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Original article

# Induced membrane technique in the treatment of infectious bone defect: A clinical analysis

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INFO ARTICLE

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ABSTRACT

*Background.* – At present, it is still a challenge for repairing a wide range of bone defect caused by various reasons. We aimed to investigate the effect of induced membrane technique in the treatment of infectious bone defect.
*Patients and methods.* – The clinical data of twenty-one patients with infectious bone defect that received induced membrane technique treatment from January 2008 to August 2017 were collected for this study. The complications were recorded, and the bone defect healing and the recovery of joint function were evaluated by Paley method. The adjacent joint activities were also evaluated.
*Results.* – One month after the first stage of surgery, one case had wound dehiscence, and others healed well without infection. Six cases had induced membrane injury during the second stage of surgery, and 4 of them received induced membrane wrapping reconstruction. At the last follow-up, bone defect healing was excellent, the joint function was restored (the rate of excellent and good was 90.5%). The joint range of motion recovered well and the rate of excellent and good was 81.0%.
*Conclusion.* – Induction membrane technique in the treatment of infectious bone defect has advantages of simple operation, rapid healing of bone defects, and low recurrence rate of infection.


## 1. Introduction

The reconstruction of segmental bone defects is one of the most common problems in clinical practice, which is mainly caused by trauma, infection, tumor and other factors [1–3]. At present, it is still a challenge for repairing a wide range of bone defect caused by various reasons. The current treatment methods are including Ilizarov technology, vascularized bone transplantation, massive allograft transplantation, and tissue engineering techniques [4,5].

In 2000, Masquelet et al. [6] used polymethyl methacrylate (PMMA) bone cement combined with autologous cancellous bone transplantation method to repair bone defect of limbs. This new technique is called induced membrane technique (Masquelet technique). The above approach is divided into two stages: debridement of the lesion site and implantation of PMMA bone cement to induce membrane was the first step, then removing bone cement and embedding cancellous bone in induced membrane at 6–8 week. The success rate of this technique in repairing bone defect was 88–100%, which could repair for 25 cm bone defect [7,8]. Currently, induced membrane technique is becoming one of the effective methods for the treatment of bone defect, especially for infectious bone defect treatment, and has been an increasingly wide utilization in the field of orthopedics [2,9–11]. It is reported that the induced membrane technique can be used for the treatment of traumatic bone defect, bone defect after resection of malignant tumor and chronic osteomyelitis bone defect. The induced membrane technique has the advantages of short treatment cycle, less complications, simple operation and satisfactory clinical effect. However, there are few reports on the influence factors and precautions of induced membrane technique.

In 2008, induce membrane technique was used in our hospital. In clinical applications, we found that it is important to understand the therapeutic principle of induced membrane technique and attach importance to the matters needing attention during operation. Therefore, in the current study, we retrospectively analyzed medical records of infectious bone defect patients treated with induced membrane technique to evaluate the treatment efficacy of induced membrane technique and analyze the main factors affecting treatments' results and cautions in clinical applications.

## 2. Materials and methods

### 2.1. Patients

The clinical data of 21 patients (15 men and 6 women) with infectious bone defect who were treated with induced membrane

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technique in our hospital from January 2008 to August 2017 were retrospectively analyzed. This study was approved by the hospital ethics committee, and all patients gave written informed consent.

### 2.2. Inclusion and exclusion criteria

Inclusion criteria: (①) limb infectious bone defect patients combined with induced membrane technique treatment; (②) patients with complete clinical and imaging data.

Exclusion criteria:(①) patients with less than 12 months follow-up; (②) patients who ignore instructions; (③) patients who with diabetes have not been effectively controlled and with skin and soft tissue defects cannot be repaired; (④) unfit for limb salvage.

