	
		2/70 bank bone graft	long leg brace	69	
			long leg brace	71	orig. lesion metaphyseal; epiphyseal plate open; recurrence was in the epiphysis

TABLE 1.

Case	Age Sex	Site	Grade	Previous Therapy	First Cryosurgery	Bone Graft	Rebiopsy Results	Repeat Cryosurgery	Fracture
17	33 F	R distal femur	II venous invasion	11/70 curet.	12/70	Fibula Strut	7/71 (+)	7/71	
18	32 F	R prox tibia	II benign osteoid	68 curet. 69 curet.	1/71	Fibula Strut	5/71 (−)		
19	43 F	R distal femur	I prominent xantho-matous areas	10/70 curet.	12/70	Fibula Strut	1/71 (−) 11/71 (−)		1/71 distal femur postop
20	46 M	R distal femur	I aneurysmal areas	None	1/71	Fibula Strut	4/71 (−)		1/71 distal femur postop
21	17 F	R distal femur	I	5/71 curet.	6/71	Fibula Strut	11/71 (−)		
22	21 M	L first metatarsal	I	None	6/71		10/71 (−)		
23	16 F	R prox tibia	I	None	6/71		12/71 (+)		
24	45 M	R distal radius	I	None	11/71	Fibula Strut	5/72 (+)	5/72	
25	13 M	L prox tibia	I aneurysmal areas	None	5/71		10/71 (−)		
26	27 F	R distal radius	II	7/69 curet.	1/72		7/72 (−)		
27	23 F	L ishium pubic ramus femoral head	I	4/72 biopsy	7/72		1/73 (−)		
28	45 M	L distal femur	I (subsequent malignant transfor-mation)	2/72 curet., bone graft 7/72 repeat	10/72	Fibula Strut	6/73 (+) 9/75 (+) Osteosarcoma above disease	None area	10/72 postop distal femur
29	15 F	R distal femur	I aneurysmal areas; benign osteoid	None	12/72		2/75 (−)		2/73 distal femur
30	26 F	L distal femur	I	1/73 biopsy	2/73	Fibula Strut	Refused by patients		3/75 distal femur
31	29 M	R prox femur	I aneurysmal areas	None	2/73	Fibula graft; nail & plate	2/75 (−) 1/76 (−)		12/75 prox femur
32	24 F	R distal femur	I aneurysmal areas; benign osteoid	11/70 curet., bone graft 12/71 repeat	5/73		1/75 (−)		
33	23 F	R distal radius	I	2/72 curet. 8/73 curet.	10/73		6/73 (−) 2/75 (−)		

Complications		*Other Treatment*		*Follow-up*	
Infection	*Others*	*Surgery*	*Other*	*Months Ned*	*Comment*
			long leg brace	70	
sinus tract 5/71			long leg brace	70	sinus tract healed spontaneously
		1/71 total knee arthroplasty 11/71 bone graft	long leg brace	66	
			long leg brace	20	
			long leg brace	71	
6/71		10/71 en bloc excision		20	Lost to follow-up after 1973
	Transient peroneal nerve palsy	12/71 en bloc excision proximal fibula		13	Lost to follow-up after 1973
	Transient peroneal nerve palsy			62	
		10/71 fibula strut graft		31	Lost to follow-up after 1974
				94	
				46	Cryosurgery of ishium; pubis bone, femoral head excised with A-M prosthesis
12/72 purulent wound drainage		10/72 bone grafting fracture site 6/73 en bloc resection; knee fusion 9/75 hip disarticulation	long leg brace	28	Malignant transformation proximal level of the tumor
		2/75 fibula bone graft 8/76 tibial osteotomy for genu varum	cast for distal femur fracture long leg brace	48	
			long leg brace	46	
		12/75 open reduction internal fixation bone grafting pathologic fracture	long leg brace	50	
				43	
3/73 superficial wound drainage	distal radius deformity	1/74 Darrach proc. tendon transfer 2/75 wrist fusion	Leather wrist gauntlet postop	42	

TABLE 1.

