Induced membrane technique for treating tibial defects gives mixed results

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Aims
This study describes the use of the Masquelet technique to treat segmental tibial bone loss in 12 patients.

Patients and Methods
This retrospective case series reviewed 12 patients treated between 2010 and 2015 to determine their clinical outcome. Patients were mostly male with a mean age of 36 years (16 to 62). The outcomes recorded included union, infection and amputation. The mean follow-up was 675 days (403 to 952).

Results
The mean tibial defect measured 5.8 cm (2 to 15) in length. Of the 12 patients, 11 had an open fracture. Eight underwent fixation with an intramedullary nail, three with plates and one with a Taylor Spatial Frame. The mean interval between stages was 57 days (35 to 89). Bony union was achieved in only five patients. Five patients experienced infective complications during treatment, with two requiring amputation because of severe infection.

Conclusion
The Masquelet technique was relatively ineffective in achieving union in this series, and was associated with a high rate of infection.

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Segmental bone defects are difficult to reconstruct. Bone grafting alone is associated with uncontrollable graft resorption, even when the recipient site is well vascularised. Historically, such defects have been associated with a high rate of amputation.

The most common methods of treating a segmental bone defect are either with the use of a vascularised fibular autograft or by bone transport using the Ilizarov technique. Although vascularised fibular autografts have distinct benefits and allow simultaneous soft-tissue coverage, problems are relatively common. These include infection and stress fracture, and can occur at both donor and recipient sites. The technique also requires specialist microsurgical expertise.

Bone transport and distraction osteogenesis were developed by Ilizarov in the 1950s, and are proven to be an effective method of salvaging a limb after severe injury. Nonetheless, bone transport can be a lengthy and challenging experience for the patient. Problems include pin site infection (up to 50%), loss of alignment, failure of bone consolidation, nonunion at the docking site (up to 44%) and a rate of revision surgery as high as 23.3%.

An alternative approach to the problem is the induced membrane technique, described by Masquelet in 1986. The first stage entails debridement of the defect, stabilisation of the limb and insertion of a polymethylmethacrylate (PMMA) cement spacer into the bony defect. This spacer has a mechanical role in preventing the ingrowth of fibrous tissue and a biological role in that it provides an environment which will support the subsequent bone graft.
Table I. Patient characteristics and operative details

<table>
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<tr>
<th>Patient (n)</th>
<th>Age</th>
<th>Gender</th>
<th>Smoker</th>
<th>Tibial defect location</th>
<th>Open injury</th>
<th>Initial debridement at Orthoplastic centre</th>
<th>Defect length (cm)</th>
<th>Mean interval to first stage (days)</th>
<th>Duration with spacer (days)</th>
<th>Fracture fixation used</th>
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<td>F</td>
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<td>Yes</td>
<td>Yes</td>
<td>3</td>
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<td>329</td>
<td>70</td>
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<td>Iliac crest</td>
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<td>16</td>
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<td>Yes</td>
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<td>4</td>
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<td>71</td>
<td>N/A*</td>
<td>IM nail</td>
<td>RIA</td>
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</tbody>
</table>

**Mean values**

- Defect length: 5.8 (2 to 15)
- Mean interval to first stage: 39.8 (3 to 329)
- Duration with spacer: 57 (35 to 89)
- Fracture fixation used: 8 IM nails/3 plates/1 TSF
- Source of bone graft: 6 iliac crest/2 distal femur/RIA

*gross infection evident at the time of re-presentation therefore the second stage impossible
†injury was initially closed but patient developed compartment syndrome requiring a fasciotomy
‡second stage attempted 49 days after the first stage, but deferred due to infection with definitive second stage surgery 40 days later
N/A, not available; IM, intramedullary; TSF, Taylor Spatial Frame; RIA, Reamer/Irrigator/Aspirator

Union rates of between 90% and 100% have been reported (see supplementary material), but significant complications can occur, including infection, amputation and fracture.15

Our unit offers a tertiary referral service for nonunion and limb reconstruction to a population in excess of two million: approximately thirty patients with nonunions are managed every year in conjunction with the on-site plastic surgery team.

In this retrospective cohort study we present the clinical course and outcome of 12 patients treated in our unit using the Masquelet technique for a segmental bone defect of the tibia.

**Patients and Methods**

We identified 12 patients from our database who had undergone limb reconstruction using the Masquelet technique between 2010 and 2015. All had received consultant-led care from fellowship-trained orthopaedic consultants.

Patient records and imaging were reviewed to determine the size and location of the defect, the nature of the initial injury; the interval elapsed between stages; the form of fixation; any diagnosis of infection or other complications; and whether the defect proceeded to union.

