Oncology

Does the addition of cement improve the rate of local recurrence after curettage of giant cell tumours in bone?

We retrospectively compared the outcome after the treatment of giant cell tumours of bone either with curettage alone or with adjuvant cementation. Between 1975 and 2008, 330 patients with a giant cell tumour were treated primarily by intralesional curettage, with 84 (25%) receiving adjuvant bone cement in the cavity. The local recurrence rate for curettage alone was 29.7% (73 of 246) compared with 14.3% (12 of 84) for curettage and cementation (p = 0.001). On multivariate analysis both the stage of disease and use of cement were independent significant factors associated with local recurrence. The use of cement was associated with a higher risk of the subsequent need for joint replacement. In patients without local recurrence, 18.1% (13 of 72) of those with cement needed a subsequent joint replacement compared to 2.3% (4 of 173) of those without cement (p = 0.001). In patients who developed local recurrence, 75.0% (9 of 12) of those with previous cementation required a joint replacement, compared with 45.2% (33 of 73) of those without cement (p = 0.044).

Intralesional curettage is a standard treatment for giant cell tumours (GCT) of long bones, with or without the use of polymethylmethacrylate (PMMA).1-5 Although wide excision with reconstruction of the joint leads to the lowest rates of recurrence, the long-term outcome is better if curettage is undertaken and the joint preserved.6-10 The rates of local recurrence and outcomes are similar for both treatment arms of curettage although some recent large studies have shown better local control after curettage with added PMMA.1,4,5 A randomised controlled trial of the two treatments has not been performed for ethical and logistical reasons.

The results from many centres which treat GCTs do not differentiate which patients receive adjuvant PMMA and conclusions cannot be made about its effect. We previously reported, in patients treated between 1970 and 1997, that Campanacci I and II11 GCTs could be treated with simple curettage, as the rate of local recurrence (7%) was very low.12 However, Campanacci III and recurrent lesions had significantly higher recurrence rates (29% and 34% respectively) when treated with curettage alone, which led us to consider that an adjuvant may be required for these patients.

Since 1997, we started to use adjuvant PMMA, primarily for Campanacci II and III lesions where the surgeon decided that curettage left the joint with insufficient bony support. Curettage without cementation was still undertaken when the surrounding cortex was considered to be sufficient.

The proponents of adjuvant cementation believe that filling the cavity with PMMA decreases the risk of local recurrence due to its thermal and toxic effects on tumour cells.1,4,5,13-15 Also, the cement gives immediate structural support, thereby allowing for more aggressive removal of tumour and early weightbearing.5,14 The disadvantages of PMMA include thermal damage to articular cartilage16 and increased stiffness of the subchondral bone leading to degenerative changes in the adjacent joint,17 although an increased risk of osteoarthritis with cementation following the treatment of GCTs has not been reported.

We undertook a retrospective study of our experience in treating GCT of bone by intralesional curettage, with or without adjuvant cementation and hypothesised that curettage with cementation would lead to lower rates of local recurrence than curettage alone.

Patients and Methods

We identified 470 patients from our database with a histological diagnosis of GCT treated between 1975 and 2008. Inclusion criteria included that the definitive curettage was done by our unit. Recurrent tumours treated elsewhere (n = 45) were excluded, as were those...
with extensive bone and soft-tissue involvement treated primarily with wide or marginal excision (n = 95). Medical records, plain radiographs, CT and MR scans were reviewed where available.

Of the remaining 330 patients (171 males and 159 females with a mean age of 32.5 years (13 to 73) treated primarily with intralesional curettage, 84 (25.5%) received adjuvant PMMA (Table I). The technique of curettage was as previously documented,12 using curettes, high-speed burrs, and a high-speed pulse lavage system when available. Since 1997, adjuvant cementation was used if the residual bone was deficient or there was an associated fracture. Bone graft was not used routinely to protect the articular cartilage from the cement as described by other authors.18 Post-operatively, patients treated with curettage alone were kept non-weight-bearing for as few as six weeks until radiographs confirmed consolidation of the cavity.12 Those treated with PMMA were allowed full weight-bearing immediately. The patients were followed-up with radiographs every three months for two years, then every six months for five years. If they requested to be seen at their local hospitals, the above plan was coordinated with the respective physicians, with instructions to refer back if indicated radiologically or clinically.

MRI studies were obtained if local recurrence was suspected. This was confirmed histologically at the time of any further surgery. Other complications, such as infection, fracture and degenerative joint disease, were recorded. Joint pain and radiological changes of arthritis were not considered complications unless they required treatment and were confirmed operatively.

### Statistical analysis
Univariate and multivariate analyses were used to determine which variables were associated with local recurrence. Kaplan-Meier survival analysis was undertaken to record recurrence-free survival and differences in joint survival between those patients who underwent curettage alone and those with added cementation. The log-rank test of equality of survivors was used to detect differences in survival between groups.

