

## ■ ONCOLOGY

# Giant cell tumours of the small bones of the hands and feet

## LONG-TERM RESULTS OF 30 PATIENTS AND A SYSTEMATIC LITERATURE REVIEW

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**Giant cell tumours (GCTs) of the small bones of the hands and feet are rare. Small case series have been published but there is no consensus about ideal treatment. We performed a systematic review, initially screening 775 titles, and included 12 papers comprising 91 patients with GCT of the small bones of the hands and feet. The rate of recurrence across these publications was found to be 72% (18 of 25) in those treated with isolated curettage, 13% (2 of 15) in those treated with curettage plus adjuvants, 15% (6 of 41) in those treated by resection and 10% (1 of 10) in those treated by amputation.**

**We then retrospectively analysed 30 patients treated for GCT of the small bones of the hands and feet between 1987 and 2010 in five specialised centres. The primary treatment was curettage in six, curettage with adjuvants (phenol or liquid nitrogen with or without polymethylmethacrylate (PMMA)) in 18 and resection in six. We evaluated the rate of complications and recurrence as well as the factors that influenced their functional outcome.**

**At a mean follow-up of 7.9 years (2 to 26) the rate of recurrence was 50% (n = 3) in those patients treated with isolated curettage, 22% (n = 4) in those treated with curettage plus adjuvants and 17% (n = 1) in those treated with resection (p = 0.404). The only complication was pain in one patient, which resolved after surgical removal of remnants of PMMA. We could not identify any individual factors associated with a higher rate of complications or recurrence. The mean post-operative Musculoskeletal Tumor Society scores were slightly higher after intra-lesional treatment including isolated curettage and curettage plus adjuvants (29 (20 to 30)) compared with resection (25 (15 to 30)) (p = 0.091). Repeated curettage with adjuvants eventually resulted in the cure for all patients and is therefore a reasonable treatment for both primary and recurrent GCT of the small bones of the hands and feet.**

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Giant cell tumour (GCT) is a relatively common benign lytic lesion that accounts for 4% to 5% of primary bone tumours and almost 20% of benign bone tumours.<sup>1</sup> It occurs mainly between the ages of 30 and 50 years and is slightly more common in women.<sup>2,3</sup> The most common sites are the meta-epiphyseal regions of the long bones (85%), with more than 50% located in the distal femur, proximal tibia and distal radius.<sup>4</sup> GCT of the axial skeleton accounts for a further 10%.<sup>2,4</sup> It is rare in the small bones of the hands and feet (between 1.7% and 5% of all GCTs).<sup>5–11</sup> The differential diagnosis includes enchondroma, fibrous dysplasia, aneurysmal bone cyst, osteomyelitis and brown tumour from hyperparathyroidism.

The standard treatment of lesions in the long bones is curettage, often with local adjuvants such as phenol, liquid nitrogen (cryosurgery) and/or polymethylmethacrylate (PMMA) to

reduce the recurrence rate, which has been reported from 12% to 34%.<sup>12–16</sup> More aggressive lesions of the long bones with soft-tissue extension, pathological fracture or involvement of joints may be treated by *en bloc* resection.<sup>14,16</sup>

Only a few studies of GCT of the small bones have been published. As most are single case reports there is no consensus about the preferred treatment, which ranges from curettage (with or without adjuvants) to *en bloc* resection and even amputation. Local recurrence rates anywhere between 0% and 100% have been reported after surgical treatment.<sup>6–8,17</sup> Most recurrences occur within two years of surgery, and *en bloc* resection has been shown to result in a lower rate of recurrence (0% to 50%).<sup>6–8,18,19</sup> However, reconstruction after resection may be difficult in cases of multi-centric GCT of the small bones, which has been reported in 7% to 18% of cases.<sup>5,20</sup> Curettage without adjuvants may not afford

