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Application of the Induced Membrane Technique for Forearm Bone Defects: Our Institutional Experience

Giorgio M. Calori, Peter V. Giannoudis,† Simone Mazzola,* and Massimiliano Colombo**

Summary: The surgical treatment of forearm fracture nonunions remains a therapeutic challenge for orthopedic trauma surgeons. Nonunions of the forearm diaphysis, although not frequent, cause severe anatomic and functional impairment related to disturbance of the interosseous membrane and dysfunction of the adjacent elbow and wrist joints. Lately the induced membrane technique has been proposed for the reconstruction of large diaphyseal bone defects. In this study we present our experience of using this technique for the treatment of diaphyseal forearm bone defects with specific emphasis on the steps of the technique.

Key Words: bone defect—forearm—induced membrane—reconstruction.

(*Tech Orthop* 2015;00: 000–000)

The majority of fractures progress to union and only a small percentage of them (5% to 10%) are associated with impaired healing requiring further surgical intervention.[1,2] Nonunion refers to a fracture that will not heal without an additional surgical or nonsurgical intervention (usually by 6 to 9 mo). According to the US Food and Drug Administration, the diagnosis of nonunion may be established "when a minimum of 9 months has elapsed since injury and the fracture shows no visible progressive signs of healing for 3 months."

Fracture healing is a complex process involving the interplay of multiple biomechanical and biological factors. To address all the factors that may be implicated in fracture nonunion, several elements need to be considered, including the cellular environment, growth factors, bone matrix, and mechanical stability. These parameters comprise the so-called "Diamond Concept," which has further evolved into "the regenerative pentagon" when vascularization is also considered.[3,4]

In 2008, we published a new classification for nonunions (NUSS)[5,6] focusing on the quality of the bone, the original fracture characteristics, the number of previous interventions, the invasiveness of previous interventions, the adequacy of previous surgery, bone alignment, presence of bone defect, the state of the soft tissues, and the American Society of Anesthesiologists grade of the patient. Each factor has been broken down into subgroups, each provided with a scoring system reflecting the difficulty that one can expect during the course of treatment. The total score would then be multiplied by 2. All the factors included in the scoring system have an impact on the complexity and difficulty of treatment of any nonunion.[7–10] The NUSS recognizes 4 groups according to severity: Score from 0 to 25 should be considered a straightforward nonunion and should respond well to standard treatments; usually the problem is mainly mechanical. The common aim of treatment is to improve stability, usually choosing a different system of fixation. Score from 26 to 50 should require more specialized care; usually the problem is both biological and mechanical. Treatment requires revision of the fixation and a biological stimulation obtained with pulsed electromagnetic fields, extracorporeal shock wave therapy, or biotechnologies, such as mesenchymal stromal cells, growth factors, or scaffold.[11–23] Score from 51 to 75 requires specialized care and specific treatments. The problem is complex and is characterized by impairment of both biological and mechanical conditions. Resection of the nonunion is usually required and consequently

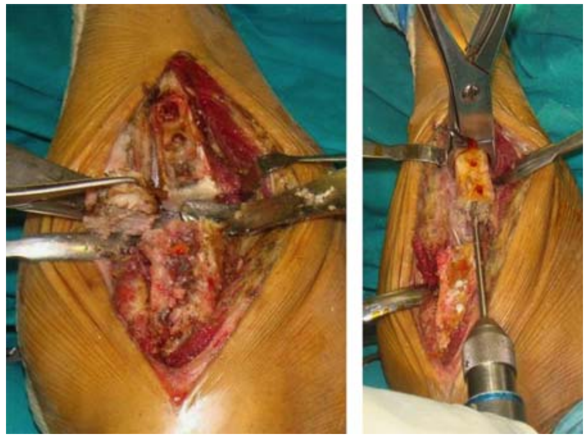

FIGURE 1. Intraoperative pictures showing the complete removal by resection of the necrotic and infected bone (left) and the reaming of the intramedullary canal with a 2.5 mm drill (right).