Case	Age Sex	Site	Grade	Previous Therapy	First Cryosurgery	Bone Graft	Rebiopsy Results	Repeat Cryosurgery	Fracture
34	23 F	R distal radius	I	2/72 curet., bone graft 8/73 repeat	10/73		1/74 (−) 10/74 (+) 12/74 (−)	10/74	
35	22 F	L distal femur	II	12/69 curet., bone graft 8/71 repeat	10/73		2/76 (−)		
36	29 F	L distal femur	II	6/71 curet., bone graft 6/72 repeat	1/74	Fibula Strut	5/74 (−) 6/75 (+)		
37	20 F	R distal femur	I aneurysmal areas	3/74 biopsy	6/74	Fibula Strut	11/74 (−) 5/75 (−)		10/74 distal femur
38	27 M	L prox tibia	I benign osteoid	3/72 curet., bone graft	12/74	Fibula Strut	5/75 (−)		
39	45 M	R prox tibia	II	12/74 curet., bone graft	2/75	Fibula Strut	Lost to follow-up		
40	19 F	L distal tibia	II aneurysmal areas benign osteoid	4/74 curet., bone graft 8/74 repeat	3/75	Fibula Strut	10/75 (−)		
41	49 M	L prox tibia	I aneurysmal areas	None	8/75	Iliac crest	1/76 (−)		
42	33 F	L distal radius	II	None	10/75	Methyl methacrylate	10/76 (−)		
43	57 F	L prox tibia	I aneurysmal areas	9/75 biopsy	11/75	Methyl methacrylate	6/76 (−)		
44	17 F	R distal tibia	II	8/75 biopsy	12/75	Methyl methacrylate	5/76 (−)		
45	25 M	L distal femur	I aneurysmal areas; benign osteoid	8/74 curet., bone graft	2/76	Methyl methacrylate	5/76 (−)		
46	24 F	R distal tibia	I	None	2/76	Methyl methacrylate	9/76 (−)		
47	9	R distal femur	I	None	6/76	Methyl methacrylate	pending		
48	42 F	R prox humerus	I benign osteoid	None	7/76	Methyl methacrylate	1/77 (−)		
49	43 M	L ilium	I benign osteoid	10/75 biopsy; 4000 rads postop	7/76	Methyl methacrylate	pending		
50	26 F	L distal femur	II	12/74 curet., bone graft	7/76	Methyl methacrylate	10/76 (−)		
51	38 M	L prox tibia	II	None	7/76	Methyl methacrylate	pending		
52	17 F	R distal tibia	II benign osteoid	curet., bone graft	8/76				

Complications		*Other Treatment*		*Follow-up Months Ned*	*Comment*
Infection	*Others*	*Surgery*	*Other*		
	distal radius deformity	1/74 wrist fusion	Leather wrist gauntlet postop	30	Recurrence from soft tissue spill distal to site of tumor
			long leg brace	44	
			long leg brace	24	Recurrence in separate focus missing at initial surgery
		5/75 total knee arthroplasty	long leg brace	30	
			long leg brace	24	
			long leg brace	3	Lost to follow-up after 5/75
			long leg brace	17	
8/75 superficial postop			long leg brace	19	
		10/76 iliac crest graft	Leather wrist gauntlet	20	
		6/76 reinsertion of methyl methacrylate plus bone graft	long leg brace	13	
		5/76 reinsertion of methyl methacrylate plus bone graft	long leg brace	21	
		5/76 iliac crest bone grafting	long leg brace	15	
	distal tibia deformity	distal tibial prosthetic replacement pending	crutches non weight bearing	10	
			long leg brace	9	
				6	
	sciatic nerve palsy		foot drop brace	11	
		10/76 reinsertion methyl methacrylate plus bone graft	long leg brace	10	
			long leg brace	8	
	skin necrosis delayed wound healing			2	

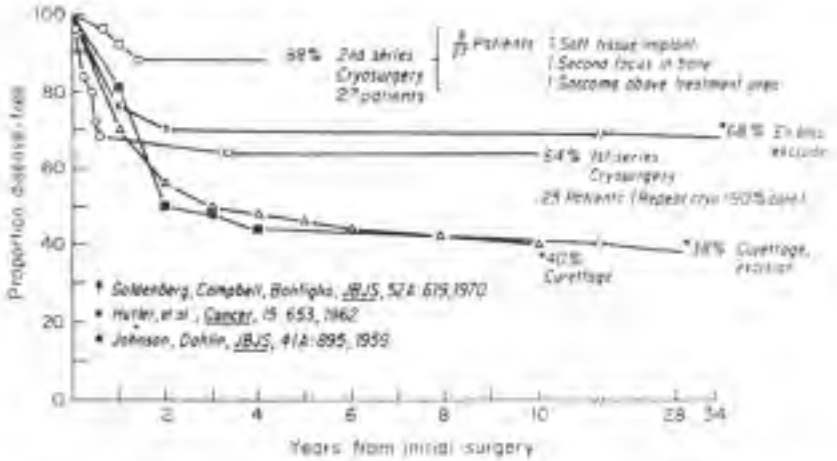


FIG. 5. Graph of recurrence rates of benign giant cell tumors.

lesion or what its presumed future behavior would have been without the second look. Thus while rebiopsy greatly facilitates the early repeat cryosurgery of any recurrent or residual lesions before further bone destruction, we remain unable to clearly predict what the clinical course of those residual areas of tumor would have been.