### 2.3. Surgical methods and postoperative management

First stage operation: the conventional surgical approach was chosen to carry out a thorough debridement of soft tissue and bone. Infection focus (including sinus, dead bone, bacterial biofilm, pus mosses, necrosis tissues, inflammatory granulation tissue and internal fixation) were eliminated. The maximum length of bone defect after debridement was 2.0–10.0 cm (average length was 5.7 cm), including 15 cases of segmental bone defect and 6 cases of partial bone defect. Segmental bone defect is a bone defect without contact ends. Partial bone defect is a bone defect with the two ends of partial contact. Sixteen patients were treated with external fixation, and 3 patients were treated with plaster fixation, and 2 patients were treated with internal fixation. Two cases of non-infected bone defect were treated with internal fixation, and 1 case was treated with external fixation, and 1 case was treated with plaster fixation. Infected bone defect were treated with vancomycin bone cement (40 g cement PMMA mixed with vancomycin 2–4 g). After debridement, all cases had skin defect, and the defect area was $1 \times 2$ cm$^2$–$6 \times 15$ cm$^2$. All of them were conducted local flap repair. Infectious bone defects were treated with sensitive or broad-spectrum antibiotics for 2–3 weeks, and then received oral antibiotics for 3 weeks.

Second stage operation: This operation was performed after 12 weeks of bone cement filling. The membrane was cut longitudinally, and the bone cement was removed. Then, autogenous cancellous bone acted as the main material for bone graft (iliac bone or proximal tibia) was implanted into the induced membrane, trying to suture the induced membrane. Among the 6 cases of induced membrane injury, 4 cases used the surrounding fascia or myomembrane to reconstruct the wrapping structure, and 2 cases did not reconstruct the wrapping structure. At the same time, the external fixation was changed to internal fixation in 14 cases. The final fixation method: intramedullary nail in 7 cases, steel plate in 9 cases, external stent in 2 cases, plaster support in 3 cases. The duration of postoperative anti-infection therapy was 3–7 days. It was no need for plaster support or brace for external fixation after the internal fixation. On 3rd days after internal or external fixation, the rehabilitation treatment was begun. After 2 weeks, the weight-bearing training was increased, and CT examination showed that patients were fully weight bearing after bony callus connection. After 6–8 weeks, plaster support was removed, and patients gradually recovered.

### 2.4. Therapeutic evaluation

Monthly follow-up was performed before bone healing, and every 2–3 months follow-up was conducted after bone healing, then every 4–6 months follow-up was executed after 6 months of bone healing. According to Paley evaluation method [12], the classification of bone defect healing and the recovery of adjacent joint function of the affected limb were evaluated. Bone healing classification includes excellent ((①) bone healing, (②) no infection or infection recurrence, (③) local deformity angle less than 7, (④) limb length discrepancy is less than 2.5 cm), good ((①) bone healing, exist one item of (②)–(④)), fair ((①) bone healing, exist two items of (②)–(④)) and poor (The bone is not healing or fracture, or all items of (②)–(④) are not satisfied). Functional classification of the affected limb included 5 observation indexes: (①) pain, (②) limp, (③) adjacent joint contracture, (④) decreased range of limb motion, (⑤) ability to perform activities of daily living or to work. Functional classification includes excellent (painless or mild pain, no limp, adjacent joint contracture was less than 5°, reduction of range of limb motion was less than 20, can complete the normal activities of daily living), good (painless or mild pain, slightly difficult to complete the can complete the normal activities of daily living, exist one item of (②)–(④)), fair (painless or mild pain, slightly difficult to complete the most of the normal activities of daily living, exist two to three items of (②)–(④)), and poor (continuous pain, cannot complete the normal activities of daily living, exist any one item of (②)–(④)). In addition, the adjacent joint activities classification includes excellent (more than 90% normal activity degrees), good (75% above normal or contralateral activity), fair (50% above normal or contralateral activity), and poor (activity less than normal or contralateral 50%).