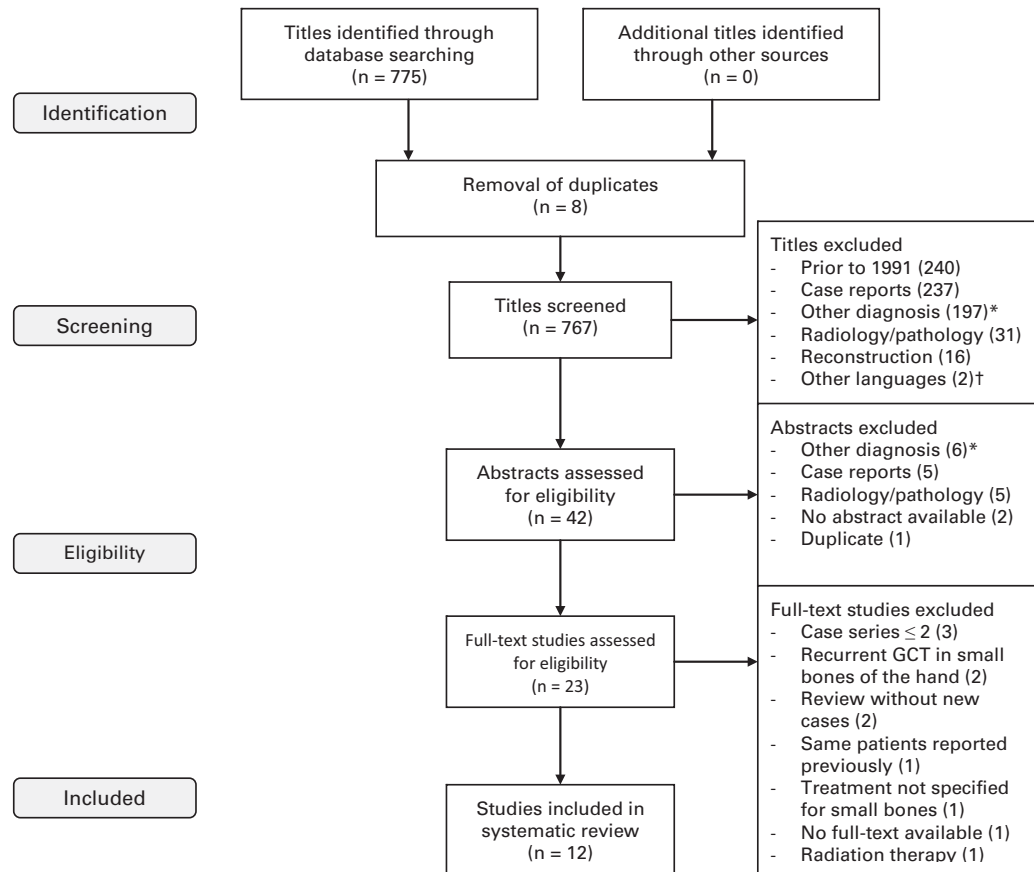


Fig. 1

Flowchart of the systematic literature search (\* including but not limited to: giant cell tumour (GCT) of the long bones (mainly distal radius), GCT of the axial skeleton, multifocal GCT, malignant GCT, other bone and soft-tissue tumours (e.g. diffuse-type GCT, GCT of tendon sheath, chondroblastoma, chondrosarcoma, osteosarcoma), GCT in animals, etc; † excluded languages were Chinese and Turkish).

complete tumour removal, resulting in a higher rate of recurrence (0% to 100%).<sup>6,8,17,21,22</sup> Radiation-induced sarcoma has been reported in 5% to 10% of patients receiving radiotherapy as adjuvant treatment, and it is therefore not recommended for primary lesions.<sup>4,8</sup>

The aims of this multicentre study were first to perform a systematic literature review of the surgical treatment of GCT of the small bones. Secondly, we aimed to evaluate the rates of complication and recurrence and attempt to define any association between patient and tumour characteristics and functional outcome after different surgical approaches.

## Patients and Methods

We performed a systematic search of the literature on GCT of the small bones published between 1 January 1990 and 17 January 2011. Search terms and MeSH headings used were 'giant cell tumours', 'GCT', 'small bones', 'hand bones', 'foot bones', and all the individual small bones separately. We identified 775 unique titles in PubMed, EMBASE, Web of Science and Academic Search Premier. All titles and abstracts were screened by two reviewers

(VCO, LH). Inclusion criteria were case series only published after 1990 in English, Dutch, Portuguese, French, Italian or German; other languages were excluded. Furthermore, we excluded papers that focused purely on radiological and/or histopathological assessment of GCT of the small bones, reviews without new clinical cases, and papers on GCT of the long bones, GCT of soft tissue (GCT-ST), diffuse-type GCT (DT-GCT) and GCT of the tendon sheath (GCT-TS). After review of the 775 titles, 42 abstracts were screened, of which 23 full-text articles were assessed. Full text assessment resulted in 11 further exclusions, leaving a total of 12 papers for systematic review (Fig. 1).<sup>6-9,17-19,21-25</sup>

In addition we retrospectively reviewed 31 consecutive patients with primary GCT of the small bones from a total of 570 consecutive patients with GCT (5.4%) treated between 1987 and 2010 in the authors' five tertiary referral centres for orthopaedic oncology. One patient with a malignant GCT after local recurrence was excluded. The 30 remaining patients had a mean follow-up of 7.9 years (2 to 26; median 5.2). No patient was lost to follow-up. There were 17 men and 13 women with a mean age of 29.6 years

