



Original article

Very long-term results of post-traumatic bone defect reconstruction by the induced membrane technique

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ABSTRACT

Introduction: The induced membrane technique for bone defect reconstruction is now well recognized, and short-term results for bone healing are consistent between published reports.

Objectives: To assess very long-term functional results in post-traumatic reconstruction using the induced membrane technique.

Method: Results for 18 patients undergoing bone defect reconstruction by induced membrane were retrospectively analyzed at 10 to 22 years' follow-up. Initial lesions were multitissue with infection in 14 cases. Reconstruction concerned the tibia in 14 cases, and the humerus, elbow, radius or ulna in 1 case each. Soft-tissue reconstruction was performed in 17 cases, by free flap ($n=8$) or pedicle flap ($n=9$). Fixation used a single-plane external fixator in 15 cases, screwed plate in 1 case (humerus), or intramedullary nail in 1 case (ulna). There was 1 crossover from external fixator to internal plate fixation (radius). Assessment comprised radiology, functional assessment, clinical examination and patient satisfaction. All patients were followed up in individual consultation.

Results: Eight of the 14 patients with lower limb lesions had unrestricted walking distance; 4 resumed leisure sports. Limb shortening ranged from 0.5 to 4 cm and was well-tolerated, although dorsiflexion was abolished or limited in most cases. Several patients underwent second procedures to improve limb function: ankle fusion, Achilles lengthening, tendon transfer, or realignment osteotomy. Radiology found a neotubular aspect, indicating peripheral densification and central resorption. Despite the multiple procedures, no patients regretted the original limb-conserving surgery. All reported that it took 2 to 3 years after consolidation and resumption of walking to achieve stable final functional improvement. No recurrent sepsis in the reconstruction zone was found.

Conclusion: The present results encourage implementing limb-conserving strategies in young patients after severe multitissue limb trauma, on condition that lesions are properly assessed, notably in terms of infection, and that the reconstruction protocol is feasible and has the patient's consent.

Level of evidence: IV, retrospective series.

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1. Introduction

The induced membrane technique for long bone defect reconstruction was first described in 2000 in a 35-case series [1]. Since 2005, many further French and English-language reports have confirmed its clinical validity [2–8]. The aim of the present study was to assess functional and radiological results in patients undergoing bone defect reconstruction by induced membrane, at more than 10 years' consolidation.

2. Material and method

Trauma patients operated on by a single surgeon were seen again with a minimum 10 years' follow-up after shaft reconstruction (Table 1). Exclusion criteria comprised tumoral and non-traumatic infectious etiology. Only patients physically present at the study consultation were included, and were examined by an investigator other than the original surgeon in 4 specific consultations during the month of June 2012.

Assessment comprised:

- radiologic assessment, with plain X-ray and long-leg full weight-bearing X-ray;

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Table 1
Case data.