## 3. Results

### 3.1. General situation of patients

According to the inclusion and exclusion criteria, 21 patients were treated with induced membrane technique. The average age of patients was 37.9 (aged from 16 to 69 years old). All patients had redness, swelling, pain and pus-like drainage or sinus tract clinical symptoms. Bacterial culture of wound secretion was performed in all patients, and 15 cases were positive. The site of bone defect: 12 cases of tibia, 2 cases of femur, 2 cases calcaneus, 1 case of metatarsal, 1 case of humerus, 1 case of ulna, 1 cases radius, and 1 case of ulna and radius (Table 1). Fourteen patients were performed 1–3 times of debridement in our hospital or the outer court before the induction of membrane technique, including 6 cases of bone infection patients with skin defects were conducted skin flap repair.

### 3.2. Postoperative condition

One month after the first stage, wound dehiscence and bone exposure were occurred in 1 case of infected bone defect. Bone cement packing and flap repair were needed to heal the wound. Partial necrosis of flap marginal happened in another 2 cases without bone exposed, conservative treatment was performed to delay wound healing. The other patients had good wound healing, with no infection or recurrence. All patients received 12–52 months follow-up (an average of 19.5 months). One case had nonunion at the end of fracture, and healed after the second bone graft. The other bone defects healed in I stage. The clinical healing time was 3–15 months, with an average of 5.5 months. All patients recovered the weight-bearing activities, and the bone defect healing was excellent at the last follow-up. Functional recovery of adjacent joints showed that 8 cases were excellent, 11 cases were good, 2

**Table 1**
General situation of patients.

| No. | Gender | Age | Bacteria | Position | Bone defect | Skin defect | First stage fixation | Induced membrane condition | Second stage fixation | Clinical healing time | Paley grading | Activity |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Man | 69 | Staphylococcus aureus and Enterobacter cloacae | Tibia | Segmental bone defect (7.3 cm) | Local flap repair | External fixation | Defect, no reconstruction | Internal fixation | 8 | Good | Good |
| 2 | Man | 22 | Pseudomonas aeruginosa | Tibia | Segmental bone defect (6.6 cm) | Local flap repair | External fixation | Intact | Internal fixation | 7 | Excellent | Good |
| 3 | Man | 56 | Staphylococcus aureus | Tibia | Segmental bone defect (6.5 cm) | Musculocutaneous flap repair | External fixation | Defect, no reconstruction | Internal fixation | 8 | Excellent | excellent |
| 4 | Man | 35 | Staphylococcus aureus | Tibia | Segmental bone defect (9.0 cm) | Local flap repair | External fixation | Intact | External fixation | 7 | Fair | Good |
| 5 | Man | 43 | Pseudomonas aeruginosa | Tibia | Segmental bone defect (6.5 cm) | Local flap repair | External fixation | Defect and reconstruction | Internal fixation | 7 | Excellent | Good |
| 6 | Woman | 28 | Staphylococcus aureus | Tibia | Segmental bone defect (6.5 cm) | Free flap repair | external fixation | Defect and reconstruction | Internal fixation | 6 | Good | Good |
| 7 | Woman | 37 | Escherichia coli | Tibia | Segmental bone defect (5.3 cm) | Local flap repair | External fixation | Intact | Internal fixation | 7 | Excellent | excellent |
| 8 | Man | 57 | Staphylococcus aureus | Tibia | Segmental bone defect (7.2 cm) | Pedicle flap repair | External fixation | Defect and reconstruction | Internal fixation | 7 | Excellent | excellent |
| 9 | Man | 25 | Streptococcus viridans | Tibia | Partial bone defect (5.1 cm) | Pedicle flap repair | External fixation | Intact | Internal fixation | 6 | Excellent | excellent |
| 10 | Man | 16 | Pseudomonas aeruginosa | Tibia | Segmental bone defect (7.0 cm) | Local flap repair | External fixation | Intact | Internal fixation | 7 | Good | Good |
| 11 | Man | 22 | Staphylococcus aureus | Tibia | Segmental bone defect (6.6 cm) | Local flap repair | Internal fixation | Intact | Internal fixation | 7 | Excellent | excellent |
| 12 | Man | 30 | Staphylococcus aureus | Femur | Segmental bone defect (6.2 cm) | Local flap repair | External fixation | Intact | Internal fixation | 4 | Good | Good |
| 13 | Woman | 36 | | Femur | Segmental bone defect (6.4 cm) | Local flap repair | External fixation | Defect and reconstruction | Internal fixation | 5 | Good | good |
| 14 | Man | 29 | Escherichia coli | Radius | Segmental bone defect (4.2 cm) | Pedicle flap repair | external fixation | Intact | Internal fixation | 3 | Good | Good |
| 15 | Woman | 50 | Staphylococcus aureus and Proteus vulgaris | Ulna | Partial bone defect (4.0 cm) | Pedicle flap repair | External fixation | Intact | External fixation | 3 | Good | Good |
| 16 | Man | 45 | | Calcaneus | Partial bone defect (4.0 cm) | Local flap repair | Plaster fixation | Intact | Plaster fixation | 3 | Good | Good |
| 17 | Man | 49 | Acinetobacter Bauman | Calcaneus | Partial bone defect (3.8 cm) | Free flap repair | Plaster fixation | Intact | Plaster fixation | 3 | Good | Good |
| 18 | Man | 40 | Staphylococcus aureus | Humerus | Segmental bone defect (5.0 cm) | Flap repair | Internal fixation | Intact | Internal fixation | 3 | Excellent | excellent |
| 19 | Man | 39 | | Metatarsal | segmental bone defect (2.0 cm) | Local flap repair | Plaster fixation | Intact | Plaster fixation | 3 | Good | Good |
| 20 | Woman | 33 | | Ulna and radius | Partial bone defect (2.5 cm) | Local flap repair | External fixation | Intact | External fixation | 3 | Fair | Good |
| 21 | Man | 35 | | Tibia | Segmental bone defect (10 cm) | Local flap repair | External fixation | Intact | Internal fixation | 8 | Good | Good |