**Table I.** Patient characteristics

Characteristic (n, %)	n = 30
Gender	
Male	17 (57)
Female	13 (43)
Site	
Foot	18 (60)
Hand	12 (40)
Treatment	
Curettage	6 (20)
Curettage with adjuvants	18 (60)
Wide or marginal resection	6 (20)
Tumour characteristics	
Soft-tissue extension	7 (23)
Pathological fracture	6 (20)
Complications	1 (3)
Local recurrence	
First recurrence	8 (27)
Second recurrence	2
Third recurrence	1
Fourth recurrence	1

(13 to 68) (Table I). As primary treatment, six patients underwent curettage, 18 curettage plus adjuvants (nine phenol, five liquid nitrogen, two phenol and PMMA, one liquid nitrogen and PMMA and one PMMA), and six resection (five *en bloc* and one marginal) (Table II). Thorough curettage was followed by three cycles of phenolisation and neutralisation with ethanol, or by three cycles of liquid nitrogen, and subsequently by filling the cavity with either bone graft or PMMA. A high-speed burr was used in nine patients treated with curettage and adjuvants (Table II). In the Leiden University Medical Center, Leiden, the Netherlands (centre 1) and the Centro Hospitalar do Porto – Hospital Santo Antonio, Porto, Portugal (centre 5), musculoskeletal pathologists graded the GCT histologically, but this did not influence the choice of surgical treatment. As extension of the tumour can be evaluated very accurately on MR imaging, the purely radiological grading system of Campanacci et al<sup>1</sup> was not used. In practice, every GCT is treated according to its tumour characteristics, such as site, the presence of a pathological fracture and/or soft-tissue extension, instead of according to a specific grading system.

Data including age, gender, tumour site, soft-tissue extension, pathological fracture, surgical treatment, local adjuvants, local recurrence, complications and further surgical treatment were collected. All data were complete. Functional outcome was assessed at final follow-up using the Musculoskeletal Tumor Society (MSTS) scoring system<sup>26</sup> and was available for 22 patients (73%). The remaining patients were discharged from follow-up (n = 1), relocated (n = 5) or had died (n = 2), and therefore could not be reached by telephone and/or post.

**Statistical analysis.** Recurrence-free survival was calculated for the three different treatment groups using Kaplan-

Meier survival analysis with 95% confidence intervals (CI), and differences between the groups were analysed using the log rank test. Associations between different patient and tumour characteristics and the resulting recurrence rates were calculated using Pearson's chi-squared test and Fisher's exact test. Unpaired t-tests were used to compare MSTS scores between different treatment groups. The results were analysed statistically with SPSS v20.0 (IBM SPSS Statistics, Chicago, Illinois) and a p-value < 0.05 was used to denote statistical significance.

## Results

**Literature search.** Data including number of cases, tumour localisation, treatment, reconstruction, local recurrences and complications from the studies included in our systematic review are listed in Table III. Within the 12 included studies, a total of 25 patients were treated with curettage alone,<sup>6,8,17,21,22</sup> 15 were treated with curettage and adjuvants<sup>6,8,9,25</sup> and 41 were treated with resection.<sup>6-8,18,19,22-24</sup> A further ten patients from the studies were treated with amputation.<sup>6-8,17,21,22,25</sup> Results from our systematic review showed that the highest mean rate of recurrence occurred after curettage alone (72% (0% to 100%); n = 18) followed by resection (15% (0% to 50%); n = 6) and curettage with adjuvants (13% (0% to 50%); n = 2). The lowest recurrence rates were reported after amputation (10% (0% to 100%); n = 1); however, this is associated with marked functional and aesthetic impairment and is only indicated rarely as a salvage procedure.

**Retrospective multicentre analysis.** In our 30 patients the anatomical distribution of the 12 cases of GCT in the bones of the hand was first, second and third metacarpal bones (two each), fourth and fifth metacarpal bones (one each), scaphoid (two), and middle and distal phalanges (one each). The anatomical distribution of the 18 GCT in the bones of the foot was: talus (five), calcaneus (three), cuneiform (two), cuboid (one), first and fourth metatarsal bones (two each), and second, third and fifth metatarsal bones (one each). No patient had a multicentric GCT. There was soft-tissue involvement in seven patients (four in small bones of the hand and three in the foot) and a pathological fracture in six (four in small bones of the foot and two in the hand; two patients had both soft-tissue extension and a pathological fracture); only one of these underwent resection. None of the patients had any intra-articular involvement and none had distant or pulmonary metastases. Two patients died respectively five and ten years after their index surgery, both from conditions unrelated to the GCT.