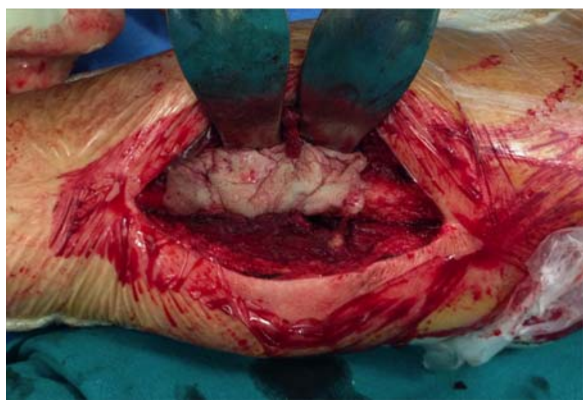

FIGURE 2. Intraoperative picture showing the implantation of the cement spacer.

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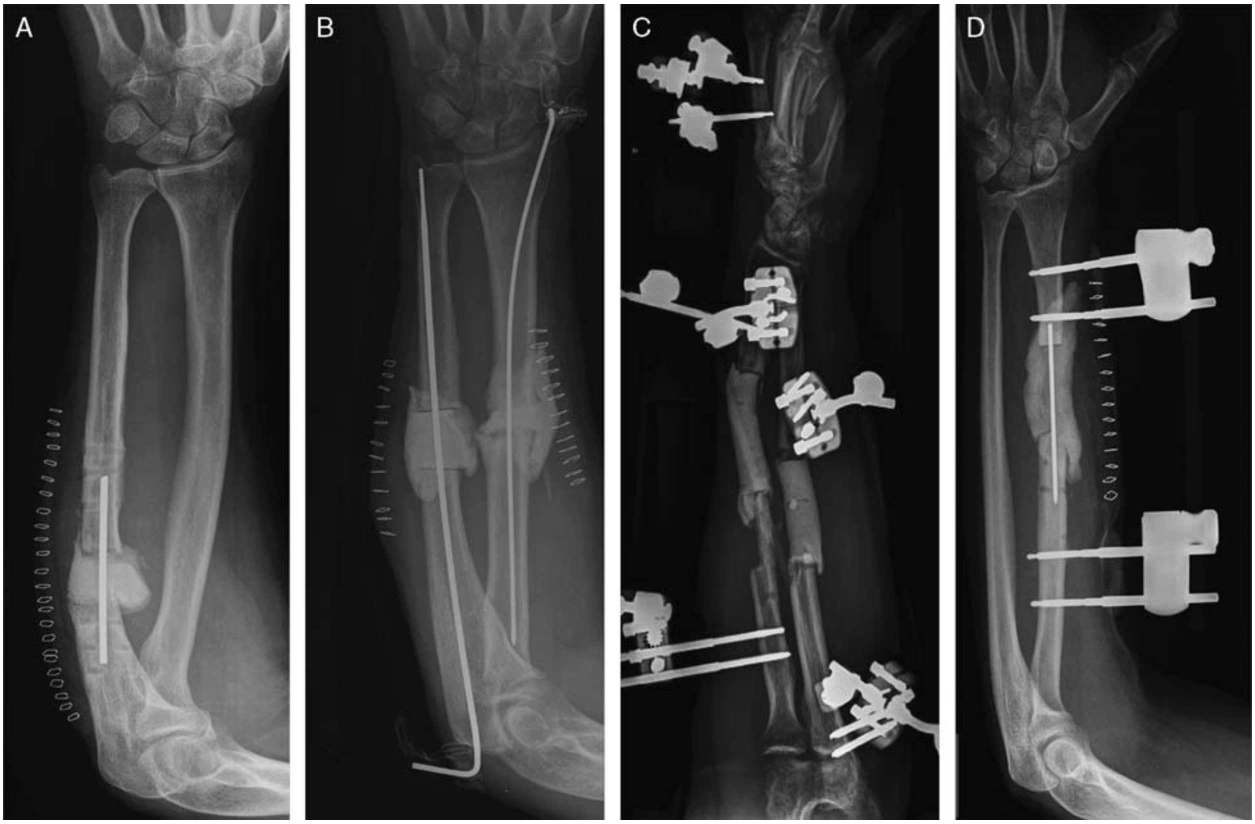