Case Gender Initial	Age at accident	Date of accident and etiology	Date: treatment; reconstruc- tion; consolidation	Segment and bone defect	Type of fixation	Soft-tissue repair	Secondary surgery	Present occupation	Walking (sports)	Knee RoM	Ankle RoM	Upper limb RoM	MWB	LLD	Residual deformity	Equipment	Pain	Satisfaction
1 M (B.)	24	Sept 1988: OF L tibia Grade 3 Road accident	May 1989 S Dec 1989 July 1990	L tibia 10 cm	External fixator	LD free flap with DVG	0	Butcher	Unrestricted	0–130°	Ankylosis at 90°		Yes	4 cm	No	Insole	No	+++
2 M (D.)	48	Oct. 1989 OF R tibia Grade 2 Road accident	March 1990 S June 1990 Jan. 1991	R tibia	External fixator	Soleus pedicle flap	TKA	Retired	Unrestricted	0–140°	PF 40° DF 0°		Yes	0.5 cm	No	No	No	++
3 F (E.)	29	Aug 1993 OF L tibia Grade 3 Road accident	Sept 1993 S Feb 1994 Aug 1994	L tibia 18 cm	External fixator	LD free flap with DVG	Ankle fusion after forefoot amputa- tion	Sales director	Unrestricted	0–130°	0		Yes	1 cm	No	Forefoot prosthesis	NO	++
4 M (F.)	32	Sept. 1993 OF L tibia Grade 3 Road accident	Oct 1993 S April 1994 Jan. 1995	L tibia 21 cm	External fixator	LD free flap with DVG	Prx tibial osteotomy for varus	Air pilot	Unrestricted	0–130°	PF 20° DF 0°		Yes	2 cm	No	No	No	+++
5 M (C.)	23	March 2000 CF L tibia Road accident	May 2000 S Aug 2000 May 2001	L tibia 6 cm	External fixator	Medial gastrocne- mius pedicle flap	Osteotomy for valg recurv	Market stallholder	Unrestricted	0–100°	10° fixed equinus		No	4 cm	Recurvatum	1 crutch for long distances	No	+
6 M (C.)	20	Feb 1992 CF L tibia Road accident	March 1992 S Aug 1992 Jan. 1993	L tibia 15 cm	External fixator	Soleus pedicle flap	0	Wine merchant (<i>négociant en vins</i>)	Unrestricted	0–130°	Squash		Yes	2 cm	No	No	No	+++
7 F (C.)	28	June 1993 OF R tibia Grade 3, + tibial plateaux Road accident	June 1993 Oct. 1993 Aug 1995	R tibia 15 cm	External fixator	Medial gastrocne- mius pedicle flap + fascio- cutaneous flap	Transfer for drop-foot	Secretary	Restricted	0–120°	PF 30° DF 0°		Yes	2 cm	Valgus	0	Weather- dependent	++
8 M (D.)	35	May 1996 OF L tibia Grade 3 Road accident	June 1996 S Oct. 1996 Aug 1997	L tibia 25 cm	External fixator	LD free flap	Distal tibial valgization osteotomy for varus	Driver	Restricted	0–130°	PF 20° DF 0°		Yes	4 cm	Residual varus	Insole + heel	No	+++
9 M (L.)	26	April 1994 CF R tibia Road accident	Jan 1995 S May 1995 March 1996	R tibia 10 cm	External fixator	Associated medial gastrocne- mius and soleus flaps	Prox valgization osteotomy, Achilles lengthen- ing	Carpet layer	Unrestricted	0–120°	PF 20° DF 0°		Yes	2 cm	No	No	No	+++
10 M (O.)	19	March 1997 OF R tibia Grade 2 Road accident	Aug 1997 S Dec. 1997 April 1998	R tibia 6 cm	External fixator	Soleus pedicle flap	0	Bank clerk	Unrestricted	0–130°	PF 20° DF–5°		Yes	1 cm	No	Compensatio- by equinus	No	++
11 M (B.)	50	Jan. 1998 OF R tibia Grade 3 and tibial plateau Road accident	Feb 1998 S July 1998 Feb. 1999	R tibia 15 cm	External fixator	LD free flap with DVG	Achilles lengthen- ing	Retired Bee-keeper	Restricted	0–25°	15° equinus		No	1 cm	Knee joint malunion	Crutch for journeys	Occasional	+++

Table 1 (Continued)

Case Gender Initial	Age at accident	Date of accident and etiology	Date: treatment; reconstruction; consolidation	Segment and bone defect	Type of fixation	Soft-tissue repair	Secondary surgery	Present occupation	Walking (sports)	Knee RoM	Ankle RoM	Upper limb RoM	MWB	LLD	Residual deformity	Equipment	Pain	Satisfaction
12 F (N.)	26	Sept. 2001 OF L tibia Grade 3	Sept. 2001 Jan. 2002 Sept. 2002	L tibia 15 cm	External fixator	LD free flap	0	Bus driver	Limp on fast walking	0–90°	PF 30° DF 5°		Yes	0	Varus 8° Knee osteoarthritis	No	Occasional	+++
13 M (B.)	26	July 1999 OF R tibia Grade 2 Road accident consolidated	Feb 2003 S (iterative fracture) May 2003 Jan. 2004	R tibia 8 cm	External fixator	Soleus pedicle flap	Complementary inter-tibiofibular graft	Warehouse driver	Restricted 1 h	0–130°	PF 20° DF 5°		Yes	4 cm	No	2 cm insole	Weather-dependent	++
14 F (S.)	53	May 2001 OF L tibia Grade 3 Boat accident	Sept. 2001 Nov. 2001 June 2002	L tibia 12 cm	External fixator	LD free flap	0	None	Restricted 30 min	0–110°	PF 20° DF 5°		Yes	2 cm	No	No	Weather-dependent	++
15 F (L.)	40	May 2001 OF L arm Grade 2 Road accident	Oct. 2001 Dec 2001 April 2002	Humerus 6 cm	Screw plate	0	0	Clothing merchant				Elbow: 0–10–130					No	+++
16 M (D.)	20	Sept. 1998 OF L forearm Grade 2 Farm accident	Oct 1998 S April 1999 July 1999	L ulna 5 cm	Plate on radius	Atypical posterior interosseous flap	Tendon transfer for finger and wrist extensor restoration	Legal expert				Elbow: 0–130° Wrist: PF 30°/DF 0° P10°/S15°					No	++
17 M (V.)	65	May 1995 OF R elbow Grade 2 Fall	Sept 1996 S Jan. 1997 (reconstruction arthrodesis) May 1998	Humerus 3 cm	External fixator	LD pedicle flap	Radial head resection	Retired				Elbow: fixed at 90° P: 70°/S: 45°					No	+++
18 M (M.)	42	Oct. 1993 OF L forearm ballistic	Nov 1993 S March 1994 Sept. 1994	L radius 10 cm	External fixator then screw plate	Serratus free flap	Extensor carpi graft; FCU transfer for finbger extension	War correspondent				Elbow: 0/15/130° Wrist: PF 20°, DF 5° PS: 0					No	+