Overall, eight patients had a first local recurrence (three in metatarsal bones, three in metacarpal bones, one in a phalange and one in the talus), with a mean time to recurrence of 14 months (6 to 31) (Fig. 2). The rate of recurrence was 50% (three of six) in patients treated with isolated curettage, 22% (four of 18) after curettage in conjunction with local adjuvants and 17% (one of six) after resection

**Table II.** Individual patient characteristics, treatments and outcomes

Patient/Gender/ Age (yrs)	Centre*	Site†	Soft-tissue extension	Pathological fracture	Treatment‡		Local recurrence						Follow- up (mths)	MSTS§	Final outcome**
					Primary	Reconstruction	n	Time to recurrence (mths)	Treatment§	Complications					
1 / F / 31	1	MT5	-	Yes	R (m)	Non-vascularised fibular graft	1	9	R + bone graft	-	78	30	NED		
2 / M / 34	1	Cuneiform	-	-	C + phenol + PMMA	-	0	-	-	-	24	-	NED		
3 / M / 35	1	MC1	-	-	C	Bone graft	1	8	C + PMMA	Surgical removal (PMMA remnants causing pain)	88	-	NED		
4 / M / 20	1	MT1	Yes	Yes (intra- articular)	C + phenol	Non-vascularised fibular graft + K-wires	2	6; 4	1) C + phenol + PMMA; 2) C + PMMA + non-vascularised fibular graft	-	94	30	NED		
5 / F / 23	1	MC2	-	-	C	Bone graft	4	20; 57; 127; 3	1) C + PMMA; 2) C + bone graft; - 3) C + bone graft; 4) C + high- speed burr + phenol + bone graft	-	267	28	NED		
6 / M / 40	1	MC2	Yes	-	C	Bone graft + K-wires	0	-	-	-	46	-	NED		
7 / M / 60	1	MC3	-	-	C + phenol	Bone graft	0	-	-	-	120	-	DOOD		
8 / F / 37	1	Talus	Yes	-	C + phenol	Bone graft	1	31	C + phenol + bone graft	-	102	28	NED		
9 / M / 20	1	MC3	Yes	-	C + PMMA	-	1	7	C + PMMA	-	117	30	NED		
10 / F / 15	1	Talus	-	-	C	Bone graft	0	-	-	-	24	-	NED		
11 / F / 13	1	MT1	-	-	C + phenol + PMMA††	-	0	-	-	-	28	28	NED		
12 / F / 22	1	MT3	-	-	C + phenol	Bone graft	1	15	C + phenol + bone graft	-	47	-	NED		
13 / F / 46	1	Ph3	-	Yes	C	-	1	14	C + phenol + bone graft	-	24	29	NED		
14 / M / 20	2	Cuboid	-	-	C + high-speed burr + phenol	Bone graft	0	-	-	-	63	30	NED		
15 / M / 24	2	Calcaneus	-	-	R (eb)	Bone graft	0	-	-	-	68	15	NED		
16 / F / 38	2	Scaphoid	-	-	R (eb)	Bone graft + screw fixa- tion	0	-	-	-	122	28	NED		
17 / F / 68	2	Calcaneus	-	-	C + phenol	Bone graft	0	-	-	-	128	30	NED		
18 / F / 22	2	MT4	-	-	R (eb)	Transposition of MT3	0	-	-	-	24	-	NED		
19 / F / 15	3	MT2	-	-	R (eb)	Non-vascularised fibular graft	0	-	-	-	105	29	NED		
20 / M / 25	3	Ph2	Yes	-	C	Bone graft	0	-	-	-	118	30	NED		
21 / M / 22	3	Talus	Yes	Yes (intra- articular)	C + high-speed burr + phenol	Bone graft	0	-	-	-	67	30	NED		
22 / M / 40	3	Talus	-	Yes	C + high-speed burr + phenol	Bone graft	0	-	-	-	24	20	NED		
23 / F / 22	4	MC1	-	Yes (intra- articular)	C + high-speed burr + liquid nitrogen	Bone graft	0	-	-	-	53	30	NED		
24 / M / 15	4	Talus	-	-	C + high-speed burr + liquid nitrogen	Bone graft	0	-	-	-	24	30	NED		
25 / M / 45	4	MC4	-	-	C + high-speed burr + liquid nitrogen + PMMA	-	0	-	-	-	30	30	NED		
26 / M / 15	4	Cuneiform	-	-	C + high-speed burr + liquid nitrogen	Bone graft	0	-	-	-	61	30	NED		
27 / M / 36	4	MC5	Yes	-	C + high-speed burr + liquid nitrogen	Bone graft	0	-	-	-	49	28	NED		
28 / F / 17	4	MT4	-	-	C + high-speed burr + liquid nitrogen	Bone graft	0	-	-	-	58	30	NED		
29 / M / 51	5	Scaphoid	-	-	R (eb)	Bone graft + K-wires	0	-	-	-	61	-	DOOD		
30 / M / 18	5	Calcaneus	-	-	C + phenol	Bone graft	0	-	-	-	32	30	NED		