### Results
The mean follow-up of the 330 patients was 76.5 months (2 to 319). The Campanacci grade was I in nine patients, II in 181 and III in 140 (Table I). Pathological fractures were noted in 62 patients (18.8%) at the time of presentation.

Adjuvant cementation was used in 36 Campanacci II patients (20%) and 48 Campanacci III patients (34%). Almost half of the patients with pathological fractures received cementation (45%, n = 28).

There was local recurrence in 85 patients (25.8%) at a mean of 22 months (3 to 133). The local recurrence occurred in 90% of cases by 42 months and 95% by five years after the primary operation.

The local recurrence rate was 29.7% (73 of 246) for curettage alone and 14.3% (12 of 84) for curettage with cementation (p = 0.001) (Fig. 1). Analysis of Campanacci II and III patients revealed similar advantages of cementation over curettage alone (Stage II: 8.3% (31 of 145) for local recurrence with cement, 21.3% (3 of 36) without (p = 0.02); Stage III: 18.7% (9 of 48) with cement, 45.6% (42 of 92) without (p < 0.001, Fig. 2)). All Campanacci I patients were treated with curettage alone.

### Table I. Univariate and multivariate analysis of variables associated with local recurrence

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total (n = 330)</th>
<th>With cement</th>
<th>With local recurrence</th>
<th>Multivariate analysis p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (n, %)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>171 (51.8)</td>
<td>48 (28.1)</td>
<td>41 (24.0) (p = 0.4)</td>
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<tr>
<td>Female</td>
<td>159 (48.2)</td>
<td>36 (22.6)</td>
<td>44 (27.7)</td>
<td></td>
</tr>
<tr>
<td>Surgery (n, %)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Curettage</td>
<td>246 (74.5)</td>
<td>-</td>
<td>73 (29.7) (p = 0.004) 0.01</td>
<td></td>
</tr>
<tr>
<td>Curettage with cement</td>
<td>84 (25.5)</td>
<td>-</td>
<td>12 (14.3)</td>
<td></td>
</tr>
<tr>
<td>Site (n, %)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Distal femur</td>
<td>95 (28.8)</td>
<td>35 (36.8)</td>
<td>23 (24.2) (p = 0.15)</td>
<td></td>
</tr>
<tr>
<td>Proximal tibia</td>
<td>85 (25.6)</td>
<td>29 (34.1)</td>
<td>21 (24.7)</td>
<td></td>
</tr>
<tr>
<td>Proximal humerus</td>
<td>22 (6.7)</td>
<td>4 (18.2)</td>
<td>3 (13.6)</td>
<td></td>
</tr>
<tr>
<td>Distal tibia</td>
<td>28 (8.5)</td>
<td>4 (14.3)</td>
<td>4 (14.3)</td>
<td></td>
</tr>
<tr>
<td>Distal radius</td>
<td>28 (8.5)</td>
<td>9 (32.1)</td>
<td>9 (32.1)</td>
<td></td>
</tr>
<tr>
<td>Axial</td>
<td>30 (9.1)</td>
<td>3 (10.0)</td>
<td>13 (43.3)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>42 (12.7)</td>
<td>0 (0)</td>
<td>21 (28.5)</td>
<td></td>
</tr>
<tr>
<td>Campanacci grade (n, %)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>9 (2.7)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>II</td>
<td>181 (54.8)</td>
<td>36 (19.9)</td>
<td>34 (18.8) (p &lt; 0.0001)</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>140 (42.4)</td>
<td>48 (34.3)</td>
<td>51 (36.4)</td>
<td></td>
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<tr>
<td>Pathological fracture (n, %)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>62 (18.8)</td>
<td>28 (45.2)</td>
<td>18 (29.0) (p = 0.51)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>268 (81.2)</td>
<td>56 (20.9)</td>
<td>67 (25.0)</td>
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</tbody>
</table>
The site of the tumour was not a significant independent variable in predicting local recurrence although the distal tibia and proximal humerus had a lower incidence (14.3% and 13.6% respectively) than other sites, whereas axial involvement had a higher incidence (43.3%, Table I).

Complications other than local recurrence are shown in Table II. Ulnar abutment with secondary collapse of the distal radius was seen in three patients treated with curettage alone but not in the nine patients treated with adjuvant cement. Despite using cement, four patients had a postoperative fracture. Two were treated conservatively and two underwent reconstruction with an endoprosthesis because of intra-articular extension of the fracture and extensive bone loss. Two patients who had curettage alone developed a painful metaphyseal cavity. At operation, there was a fluid-filled space with no signs of local recurrence and cementation of the area relieved the pain in both cases.

Three patients treated with curettage alone subsequently developed osteoarthritis with much local bone loss; they underwent total knee replacement using revision components.