FIGURE 3. Different possibilities of stabilization. A, Intramedullary K-wire for stable case in which only 1 bone is involved and the bone defect is <3 cm. B, Double long K-wires for radius and ulna lesions that do not exceed 3 cm of bone loss. C, External fixator for radius and ulna large bone defects (> 3 cm). D, External fixator + intramedullary K-wire for radius defect wider than 3 cm.

a bone defect must be treated. Traditional treatments may be used, such as bone transport with external fixator, autologous iliac crest grafts or microvascular fibula grafts, and the application of biotechnological products, including cells, scaffold, and growth factors, according to the principles of the "biological chamber"[24,25] and "polytherapy."[26–29]

Score from 76 to 100 may indicate the need for primary amputation, arthrodesis, prosthesis, or megaprosthesis implantation depending on the patient's condition, the severity of the bone loss, and the anatomic localization.[30,31]

The surgical treatment of forearm fracture nonunions remains a therapeutic challenge for orthopedic trauma surgeons. Nonunions of the forearm diaphysis cause severe anatomic and functional impairment related to disturbance of the interosseous membrane and dysfunction of the adjacent joints, elbow, and wrist.[32–35] Diaphyseal fractures of the forearm differ from other

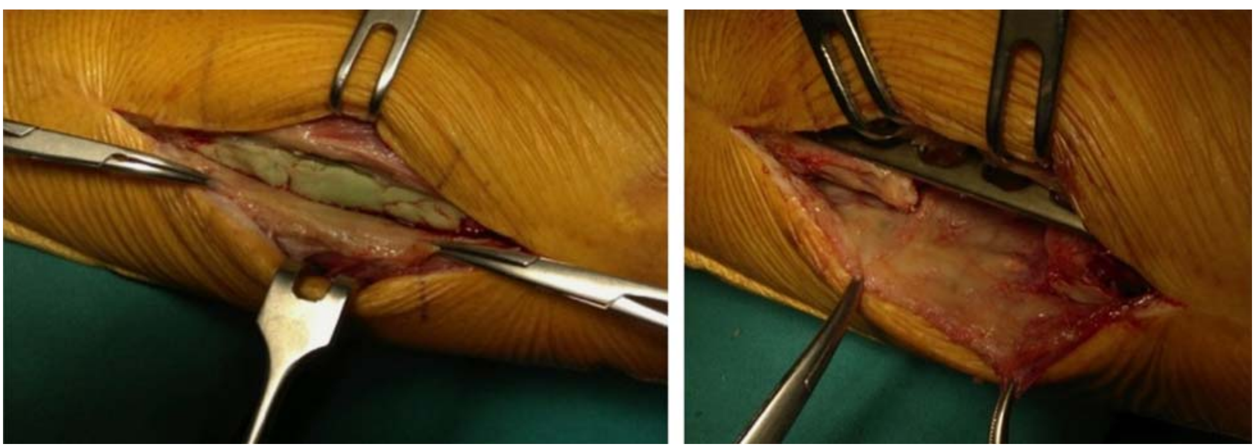

FIGURE 4. Intraoperative pictures showing the gentle incision of the membrane revealing the spacer (left) and the good status of the membrane after spacer removal. full color online

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FIGURE 5. Intraoperative pictures showing implantation of RIA + rh-BMP-7 (left) and the final result after the grafting. full color online

diaphyseal long bone fractures because of the intimate relationship between the radius and ulna and their reciprocal movements.[36] The shape, length, and distance between the radius and the ulna are reflected in movements of the elbow and fine movements of the wrist/hand, and these should be restored. Pronation and supination of the forearm occur at the radio-humeral, proximal radio-ulnar, and distal radio-ulnar joints. Therefore, any change in the relationship between forearm bones can lead to a malfunction in proximal or distal articulation.