**Fig. 1.** Typical cases. X-ray and appearance of bone infection after internal fixation of tibial shaft fracture (A). Patients treated with induced membrane technique. In the first stage operation, the bone cement filling material was made by the method of in vivo formation (B). In the second stage of operation, the membrane injury and defect were found when the packing was taken out (C). In the second stage, X-ray and appearance of postoperative bone infection recurrence (D). X-ray and appearance of bone healing and internal fixation after surgical intervention (E).

cases were fair, and the total excellent rate was 90.5%. Classification of adjacent joint activities showed that 7 cases were excellent, 10 cases were good, 3 cases were fair, and 1 case was poor (the total excellent rate was 81.0%). Bone cement leakage, fixator fracture, and fracture after bone healing was not observed. Postoperative infection recurred in 4 cases. Two of them were ineffectual in conservative treatment, and bone infection was controlled by reoperation intervention. The 2 cases had induced membrane injury without wrapping structure reconstruction, but the bone defect was healed and no need bone grafting. The other 2 cases received conservatively to control infection and they had intact induced membrane (Table 1). Typical cases were shown in Fig. 1.

## 4. Discussion

### *4.1. Influencing factors of induced membrane technique in repairing bone defect*

The procedure of induced membrane technique was follows: firstly, induced membranes were developed in vivo; then, cancellous bone graft materials were implanted in induced membranes in the absence of infection; finally, new bony callus formation was developed by blood and osteogenic factors supply from the induced membranes. Previous studies indicated that induced membranes had abundant vascular system perpendicular to the long axis of the bone and secreted various osteogenic growth factors (TGF-β1, BMP-2, VEGF), thus playing an important role in the vascularization and osteogenesis of transplanted bone [13–16]. The induced membranes is rich in mesenchymal stem cells, so it has biological osteogenic activity. Moreover, the induced membranes also had the function of mechanical isolation, wrapping and auxiliary fixation of the transplanted bone. Implantation cancellous bone graft in the membranes could avoid bone loosening and bone resorption [6]. Therefore, induced membrane technique was an improved free bone graft, and the way of healing was to form a new bone connection rather than longitudinal bone growth.