The use of cement was associated with a higher risk of subsequent joint replacement regardless of local control (Fig. 3). In patients without local recurrence, 18.1% (13 of 72) of those with cement needed a joint replacement, compared with 2.3% (4 of 173) of those without cement (p = 0.001). In patients who developed local recurrence, 75.0% (9 of 12) of those with previous cementation required a joint replacement, compared with 45.2% (33 of 73) of those without cement (p = 0.044). Multivariate analysis showed that curettage with cement and local recurrence were independently associated with joint salvage.

**Discussion**

Along with others, we found that curettage with adjuvant cementation was associated with a lower risk of local recurrence,1,4,5 in Grade II and III GCTs. An important difference in our protocol compared with other centres is that we continue to treat some Grade II and III tumours with curettage alone. The decision to use PMMA is made at operation and herein lies a limitation to our study, as this decision is left to the surgeon’s experience and has not been quantified. It could be argued that only larger tumours leaving a weak cavity after curettage were cemented. This may be a possible bias towards cement, as smaller lesions have been shown to be associated with higher local recurrence.19 However, this highlights the importance of a detailed curettage as the primary determinant of local control, and small lesions may be underestimated with a sub-optimal curettage being done. Suzuki et al20 found that in GCTs located within 5 mm of the articular surface, local recurrence was likely to occur at the articular side of the lesion. They correlated this with their less aggressive curettage, which avoided a burr and electrocautery, to lessen damage to cartilage.

The importance of our use of PMMA is that it allows the surgeon to do an aggressive curettage without compromising on thoroughness. This advantage of cement has also been noted by others.5,14 The disadvantage of using cement close to the articular surface is the risk of cartilage damage.
and early onset of joint degeneration. The biomechanical
deficiencies of using PMMA to replace subchondral bone
are recognised,17,21,22 with the resulting degeneration
mostly documented through animal studies or post-opera-
tive radiological changes.17,20,21 Szalay et al17 compared
GCTs treated with curettage and bone grafting or cement-
ing and found significant acceleration of degenerative
changes in the latter group. The degenerative changes were
based on radiological changes alone and functional knee
scores at medium-term follow-up showed no differences
between the groups.

We considered the need for subsequent joint replacement
as the determinant of degenerative changes. As local recur-
rence contributes to deterioration of the joint,19 we evaluated
the rate of joint replacement for those who did not have
local recurrence and found that patients treated with
cementation had a significantly higher rate of joint replace-
ment surgery (Fig. 3). In the 11 patients with cementation
who subsequently underwent knee replacement for osteo-
arthritis (Table II) cement had migrated through the articular
cartilage and was found within the joint. Whether these
patients with extensive joint involvement or cavities with
greater than 50% circumference would have been better
treated initially with an endoprosthesis is beyond the scope
of this study. The high rate of joint failure in our patients
who were treated with PMMA could also be explained by
the lack of support by internal fixation. Fraquet et al13 re-
commend routine osteosynthesis to support large cavities
filled with cement to prevent the remaining joint surface
from ‘rolling’ around the cement block and fracturing.13

Curettage alone was associated with higher rates of local
recurrence (30%) but this was comparable with those (18% to
51%) from other centres.1,2,4,5 The advantage of curettage
alone was the lower rate of joint replacement. We re-
ported earlier that with curettage alone, the empty cavity
gradually consolidates.12 In a more detailed study, Hirn
et al23 found that most cavities occupying < 60 cc filled
spontaneously but those > 60 cc did not do as well. In this
study, we identified patients (Table II) where, although new
bone formed around the cavity, its volume remained signif-
icient enough to cause structural weakness and symptoms
which were relieved with subsequent cementation. The fact
that joint replacements in these patients required revision
implants indicates the amount of bone loss still present after
ten years. Given this, structural fillers should still play a role
in the treatment of GCTs with large subchondral defects.

Bone allografts have been used as fillers2,24,25 but they do
not provide immediate stability and have inherent risks
of infection and graft failure. A layer of bone graft between
the cement and articular cartilage is an attractive solution but
has yet to gain popularity or show better results.18 Osteo-
conductive calcium phosphate bone graft substitutes can
provide support to articular cartilage and have the capacity
to be resorbed and replaced by host bone.26 However, the
quantities required to fill curetted GCT cavities (50 cc to
100 cc) are unlikely to be technologically or financially feasible.

Although adjuvant cement gives better local control rates
for curettage of GCTs of bone, it leads to an increased risk
for joint replacement, regardless of the control of the disease
and discussions with patients must take this into account.

No benefits in any form have been received or will be received from a com-
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Fig. 3a
Kaplan-Meier survival curves showing joint survival for patients with giant cell tumor by treatment (curettage versus curettage with cement) and
a) no local recurrence and b) local recurrence.
DOES THE ADDITION OF CEMENT IMPROVE THE RATE OF LOCAL RECURRENCE AFTER CURETTAGE OF GIANT CELL TUMOURS IN BONE?