The aims of surgical treatment of forearm nonunions are to restore the appropriate bone length and rotation minimizing the risk of a compromised functional capacity. The surgical technique must provide bone stability and stimulation of bone repair thus restoring normal flexion-extension of the elbow and pronation and supination and grip strength of the wrist. Key to success in the management of these demanding conditions is to develop a comprehensive treatment concept, which considers the forearm and its adjacent joints, the elbow, and wrist, as a complex functional unit.

Aseptic forearm nonunion is an uncommon complication of forearm diaphyseal fractures due to the wide use and success of the new developed surgical techniques and implants.

Infected forearm nonunion is an infrequent complication of diaphyseal fracture of the forearm, being associated with a number of challenges. Reviewing the literature, most reports on the treatment of infected nonunions refer to the lower extremity, particularly the tibia.[37–40]

In general terms infected nonunion in the upper extremity is a rare event, especially in the forearm. Such patients usually have had numerous previous surgical interventions, resulting in bone defects and soft tissue compromise.[41,42] The problem is complex due to the presence of bone necrosis, segmental bone loss, sinus tract formation, fracture instability, and scar adhesion of the soft tissues.[41–43]

Overall, different modalities of treatment have been described, but the results of the treatment are not completely satisfying.[44–47] The mainstay of treatment involves eradication of the infection (converting a septic to an aseptic nonunion) and to promote a successful osteogenic response. For the osteogenic stimulus component various methods have been used including bone grafting, nonvascularized fibular graft, vascularized fibular graft, and bone transport. Bone grafting remains the most common treatment for forearm bone defects. However, bone defects

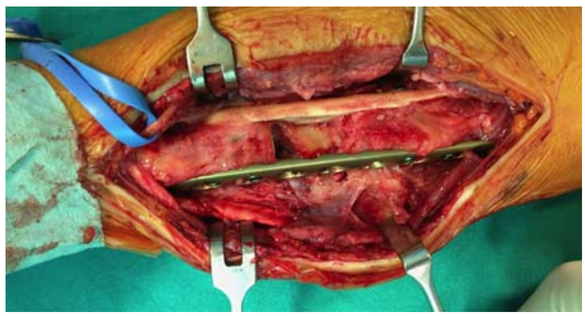

FIGURE 6. Intraoperative picture showing the definitive stabilization using LCP plate and fibula allograft "stick" from the tissue bank. full color online

FIGURE 7. Intraoperative pictures showing the membrane after the grafting (left) and the closure of the "Biological Chamber" utilizing the membrane. full color online

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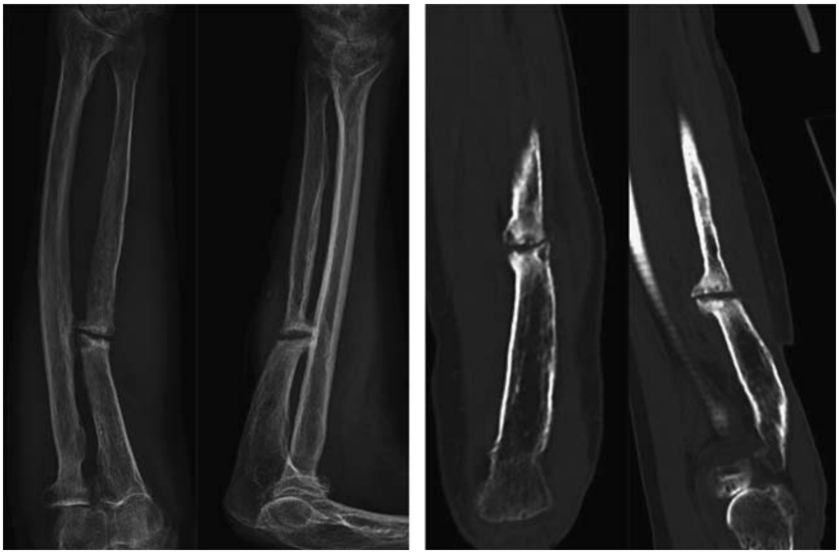

FIGURE 8. Case 1: M.R. Female, 45 years old. Posttraumatic septic nonunion of the ulna. NUSS score 64 points. Preoperative X-ray and computed tomography scan of the affected forearm showing the nonunion.