\* 1, Leiden University Medical Center (Leiden, the Netherlands); 2, Centro Traumatologico Ortopedico AOU-Careggi (Florence, Italy); 3, Nuffield Orthopaedic Centre (Oxford, United Kingdom); 4, Radboud University Medical Center (Nijmegen, the Netherlands); 5, Centro Hospitalar do Porto – Hospital Santo Antonio (Porto, Portugal)

† MT, metatarsal; MC, metacarpal; Ph2/3, middle/distal phalanx

‡ R (m/eb), resection (marginal/en bloc); C, curettage; PMMA, polymethylmethacrylate; K-wire, Kirschner wire

§ including reconstruction

¶ MSTS, Musculoskeletal Tumor Society score

\*\* NED, no evidence of disease; DOOD, died from other disease

†† PMMA was replaced with a non-vascularised fibular graft five months after the index surgery, to allow for better function in the long term for this young patient

(Table II). The Kaplan-Meier five-year estimated recurrence-free survival was 50% (95% confidence interval (CI) 1.6 to 2.4) for curettage, 76% (95% CI 1.7 to 2.2) for curettage with adjuvants and 80% (95% CI 1.6 to 2.3) for resection (log rank test,  $p = 0.404$ ) (Fig. 3). The five-year estimated recurrence-free survival was 69% (95% CI 1.8 to 2.2) for all intra-lesional treatments and 80% (95% CI 1.6 to 2.3) for resection (log rank test,  $p = 0.661$ ). Surgical treatment of the first local recurrence consisted of repeated curettage with adjuvants (three with phenol and four with PMMA) and repeated resection (one). One patient, who had a total of four local recurrences, is currently free of disease at 26 years after repeated curettage procedures with variations of phenol, bone grafting and PMMA (Table II).

There was no statistical association between the use of different local adjuvants and the respective recurrence rate ( $p = 0.28$ ; chi-squared test) or the number of recurrences ( $p = 0.40$ ; chi-squared test). The same held true for

recurrence rate and type of intervention ( $p = 0.12$ ; chi-squared test), pathological fracture ( $p = 0.62$ ; Fisher's exact test) and soft-tissue extension ( $p = 0.31$  Fisher's exact test).

The only minor complication reported was pain caused by remnants of PMMA in one patient that resolved completely after surgical removal of the PMMA fragment. No other complications were reported in this series.

The mean MSTS for functional outcome at final follow-up was 25 (15 to 30) for the four patients who underwent resection and 29 (20 to 30) for the 18 treated by curettage with or without adjuvants ( $p = 0.091$ ; unpaired  $t$ -test) (Table II).

## Discussion

GCTs of the small bones are believed to behave more aggressively than GCT of the long bones<sup>27-29</sup>; high recurrence rates have been described after different types of surgery.<sup>6,8,17,21</sup>

Local recurrence rates from this study were comparable to those described in the literature: 50% *vs* 72% for curettage, 22% *vs* 13% for curettage with adjuvants and 17% *vs*