In evaluating the complications in our patients it is important to note at first that this series of cases is primarily a referral one in which 50% of the cases had undergone at least one unsuccessful previous surgical attempt at treatment and 9 had been subjected to multiple procedures. The lesions we have treated have been typically large (Figs. 2A and B) and 70% of our cases occurred in the major weight bearing bones around the knees (in contrast to 34–54% in other large series).[5–7, 9, 15, 16] Because of the stresses of weight bearing and the generally large size of these lesions, the knee is an especially difficult area from which to eradicate tumor while preserving function. The dismal alternatives of performing primary amputation or bloc resection with arthrodesis have therefore often been utilized for large lesions at this site.[8] The time needed for the bone to heal after cryosurgery was prolonged in our patients since the tumors were usually large and the shell of surrounding bone was often very thin. That reason as well as the bone necrosis following cryosurgery requires supplementary support during the healing period. As a result we no longer use structurally nonsupportive cancellous bone chips but instead we use either iliac (Figs. 2C–F) or fibular strut grafts for support and/or methylmethacrylate insertion occasionally surrounded by onlay grafts. This provides internal support to help prevent postoperative fracture and stimulates reconstruction of the surrounding cortex. Adequate fracture healing following massive tumor destruction and cryonecrosis can take as long as 2 years,[3] bone scan activity may be present for 5 years; therefore, long leg ischial weight bearing braces are now used for extended periods after treatment of large tumors until sufficient bone consolidation is well underway. The earliest sign of bone healing has been peripheral sclerosis of the treated area seen on X-ray following cryosurgery. Histologically this is new bone formation.

Infection seems to be a particular problem in any type of therapy for giant cell tumors. Goldenberg *et al.*[5] reported an overall infection rate of 7% in their series and 12% for patients with tumors of the knee. In our first series of 25 cases only one serious infection (3.5%) occurred (in a lesion about the knee). We doubt that cryosurgery itself increases the risk of infection since we observed only 2 instances of infection in over 600 other

cryosurgical procedures in which primary and metastatic neoplasms other than giant cell tumors were being treated. In the series by Goldenberg *et al.*[5] 4 out of 15 infections led to amputation while only one of our 10 cases resulted in limb ablation and that, only following development of pulmonary metastasis. We now feel that refinement of our surgical technique with special care given to wide skin and subcutaneous tissue retraction, thorough irrigation and meticulous closure as well as routine use of preoperative and postoperative bactericidal antibiotics has reduced the incidence of serious infection to only a single case in our last 27 cases.

The last point of interest is our one frank malignant giant cell tumor out of 52 cases (1.9%). The previous series at Memorial Hospital had a 16% fully malignant complication rate.[7] It is a very real possibility that the quick and thorough eradication by cryosurgery shortens the course of this disease and the time exposure interval during which a malignancy may develop.

The advantages of salvaging good knee function is obvious.

SUMMARY

Fifty-two cases of giant cell tumor of bone have been treated by cryosurgery—an extensive freezing of residual tumor after curettage. Cryosurgery is performed by direct pouring of liquid nitrogen into the tumor cavity through a funnel. The cavity is filled with methylmethacrylate and corticocancellous onlay grafts until peripheral bone regeneration occurs to provide bone stability and prevent postoperative pathologic fracture. Patients with lesions in a weight bearing bone are placed in a long leg ischial weight bearing brace until sufficient healing has taken place. Rebiopsy (a second stage diagnostic procedure) is performed 3–6 months after the original cryosurgery. By comparison of pathology, results and complications between our first series of 25 cases and the additional 27, we have observed only one frank malignant giant cell tumor (1.9% incidence). This is much lower than the previously reported 16% fully malignant complication rate, and may be the result of the rapid elimination of the giant cell tumor by cryosurgery.

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