>4 to 5 cm are considered difficult to treat successfully[48] as containment of the graft, resorption, and prevention of forearm bone synostosis remain the issues to overcome.[38] The use of nonvascularized fibular graft has been successful in the treatment of bone defects, but the method relies on revascularization, and it may take many months to be incorporated during which time they lose much of their strength and are susceptible to fracture.[49] Vascularized fibular graft has been introduced in the treatment of massive bone defects. Its advantage is that it does not rely on revascularization and therefore should become fully incorporated sooner. Nevertheless, it is a technically demanding procedure with a high rate of infection and thrombosis of the graft vessels.[50–52] Donor-site morbidity is also common.

Bone transport has been successfully used in lower limbs, being less invasive and more versatile compared with other methods, and it can treat infected nonunion with bone defects of any length. However, it is not very common and easy to perform in the treatment of forearm defects.[43,53]

In 1986, Masquelet conceived and developed an original reconstruction technique for large diaphyseal bone defects,

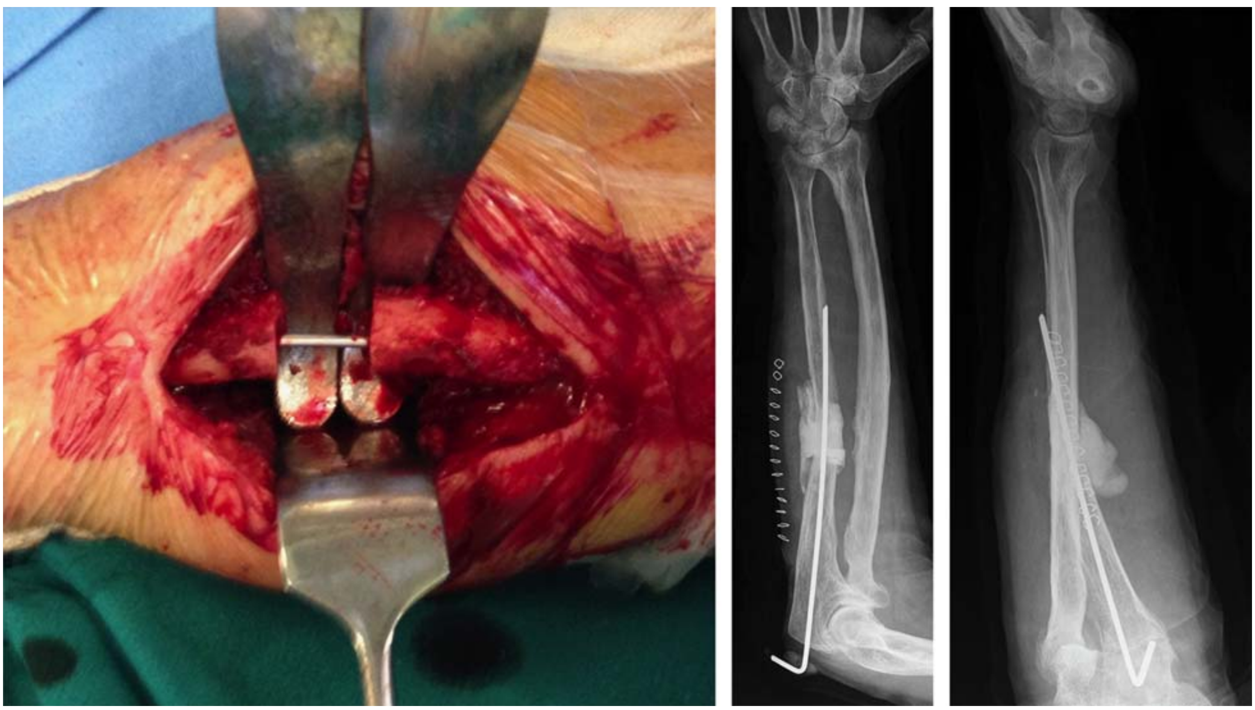

FIGURE 9. Intraoperative pictures showing the bone defect after the resection and the positioning of an intramedullary K-wire before the spacer implantation (left); postoperative X-ray (right). full color online