RoM: range of motion; MWB: monopodal weight-bearing; LLD: limb-length discrepancy; OF: open fracture; CF: closed fracture; S: septic; BD: bone defect; LD: latissimus dorsi; FCU: flexor carpi ulnaris; TKA: total knee arthroplasty; DVG: double vein graft; PF: plantar flexion; DF: dorsiflexion; P: pronation; S: supination; PS: pronation-supination.

- functional assessment:
 - walking distance,
 - sports activity (if any),
 - use of equipment or device to compensate for limb shortening,
 - ≥ 5 seconds' monopodal weight-bearing test,
 - under- and over-lying joint range of motion,
 - pain and occupational status,
 - patient satisfaction (dissatisfied = 0, moderately satisfied = +satisfied = ++, very satisfied = +++) and opinion in hindsight of the original limb-sparing strategy as compared to possible amputation.

3. Results

The series comprised 18 patients, 15 of whom had been among the 35 patients for whom short-term results were reported in 2000 [1]. M/F sex ratio was 12/6. Mean age at trauma was 33 years (range, 19–65 years). Fourteen cases involved road accidents. Fourteen cases involved infected fracture or septic nonunion. The reconstructed segment was the tibia in 14 cases, and the humerus, elbow (fusion), radius or ulna in 1 case each. Soft-tissue flap reconstruction following extensive wound care was required in 17 of the 18 cases. Fixation used an external fixator kept in place until consolidation was achieved in 15 cases, screwed plate for 1 case of aseptic humeral defect, and intramedullary nail for 1 case of ulnar defect. There was a single crossover from external fixator to screwed plate in a case of radial defect.

3.1. In the lower limb

In the lower limb (14 tibias), mean defect size was 13 cm (range: 6–25 cm), exceeding 15 cm in 7 cases.

Two patients (No. 7 and No. 12) were managed in emergency. In the other 12 cases, trauma-to-surgery (induced membrane) interval ranged from 1 to 9 months, for a mean 3.5 months. Intervals between steps 1 and 2 ranged from 2 to 7 months, for a mean 4 months. Radiologic consolidation time was 4 months, but time to total non-protected weight bearing ranged from 4 to 10 months, for a mean 7.7 months after reconstruction grafting.

Secondary procedures comprised: 1 total knee replacement, 1 talocrural fusion, 3 tibial realignment osteotomies, 1 tendon transfer, and 2 Achilles lengthenings.

3.2. In the upper limb

In the upper limb, mean defect size was 6 cm (range: 3–10 cm). Trauma-to-surgery interval ranged from 1 to 16 months, for a mean 6 months. Intervals between steps 1 and 2 ranged from 2 to 6 months, for a mean 4 months. Radiologic consolidation time ranged from 3 to 6 months, for a mean 4 months.

Two of the 4 patients underwent secondary surgery: tendon transfer for finger and wrist extensor restoration.

3.3. Functional assessment (June 2012)

Mean follow-up at assessment was almost 15 years (range: 10–22 years).

3.4. Lower limb assessment

Walking and sports:

- 8 patients had unrestricted walking distance;
- 5 patients could not walk for more than 1 hour without a break;
- 1 patient limped when walking fast;

- 2 patients had resumed leisure sports: squash and soccer, respectively; two others were regular swimmers.

Range of motion:

- knee range of motion was normal or subnormal for 12 of the 14 patients; it was limited to 25° for 1 patient with epiphyseal-metaphyseal-diaphyseal proximal tibial fracture requiring diaphyseal reconstruction; it was limited to 90° for 1 patient with tibial reconstruction underlying a femoral fracture.