**Table III.** Overview of the literature on surgical treatment of giant cell tumour (GCT) of the small bones

Author/s	Patients/ Lesions (n)	Mean age (yrs) (range)	Mean follow-up (yrs) (range)	Site*	Primary treatment†	Reconstruction‡	Local recurrence		Complications§	Functional Metastasis outcome** (n, %)	
							n (%)	Mean time to recurrence (mths) (range)			
Picci et al <sup>22</sup>	52 (9) <sup>††</sup>	31.1 (SD 14.7)	2	MC (4), P (2), Cb (1), MT (1), Cc (1)	Amputation (2); Marginal resection (6); Curettage (1)		0	-	-	NR	NR
Sanjay et al <sup>19</sup>	7 (7)	24.6 (14 to 35)	10.9 (7 to 15)	MC (6), P (1)	Wide resection (7)	Internal fixation with K-wires (4); Bone graft (3); Index finger transposition (1)	1 <sup>‡‡</sup> (14)	3	Resection	NR	1 (14)
Athanasiou et al <sup>2</sup>	14 (13) <sup>§§</sup>	32.7 (11 to 54)	5.8 (1 to 39)	MC (7), P (5), S (1)	Wide resection (2)	-	1 (50)	17	Pending (lung metastasis)	1 gross intralesional contamination after resection	NR
					Amputation (1)	-	0	-	-		
					Curettage (8)	Bone graft (5)	7 (88)	6 (3 to 10)	<b>First (6):</b> Curettage (3, 1 with phenol); Resection (4, 1 with EBRT). <b>Second (6):</b> Curettage with phenol (1); Resection (5, 1 with EBRT)		2 (15)
Biscaglia et al <sup>6</sup>	29 (26) <sup>¶¶</sup>	27.4 (26 to 59)	6.75 (1 to 28)	T (9), MC (8), Cb (3), Cn (3), MT (3), N (2), Cc (1)	Resection (6)	-	1 (17)	5	Amputation	NR	0
					MC disarticulation (1)	Arthrodesis (1)	0	-	-		
					Curettage (11)	Bone graft (14)	7 (64)	15	Resection (3); Curettage with phenol (2); Curettage (1); Amputation (1)		
Patradul et al <sup>23</sup>	3 (3)	23 (18 to 31)	3	MC (2), P (1)	Curettage with phenol (8)	-	0	-	-		
					Resection (3)	Bone graft and osteosynthesis (K-wires) (3)	1 (33)	12	Marginal resection	NR	Satisfactory§§
Wittig et al <sup>9</sup>	3 (3)	23.7 (16 to 33)	4.5 (4 to 5)	P (2), MC (1)	Curettage with liquid nitrogen and PMMA (3)	Osteosynthesis (K-wires) (3)	0	-	-	1 minor wound necrosis	ROM and grip strength within normal limits
Kamath et al <sup>25</sup>	8 (3) <sup>§§</sup>	28.8 (13 to 47)	3 (3 to 15)	Cc (1), T (1), Cn (1)	2 curettage with burr and H <sub>2</sub> O <sub>2</sub>	Bone graft (2)	1 (50)	24	Curettage with PMMA	NR	NR
					1 amputation	-	0	-	-		
Ozalp et al <sup>21</sup>	5 (5)	41.6 (27 to 74)	7.8 (4 to 17)	MC (2), P (3)	4 curettage	Bone graft (2); Arthrodesis (1)	3 (75)	8 (2 to 18)	<b>First (3):</b> Wide resection (1); Marginal resection (1); Ray amputation (1). <b>Second (1):</b> Ray amputation	NR	0
					1 ray amputation	-	1 (100)	6	<b>First:</b> Soft-tissue resection. <b>Second:</b> Advanced amputation***		
Ropars et al <sup>17</sup>	4 (4)	40.5 (25 to 72)	3 (2 to 8)	P (3), MC (1)	3 amputation	-	0	-	-	NR	NR
					1 curettage	Bone graft (1)	1 (100)	4	<b>First:</b> Resection. <b>Second:</b> Resection		Limited ROM
Minhas et al <sup>7</sup>	19 (7) <sup>§§</sup>	24.3 (SD 5.7)	4.5	MC (4), P (3)	6 wide resection; 1 ray resection	Bone graft (6)	0	-	-	0	NR
Vergara et al <sup>24</sup>	3 (3)	27 (18 to 38)	NR	P (1), Carpal bone <sup>†††</sup> (1), MC (1)	3 resection	Bone graft (1); Bone elongation (2); MCP joint arthroplasty (1)	0	-	-	NR	Limited ROM
Ge et al <sup>18</sup>	8 (8)	28.5	3.8	MC (3), MT (4), P (1)	Wide resection (8)	Bone graft and osteosynthesis (8)	2 (25)	12 (11 to 14)	Wide resection (2)	NR	Excellent <sup>§§§</sup>
Current study	30 (30)	29.6 (13 to 68)	7.9 (2 to 26)	MC (8), MT (7), T (5), Cc (3), S (2), P (2), Cn (2), Cb (1)	Curettage (6)	Bone graft (5)	3 (50)	14 (8 to 20)	<b>First (3):</b> Curettage with phenol (1); Curettage with PMMA (2). <b>Second (1):</b> Curettage. <b>Third (1):</b> Curettage. <b>Fourth (1):</b> Curettage with phenol	Pain due to cement remnants after treatment of a recurrence (1)	0
					Curettage with adjuvants (18: 9 phenol, 2 phenol and PMMA, 1 PMMA, 5 liquid nitrogen, 1 liquid nitrogen and PMMA)	Bone graft (13); Non-vascularised fibula with K-wires (1)	4 (22)	15 (6 to 31)	<b>First (4):</b> Curettage with phenol (2); Curettage with PMMA (2). <b>Second (1):</b> Curettage with PMMA		See above
					Resection (6)	Bone graft (3: 1 with K-wires); Non-vascularised fibula (2); Transposition MT3 (1)	1 (16)	9	Resection		MSTS: mean 25 (15 to 30)