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FIGURE 10. Postoperative X-ray afer the second step (RIA grafting + rh-BMP-7 + mesenchimal stromal cells + LCP osteosynthesis + homologous fibular stick implantation).

based on the notion of the induced membrane.[54–58] The induced membrane technique has the advantage of being simple, although technical execution must be carefully performed. The 2-stage procedure is an advantage in case of infection because the aim of the first step is to cure infection and to restore the surrounding soft issue envelope. Repeated debridement may be necessary, which makes the choice of implant stabilization difficult. External fixation makes revision surgery possible. The advantages of inserting a spacer include maintaining a well-defined void to allow for later placement of graft, providing structural support, offloading the implant, and inducing the formation of a biomembrane. The spacer also maintains the defect and inhibits fibrous ingrowth. Masquelet and Beguè proposed that this membrane prevents graft resorption while enhancing vascularity and corticalization of the graft material.

It has been described that, after the initial placement of the antibiotic impregnated spacer, an interval of 4 to 6 weeks is needed for development and maturation of the biologically active membrane that is suitable for grafting.[59] Recent literature has shown that this biomembrane can be 0.5 to 1 mm thick[60] with a hypervascular profile.[61] Pelissier et al[61] also reported that the induced membrane has the capacity to secrete growth factors thus stimulating bone regeneration.

In this study we present our experience applying the induced membrane technique in the treatment of patients with forearm diaphyseal aseptic/septic nonunion with a NUSS score between 51 and 75 points.

THE SURGICAL TECHNIQUE

The technique requires a 2-staged approach.

FIRST SURGICAL STEP

A tourniquet is applied and can be inflated if it is thought that the procedure will not last >2 hours. Alternatively, the tourniquet can be applied but not inflated. Antibiotics should

FIGURE 11. X-ray at 9 months after the procedure showing the restoration of the ulna with good integration of the grafts.

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FIGURE 12. Pictures showing the clinical and functional outcome. full color online

not be administered at induction until intraoperative tissue cultures have been taken.

During the first surgical step a complete debridement and removal of the pathologic, necrotic, and infected bone and soft tissues is performed. Thorough debridement and irrigation are critical, especially if infection is the cause of the defect. In patients with infected nonunion or osteomyelitis, this 2-stage technique ensures that adequate debridement has been undertaken at the first operation with no evidence of recurrence. Bone edges of the bone fragments should be healthy with a viable bleeding bed. In all cases and most of all in case of infection, the intramedullary canal should also be debrided using a 2.0/2.5 mm drill and irrigated. At least 6 tissue cultures from both the bone and the soft tissues must be harvested and be sent to microbiology for culture and sensitivity. Then a polymethyl methacrylate antibiotic-loaded cement spacer is implanted at the site of the bone defect and the forearm is stabilized with an external fixator or K-wires (Fig. 1).

CEMENT SPACER

For optimum membrane induction and better stability of the construct, the cement should be placed over the edges of the bone and inside the canal and should maintain the space of reconstruction (Fig. 2).

The cement spacer has also a mechanical role as it maintains the space between the edges of the bone avoiding a fibrous tissue invasion of the site.[61] The spacer sterilizes the site of infection and it creates, in 2 months, an excellent microenvironment with adequate local conditions for bone grafting. Another role of the spacer as previously stated is the induction of the biological active membrane.

If the defect area is known to be sterile, free of pathogens, then the cement can be implanted without being loaded with antibiotics. If there is a doubt of sepsis or there is an environment of sepsis but the pathogen responsible is not known as yet, then we prefer to use an antibiotic-loaded cement with gentamicin and clindamycin.