The ankle showed perpendicular ankylosis or fusion in 2 patients, and moderate equinus fixation in 2 others. The other patients showed no or $< 5^\circ$ dorsiflexion.

Monopodal weight bearing was possible for 11 patients, possible with orthosis for 1 (with forefoot amputation), and impossible for 2 patients due to fixed equinus.

Shortening ranged from 0.4 to 4 cm. Shortening of 3–4 cm was systematically managed by a heel and/or insole incorporated in the footwear. One patient (No. 8) showed clinically asymptomatic severe persistent 8° varus malalignment.

Four patients with restricted walking distance reported occasional pain on effort or depending on the weather.

There were no cases of septic recurrence along the reconstructed shaft. Two patients underwent revision surgery for chronic infection of an external fixator pin orifice.

Radiology of the reconstructed segment showed a tubular aspect, with peripheral densification and central resorption, restoring long bone morphology (Fig. 1). This tubular aspect was found at least 2 years after resumption of weight bearing.

3.5. Upper limb assessment

In the upper limb, the 2 patients with reconstruction of 1 of the 2 forearm long bones showed limited wrist motion due to the severity of the initial trauma and the secondary tendon transfers (Fig. 2). The radiological aspect of the reconstruction had not progressed toward a tubular morphology (Fig. 3).

3.6. Patient satisfaction and outcome

Nine patients were very satisfied, 6 satisfied, and 3 moderately satisfied. None of the lower limb patients regretted the limb-conserving strategy, despite treatment duration and multiple surgery. All reported that it took 2 to 3 years after resumption of complete weight bearing for sequelae to resolve and function to improve adequately – to the point where the limb was “forgotten” for 4 patients.

All patients returned to work, at various intervals. Some returned to their previous job, despite its hardship (No. 1 and No. 9) or high demands (No. 5, who regained his professional air pilot's license).

4. Discussion

It may be supposed that the patients who responded to our invitation for assessment were those with the best results in terms of function and resumption of activities, inducing a bias. The cases of failure in the initial series [1], which included 14 of the present patients, had all been managed using techniques other than induced membrane. The aim of the present study was to assess very long-term functional outcome in limb segment reconstruction by the induced membrane technique. Review of files [already reviewed previously for the 2010 symposium of the French Society of Orthopedic Surgery and Traumatology (SoFCOT)]



Fig. 1. Case No. 6. Infected open tibial fracture, treated by emergency nailing. Wound care left a 15 cm defect. a: induced membrane technique step 1, associating external fixation, cement spacer and soft-tissue reconstruction by soleus muscle flap. b: radiologic bone healing 1 year after grafting. c: radiologic aspect at 19 years' follow-up: peripheral densification and central resorption in the reconstructed segment. d: good functional outcome: the patient plays squash.

and examination of the patients further answered a number of questions in the light of current advances in the technique.

1. Intervals between trauma and reconstruction were particularly long in the present series; this was because referral of 16 of the 18 patients was late, at the stage of infection or septic nonunion, after multiple surgeries elsewhere. We did not attempt to count the total number of procedures per patient between emergency care and final consolidation. The intervals between the 2 operative steps were also very long, due to iterative wound care and soft-tissue healing time. Recovery of soft-tissue flexibility, especially as regards muscle flaps, is a prerequisite for step 2. There were a remarkable number ($n=8$) of microsurgical free flaps, partly due to the “microsurgery vogue” of the 1980s and 1990s, and partly to the limited availability of locoregional solutions. Such microsurgical tissue transfer has nowadays

become a thing of the past, thanks to lower severity of multitissue lesions, better emergency treatment of open fractures with the spread of the “orthopedic damage control” attitude, earlier referral to specialist centers, and technical progress in pedicle flap surgery.

The interval between the two operative steps actually turned out not to be as important as is often claimed [9]. The discovery of stem cells within the membrane [10–12] makes the previous recommended interval of 4–6 weeks less critical [13].

Time to lower limb weight bearing was in line with the initial study and subsequent reports in the international literature [2,3,5,8]. The mean wait-time of 7–8 months after graft reconstruction refers to the possibility of resuming complete weight bearing without protection. A radiologic aspect of bone healing, regardless of defect size, is achieved in around 4 months, as in the upper limb;



Fig. 2. Case No. 15. Infected open humeral fracture with multiple procedures. a: radiologic aspect prior to induced membrane technique; 6 cm defect after wound care. b: radiologic aspect at 10 years' follow-up; slight peripheral densification and persistent central bone density.

however, the stress inherent to full lower limb weight bearing led us to be cautious and to advise only gradual resumption.