\* MC, metacarpal; P, phalanx; Cb, cuboid; MT, metatarsal; Cc, calcaneus; S, scaphoid; T, talus; Cn, cuneiform; N, navicular

† PMMA, polymethylmethacrylate; H<sub>2</sub>O<sub>2</sub>, hydrogen peroxide

‡ K-wire, Kirschner wire; MCP, metacarpophalangeal; MT3, third metatarsal § EBRT, external beam radiation therapy

¶ NR, not reported

\*\* ROM, range of movement; MSTS, Musculoskeletal Tumor Society score

†† the other patients had non-GCT lesions of the small bones of the hands and feet. Two of the nine GCTs were referred with local recurrence

‡‡ soft-tissue recurrence only §§ the other patients had GCT in sites other than the small bones of the hands and feet

¶¶ only 26 patients underwent surgical treatment; the remaining three were under observation

\*\*\* forearm amputation because of soft-tissue extension ††† not further specified §§§ not specified which method was used to assess functional outcome

15% for resection. The rate of recurrence of GCT of the small bones in the literature and in our group were at the higher end of the ranges reported in the literature for GCT of the long bones, which are 27% to 65% after

curettage,<sup>1,12</sup> 12% to 34% after curettage with adjuvants<sup>12,13,16</sup> and 0% to 12% after resection.<sup>12,14</sup> Risk factors for recurrence such as soft tissue extension were not more common (23%) than in those reported for long bones



Fig. 2a



Fig. 2b



Fig. 2c

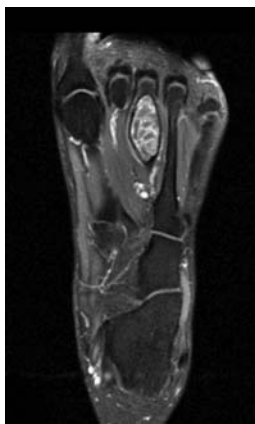


Fig. 2d



Fig. 2e



Fig. 2f

Imaging of a 22-year-old female patient (no. 12) with giant cell tumour of the third metatarsal bone of the right foot. Figure 2a and 2b – radiographs a) pre-operatively, showing an expanding lytic lesion without cortical disruption in the metaphysis of the third metatarsal bone and b) at three months after primary curettage with phenol and bone grafting. Figures 2c and 2d – radiograph (c) and T<sub>2</sub>-weighted MR scan (d) at one year post-operatively, showing signs of local recurrence with secondary aneurysmal bone cysts. Figures 2e and 2f – radiographs e) at three months after repeat curettage, phenol and bone grafting and f) at one year after treatment for local recurrence, showing complete incorporation of the graft. At a final follow-up of four years there are no signs of further recurrence or pulmonary metastasis.

(22% to 25%).<sup>15,30</sup> Complete removal of GCT of the small bones can be difficult for both intra-lesional and wide resections, which may be explained by the technically challenging anatomical locations, the difficulty of applying adequate local adjuvants due to anatomical restrictions, their very rare incidence, which is likely to result in the surgeon's relative lack of experience. The differences between the rates of recurrence with the various treatment options in our study were not statistically significant and our sample size was too small to detect differences after the use of various local adjuvants. The mean time to local recurrence in our series was also consistent with the literature about GCT of both long and small bones: only one patient had a first recurrence more than two years after surgery (Tables II and III).

*En bloc* resection and ray amputation have been advocated in technically challenging cases, as they are believed

to minimise the risk of recurrence.<sup>6,8,17,21,22,25,27</sup> However, similar recurrence rates have been reported for both resection (15%) and curettage with adjuvants (13%), indicating that resection is not necessarily better.<sup>18,23</sup> Wide resection may also be associated with reduced function of the affected hand or foot. Reconstruction of a defect is often required such as bone grafting, osteosynthesis or joint replacement, thereby increasing the duration of rehabilitation and the risk of late complications.<sup>18,23,24,31</sup>

In this multicentre series the recurrence rate after curettage with adjuvants (22%) was somewhat higher than the mean rate of recurrence reported in the literature (13%)<sup>6,8,9,25</sup> for GCT of the small bones but remained within the range reported after curettage with adjuvants for GCT of the long bones (12% to 34%).<sup>12-16</sup> Furthermore, in our study all first recurrences except one were successfully treated with repeated curettage and local adjuvants,