In those cases in which a pretreatment culture was performed with identification of the pathogen, the choice of the antibiotic to be loaded to the cement is based on the sensitivity of the bacteria.

STABILIZATION

The forearm is a complex segment from a biomechanical point of view and subjected to high shear and torsional forces. The mechanical stability after osteotomies, especially in extensive resections, is severely compromised. In cases of

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FIGURE 13. Case 2: O.F. Male, 34 years old. Posttraumatic septic nonunion of radius and ulna (motorbike accident with bone exposure). NUSS score 68 points. Preoperative X-ray showing the septic nonunion of both radius and ulna.

large resections and in which both radius and ulna are involved, instability is complete. In every case a sustainable stabilization is needed to prevent such problems as secondary mobilization of the spacer and possible neurovascular, ligament, or tendon injuries. Stabilization of the segment is based on the proper placement of the spacer. Optimum spacer placement can be achieved with the introduction of a K-wire introduced in the 2 bone fragments and the spacer itself. We reserve the fixation with K-wires to cases in which a single bone segment is involved (radius or ulna) and in which the bone loss is not >3 cm or rarely in lesions of both radius and ulna but when the gap is 1 cm maximum.

We believe that in all these cases there is adequate internal stability present and a brace or a plaster of Paris externally will be sufficient to provide the additional stability necessary to maintain alignment and a painless first-stage period.

In cases in which both forearm bones are affected, or in cases with a gap of >3 cm, we prefer to perform stabilization of the affected extremity with an external fixator. The placement of the pins is essential to optimize stability, but also not to interfere with the next incision or future plate position if possible. Meticulous pin site care is crucial to minimize the risk of infection. A combination of internal K-wiring and external fixator application can also be considered for optimal structural support (Fig. 3).

Although the initial first-stage stabilization is temporary and not definitive, it is still necessary to correct length, mechanical axis, and the rotation of the extremity to preserve the relationship between radius and ulna in both cases whether the temporarily stabilization has been performed with an external fixator and/or with K-wires.