**Results**

Nine patients were male, with a mean age of 36 years (16 to 62). All injuries were initially open except for one in which a fasciotomy had been performed for compartment syndrome, secondary to a fracture of the tibial plateau. The mean size of tibial defect was 5.8 cm (2 to 15). Nine patients (eight male, one female) were treated within 30 days of injury. The fractures mostly involved the diaphysis (Table I).

The mean follow-up was 675 days (403 to 952), and was defined for the purposes of this study as the length of time that had elapsed between completion of the second surgical stage and discharge from the clinic. In the two patients still under follow-up, the time between second stage and most recent consultation was recorded (Table II).

The cement spacer used in all cases was PMMA (Palacos; Heraeus Kulzer GmbH, Hanau, Germany) (Fig. 1). Vancomycin was added in seven cases. Soft-tissue coverage was achieved at this stage with a local muscle flap (n = 5), a split thickness skin graft (n = 3), a free flap (n = 3) or primary closure (n = 1). The spacer was left in situ for a mean of 57 days (35 to 59).

In one case, the second stage was delayed due to a serous discharge arising from beneath the wound edge when surgery was attempted on day 49. After debridement, both metalwork and spacer were retained. Microbiology identified a coagulase-negative staphylococcus, and surgery was carried out successfully some 40 days later after a course of antibiotics.

Five patients developed infective complications (Table II), of whom two did not proceed to the second stage as they were lost to follow-up and had developed deep infection prior to re-presentation. They subsequently underwent transtibial amputation (Figures 2 and 3 illustrate one of these cases).

In five patients, bone morphogenetic protein (BMP-7) was used to augment the bone graft.

Bony union without any further intervention was achieved in five patients. Figures 4 and 5 demonstrate the radiological progression of the technique in a single patient.

Five patients went on to develop nonunion. At second stage surgery, the pseudomembrane was not to have formed in two patients by days 35 and 48. One patient, in whom the plate failed, continued to be symptomatic, hav-
having undergone revision to an intramedullary nail. One patient had an exchange nailing which included a period with a temporary antibiotic nail. A CT scan showed incomplete union but the patient declined further intervention. Two patients proceeded to union after exchange nailing, and another after debridement of infected bone, distraction osteogenesis with a circular frame and intramedullary nailing.

**Discussion**

Significant bone defects are rare: one study reported an incidence of 0.4% of all patients admitted to hospital with a fracture.\(^7,16\) Consequently, it is difficult to make a meaningful assessment of treatment options and outcomes: there are few robust clinical trials which address the problem.\(^7\) Although a multicentre, randomized controlled trial comparing the Masquelet technique with other approaches would be ideal, such a study would present many methodological problems due to the heterogeneity of the patient population and the low incidence of such injuries. To date, most studies that have evaluated the Masquelet technique are case series and report a very high rate of union (see supplementary material). Our case series, the largest so far from the United Kingdom, suggests a less predictable outcome with fewer than half of the patients achieving bony union without further surgery. This has been presaged by a recent Scandinavian study which commented on the unpredictable time taken to proceed to consolidation.\(^10\)

Infection is the most common major complication.\(^15\) In our series, it occurred in almost half our patients, two of whom went on to amputation as a result. The quality of the initial debridement of an open fracture is a key factor influencing infection, and hence of the outcome of the technique.

<table>
<thead>
<tr>
<th>Table II. Patient outcomes and follow-up</th>
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<tbody>
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<td>Patient (n)</td>
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</tr>
<tr>
<td>12</td>
</tr>
</tbody>
</table>

Mean values 675 (403 to 952) Union achieved in 5/12.

* gross infection evident at the time of re-presentation therefore the second stage impossible
† discharged from fracture clinic but being followed up by the Knee surgery team for an ACL injury which occurred during the initial injury
N/A, not available; BKA, below knee amputation; TSF, Taylor Spatial Frame

Fig. 1

Intra-operative photograph showing cement spacer being placed around an intramedullary nail for a mid-shaft tibial fracture with bone defect.
In our study, half the patients underwent initial debridement at a smaller district general hospital, possibly by surgeons less experienced in managing these complex injuries. While more infections were seen in this group, three of six patients treated elsewhere against two of six treated primarily in our centre, low sample sizes preclude any meaningful conclusion being drawn.

The use of antibiotics in the cement spacer remains contentious. Aparad et al suggest that they may mask the effect of an inadequate debridement by suppressing but not eradicating any resultant infection. In the only patient in our series with clear clinical signs of infection at second-stage surgery, the infection was recognised and managed appropriately. It is not clear whether the two patients in whom deep infection was established would have had a recognisable infection at second-stage surgery, as they had failed to comply with follow-up at this point.