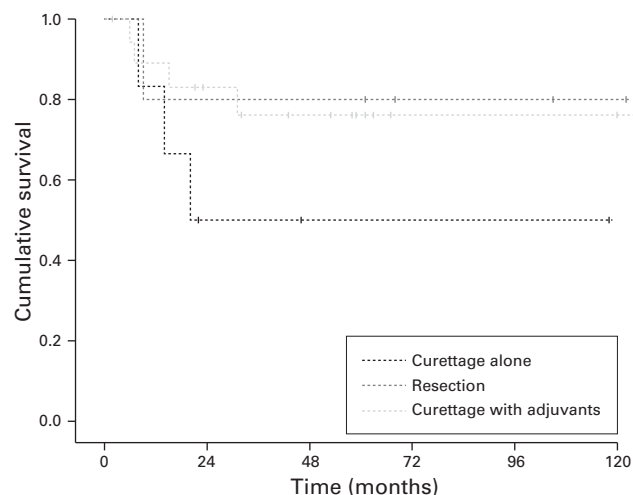


Fig. 3

Kaplan-Meier survival curve showing the estimated five-year recurrence-free survival after curettage (50% (95% confidence interval (CI) 1.6 to 2.4)), curettage with adjuvants (76% (95% confidence interval (CI) 1.7 to 2.2)) and resection (80% (95% confidence interval (CI) 1.6 to 2.3)) for giant cell tumour of the small bones (log rank,  $p = 0.160$ ).

thereby avoiding a more aggressive surgical approach. Finally, all patients were free of disease. This suggests that curettage with adjuvants can be a feasible treatment option for both primary and recurrent GCT of the small bones.

Neither the type of local adjuvant or surgical treatment nor the presence of a pathological fracture or soft-tissue extension was associated with a higher risk of recurrence. To our knowledge, such associations for GCT of the small bones have not previously been studied. In the literature, authors often referred to the potentially more aggressive behaviour of GCT of the small bones, which reflect the higher rates of multicentricity (7% to 18%)<sup>5,20</sup> compared with the rate of multicentricity in GCT of the long bones (approximately 1%).<sup>28</sup> Of all multicentric GCTs, up to 61% have been reported in the small bones of the hands and feet.<sup>28,29</sup> Interestingly, our study does not describe any patient with multicentric GCT and are unable to corroborate previous reports.

Only a few studies reported post-operative complications, which included a reduced range of movement and wound necrosis after curettage with adjuvants.<sup>8,9,31</sup> We encountered only one minor complication of pain after curettage with PMMA due to cement remnants.

The role of different local adjuvants should be considered, considering the complications they may cause. Phenol in high concentrations is toxic to soft tissues and some studies have questioned its efficacy,<sup>15,16</sup> whereas others reported no difference between phenol and other adjuvants.<sup>32,33</sup> The use of a high-speed burr allows the removal of tumour cells from the walls of the tumour cavity but also destroys healthy cancellous bone and carries the risk of dissemination of tumour.<sup>34</sup> Cryosurgery may result in thermal injury

to surrounding healthy soft tissues, bone or cartilage.<sup>35</sup> PMMA is used both as a local adjuvant and as filling material, which is believed to substantially reduce the risk of recurrence due to thermal necrosis and its direct toxic effect on tumour cells but without producing major complications.<sup>36</sup> However, it is not always necessary to fill the defect in a small bone. Nevertheless, to reduce the risk of recurrence we recommend the use of local adjuvants after curettage.

Few authors have described functional outcome after surgery for GCT of the small bones.<sup>9,18,23,24</sup> In two studies it was described as satisfactory or excellent but the method of assessment was not reported.<sup>18,23</sup> Three other studies reported a limited or normal range of movement after resection or curettage for GCT of the bones of the hand.<sup>9,17,24</sup> In this study we assessed functional outcome using the MSTs scoring system with the results being slightly better after intra-lesional surgery than after resection.

Our study has several limitations. First, it was retrospective and even recruiting from several centres, to obtain a larger group of patients, the sample size remained too small to comment with confidence on differences in the rates of recurrence after the use of various adjuvants. Second, the multicentre design implies that multiple treatment strategies have been applied, which may have resulted in selection and treatment bias.

In conclusion, we found the lowest rate of recurrence for resection, followed by curettage with adjuvants. Curettage alone was consistently associated with the highest rate of recurrence. We were unable to identify any factors that were associated with a higher risk of complication or recurrence. From the literature *en bloc* resection and ray amputation are associated with functional and aesthetic disability and are rarely indicated as a salvage procedure. Repeated curettage with adjuvants eventually resulted in the cure of all patients in our series. Therefore, curettage with adjuvants is a feasible treatment option for both primary and recurrent GCT of the small bones of the hands and feet.

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