2. What kind of cement should be used for the temporary spacer? Despite recent advances combining internal fixation material and antibiotic-loaded cement [14,15], we still use a cement spacer without antibiotics: antibiotic-loaded cement could mask insufficient debridement and resection of bone and/or soft-tissue. Recurrence of infection after step 1 of the induced membrane technique is always due to insufficient resection. Complete definitive control of infection is a prerequisite for continuing with graft reconstruction.

A recent study [16] showed that the antibiotics included in the cement affect the physical properties of the membrane, although it was not specified whether this impaired osteogenesis. It is likely that spacer component properties impact membrane properties [17].

3. Long-term radiologic progression concerns the lower limb segments subject to axial compression forces. In hindsight, this

justifies the use of intramedullary nails, previously thought to reduce useful graft volume. Given the gradual loss of mechanical properties in the central part of the graft, in step 2, if the limb is not stabilized by a nail, a spacer may be useful in the graft center, reducing the volume of bone harvesting [18].

4. Regarding primary stabilization and maintenance procedures to enhance range of motion, a large majority of patients wore an external fixator until end of treatment. The advantage of intramedullary nailing is that weight-bearing can be resumed at 4 months, at radiologic consolidation [19]. Immediate nailing, however, incurs a risk of recurrence of sepsis; an approach worth exploring is to cross over from external to internal fixation in step 2, as in the present case of radial reconstruction (No. 18).

The rate of secondary lower limb osteotomy reveals the difficulty of maintaining good alignment with a single-plane fixator. This is in fact mainly a matter of lack of vigilance in maintaining the lower limb axis. In severe defect (>20 cm), a circular or hybrid external fixator is preferable to a single-plane model;



Fig. 3. Case No. 8. Infected open tibial fracture. Iterative wound care left 25 cm defect. a: cement filling and soft-tissue repair by latissimus dorsi flap. Single-plane external fixation clearly insufficient, with gradual leftward drift of the apparatus leading to consolidation in varus, whereas primary alignment had been satisfactory. Partial correction osteotomy by resection of a lateral corner of the distal metaphysis was performed after consolidation. b: at 15 years' follow-up, good peripheral corticalization of the reconstruction, but insufficient axial correction. The patient was asymptomatic. 4 cm limb-length discrepancy, managed by insole and heel.

intramedullary nailing is not effective here either, due to the degree of stress exerted entirely on the locking screws.

Ankle function results were relatively poor (Table 1). Apart from fixed equinus in cases 12 and 13 and ankle stiffness in case 1, most patients lacked talocrural dorsiflexion. Systematic intertibiobial grafting may be blamed for this, but it is in fact more a question of failure to prevent ankle stiffness due to prolonged immobilization. We now recommend daily unscrewing of the part of the fixator that immobilizes the foot.

The need for secondary procedures should not be underestimated, but these are not completely unavoidable, given the source of progress provided by follow-up studies.

5. The final question regards the criteria for implementing bone reconstruction, and thus limb conservation. This particularly concerns the tibia, and the alternative of amputation. The relevant

parameters are the extent of soft-tissue lesions, the severity of infection, foot status and the patient's subjective context (motivation, active participation, smoking cessation, etc.). We did not use any quantitative scores, deeming each case to be individual. The key points are control of infection and the success of soft-tissue repair.

5. Conclusion

The lessons to be drawn from the present study confirm the guidelines set out in the 2010 SoFCOT Symposium on the subject:

- the tibial segment is the most at risk in traumatology, due to frequent multitissue lesions. Emergency management of open

fracture is therefore essential, and should adopt an “orthopedic damage control” strategy;

- in case of complications, and notably infection, early radical debridement with extensive wound care, to dry out the infection, is a prerequisite for bone reconstruction;
- bone defect size is not in itself a prognostic factor. Prognosis in the lower limb depends rather on foot quality, infection and soft-tissue lesions;
- apart from debridement and wound care, the key to reconstruction lies in repairing the soft-tissue envelope, at least for the induced membrane technique;
- in the lower limb, special attention should be paid to alignment, external fixator stability and care of all foot and ankle joints;
- given the above, the present very long-term results, despite the retrospective study design and considerable loss to follow-up, encourage long bone reconstruction in complex situations of multitissue defect; functional outcome can safely be expected to be satisfactory, on condition that lesions are properly assessed, the reconstruction protocol is feasible, and the patient fully adheres to the strategy.

Disclosure of interest

The authors declare that they have no competing interest.

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Author contributions

A.C. Masquelet: surgery.
T. Kishi: file review.
P.E. Benko: patient follow-up.

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