The optimum composition of the cement spacer is a further area of uncertainty. One recent animal study demonstrated that both the type and antibiotic content of the cement influenced the thickness and elasticity of the pseudomembrane in a rat model. This is an area where further research would help.11

The timing of the second stage of surgery may also influence outcome. Traditionally, the interval between the first and second stages has been six to eight weeks but a recent study has shown that the osteogenic potential of the pseudomembrane decreases markedly with time. Levels of VEGF, interleukin-6 (IL-6) and collagen I (Col-1) peaked at one month but had dropped to half by two months post-operatively, suggesting that delay could be detrimental. In our small series, we saw no statistical relationship between timing and outcome.

We used bone graft from a number of sites in these patients. Cancellous autologous bone graft has been described as the benchmark but its use is limited in the treatment of very large defects. The Reamer/Irrigator/Aspirator (or RIA) system permits the collection of large volumes of bone graft from the medullary canal of the
femur. It has been shown to contain higher levels of key growth factors and osteogenic elements than iliac crest graft.\textsuperscript{10,15} It may also entail less donor site pain than iliac bone graft, but does risk fracture of the donor site.\textsuperscript{20,23,24} While the original technique used external fixation to confer stability, both plates and nails have subsequently been shown to be safe and effective.\textsuperscript{25} Nailing may allow earlier weight-bearing and negates the risk of pin-track infection.\textsuperscript{7} The presence of the nail in the defect also reduces the volume of graft needed to fill it, but affords a high surface area for the formation of a biofilm.\textsuperscript{10,15}

The degree of stability conferred by the implant must also be considered: very rigid fixation risks stress shielding which may reduce bone graft integration.\textsuperscript{4} Conversely, micromotion may result in a weak and poorly vascularized pseudomembrane, which is potentially detrimental.\textsuperscript{19}

The largest case series to have reported results of the technique achieved a 90% rate of union in 54 patients at one year. The authors advised that weight-bearing was delayed until union had been achieved at a mean of 17.4 months.\textsuperscript{2} This prolonged period of restricted weight-bearing may result in other complications such as muscle wasting and contractures, risking a poorer overall recovery. One limitation of our study was the difficulty in making an accurate assessment of the time at which patients began fully weight-bearing from medical records.

The key strengths of this study include a homogeneous population of adults with a single fracture who all underwent definitive reconstruction in a single centre. Variables that could influence outcome, such as smoking, method of fixation and the source of bone graft have been recorded. The long follow-up has allowed us to identify patients who experienced late problems.

Limitations include its retrospective nature, the relatively small cohort and the heterogeneity of injury sub-type. We experienced some unwillingness to engage in the process. The loss to follow-up, coupled with limb loss, is a key example of the importance of patient selection.\textsuperscript{11}

It is not possible from this study to explore the effect of initial debridement elsewhere on outcome. Other studies on the management of open tibial fractures, including those from our unit, have shown that patients who undergo initial surgery in a smaller unit have an increased rate of complications and a greater need for revision surgery.\textsuperscript{24,27} This trend may be replicated by patients undergoing the Masquelet technique, although the numbers in this study are too small to determine this definitively.

It is essential that patients transferred from peripheral hospitals are re-staged at the definitive treatment centre. The team undertaking definitive management should start with a meticulous assessment of the quality of initial debridement, and be confident that there is no residual infection before proceeding with the Masquelet technique.

It is important that surgeons do not consider reconstructive options to be mutually exclusive: one advantage of the Masquelet technique is that it does not preclude other techniques should it fail.\textsuperscript{1,22}

**Take home message:**
- This paper shows that the Masquelet technique produced poor results in this patient cohort in terms of union rates and infections when compared with previous studies.
- A higher rate of nonunion was seen following the Masquelet technique in smokers (five of seven patients) than non-smokers (two of five patients).
- Two patients required amputation.

**Supplementary material**

A table showing previous studies of induced membrane technique can be found alongside the online version of this article at www.bjoline.org.uk

**Author contributions:**
R. Morris: Collected and analysed data for the study, Completed writing up, Coordinated the editing of the paper with co-authors, Submitted the final version, Corresponding author for the study.
M. Hossain: Collected and analysed data for the study, Contributed to editing of manuscript, figures and tables.
A. Evans: Contributed to editing and revising parts of the paper following initial drafts, prior to final submission.
I. Pallister: Contributed to editing and revising parts of the paper following initial drafts, prior to final submission.

No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article.

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**References**