### *4.2. Operation precautions of induced membrane technique in repairing bone defect*

First of all, it was necessary to have a good soft tissue to completely cover the bone defect area during the application of induced membrane technique [6], also tension-free suture was required during repaired skin flap. Bone defects are often associated with soft tissue defects, and flap transplantation was performed simultaneously when packing cement. Then, bone cement stimulated the surrounding soft tissue to lead allergic reaction and induce the formation of membrane. In the current study, because suture tension was too large during repaired skin flap, the wounds of 1 case were gradually split at 1 month after the operation, and bone cement exposed.

The second point, the quality and integrity of induced membrane formation are closely related to the therapeutic effect. The volume of bone cement filling material should not be less than bone defect volume. Through our previous papers (published in Chinese), the effect of bone cement filling material with multi column structure in vitro was better than traditional method in vivo. Multi column structure is a method of bone cement filling in vitro. Briefly, bone cement filling material is made according to the volume of bone defect in vitro, and is longitudinally cut into 3–4 multi column structures before it hardens. Then, the filling material and the bone extremities are connected by bone cement (it is called bone cement 'collar', Fig. 2) [17]. In this way, the bone cement filling is easy to be taken out in the second stage without damaging the inducible membrane. Compared with this method, the disadvantages of traditional method forming in vivo were as follows: 1) the packing of bone cement was large, and hard to remove; 2) bone cement fever (up to 61–72 °C) resulted 1–2 mm bone tissue necrosis; 3) the surface area of the whole solid bone cement filling was small, and antibiotic elution rate was low, which could not cope with the osteomyelitis of medullary cavity lavage [18]. In the current study, small induced membrane happened in 3 cases with bone cement filling in vivo, which resulting in the induced membrane injury in

**Fig. 2.** Multi column structure and bone cement 'collar'. Multi column structure is a method of bone cement filling in vitro. Briefly, bone cement filling is made according to the volume of bone defect in vitro, and is longitudinally cut into 3-4 multi column structures before it hardens. Then, the filling material and the bone extremities are connected by bone cement (it is called bone cement 'collar').

the second stage of surgery, the membrane could not be completely wrapped bone graft, and bone healing time is relatively long. One of them had nonunion at the connecting end, suggesting that the quality of induced membrane affected the effect of bone defect repair. Postoperative infection recurred in 4 cases. Two of them were ineffectual in conservative treatment, and bone infection was controlled by reoperation intervention. The other 2 cases received conservatively to control infection and they had intact induced membrane. The results indicated that induced membrane had certain protective effect on infection or recurrence after operation, and the integrity of induced membrane should be maintained as far as possible.

The third point, how to bone graft and take bone? After implanting bone graft, induced membrane need to suture. If the membrane was injury, the surrounding fascia could be used for bone graft.

## 5. Conclusion

According to the clinical application of induced membrane technique in 21 cases, we found that the technique in treatment of infectious bone defect had the advantages of simple operation, low requirement of recipient area, rapid healing of bone defects, no correlation between healing time and long bone defect, and low recurrence rate of infection. However, the development of induced membrane technique required certain conditions (such as skin coverage, many cancellous bone, etc.). Thus, its popularity was not as good as Ilizarov technology. Therefore, the surgeon must understand the principle of treatment and pay attention to the influence factors in order to avoid surgical error and reduce complications.

## Disclosure of interest

The authors declare that they have no competing interest.

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None.

## Authors' contribution

Jianbing Wang conceived the study and Qudong Yin designed the study and drafted the manuscript. Sanjun Gu collected the data and Yongwei Wu analyzed the data. Yongjun Rui put forward the concept of the study and reviewed the manuscript. All authors read and approved the final manuscript.

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