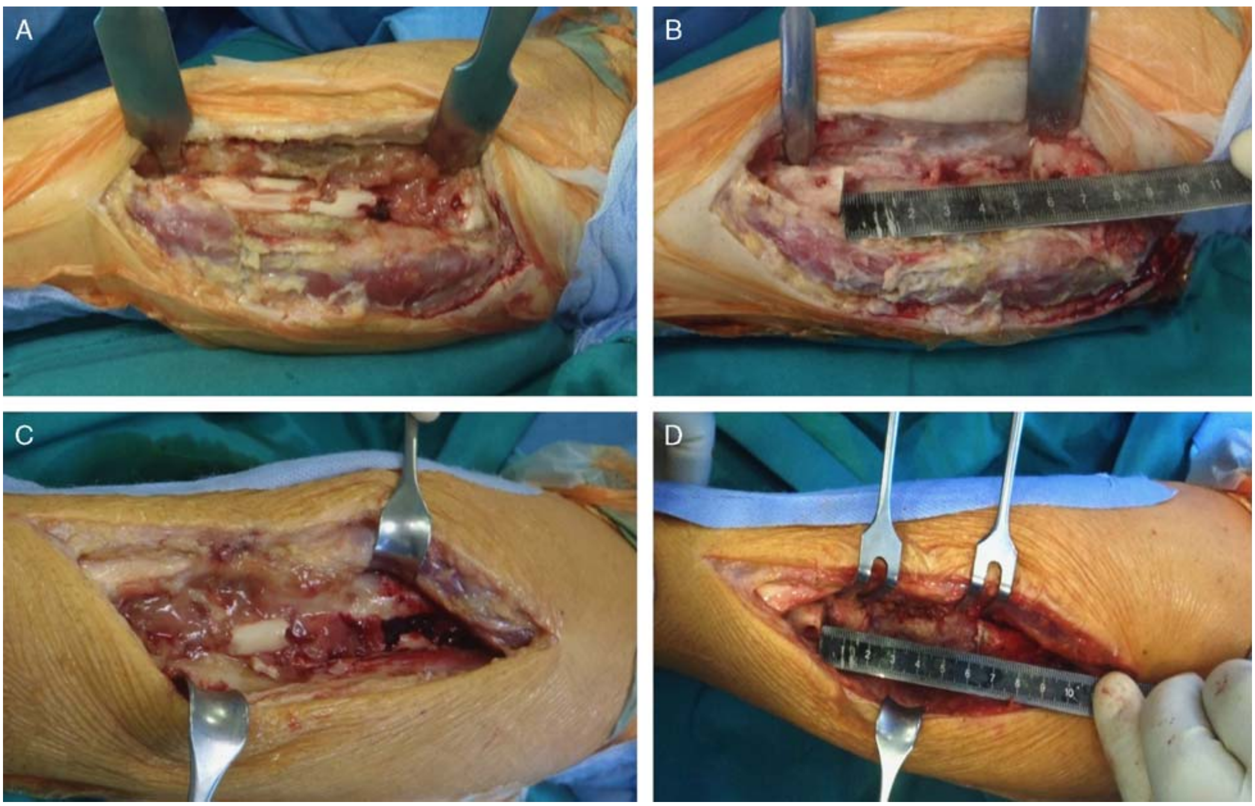

FIGURE 14. Intraoperative pictures showing the septic condition of the radius (A) and of the ulna (C) with necrotic bone and pathologic soft tissue and the bone defects of radius (B) and ulna (D) after the resection and debridement. full color online

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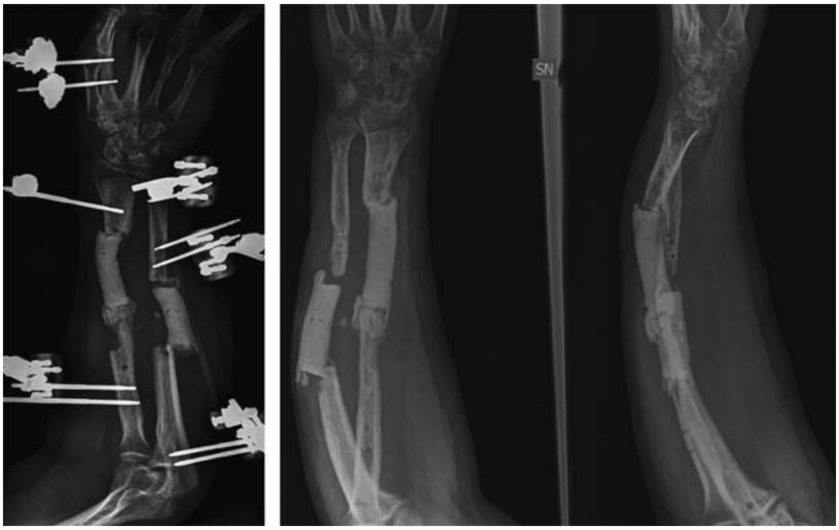

FIGURE 15. X-ray showing the temporary stabilization with external fixator (left) and after the removal of the implant (3 mo later).

FIGURE 16. Intraoperative picture showing the harvesting of the vascularized fibula. full color online

CLOSURE

Finally, in the first stage of the Masquelet technique, the soft tissue envelope is repaired. Good soft tissue coverage is essential and free tissue transfer may be required. Wound closure must not be under tension.

SECOND SURGICAL STEP

Tourniquet is applied and inflated. Antibiotics should not be administered again at induction until tissue cultures for microbiology have been harvested. During the second stage, approximately 6 to 8 weeks later, the plan is to remove the cement spacer carefully ensuring that the formed "induced membrane" is minimally disturbed. The cement spacer is removed with a saw or an osteotome with caution not to break the bony edges or to damage the membrane (Fig. 4). The ntramedullary canal is carefully prepared with a 2.5 mm drill or a curette and debrided if needed. Bone edges of the bone fragments should be healthy with a viable bleeding bed. All nonvital tissues must be removed again.

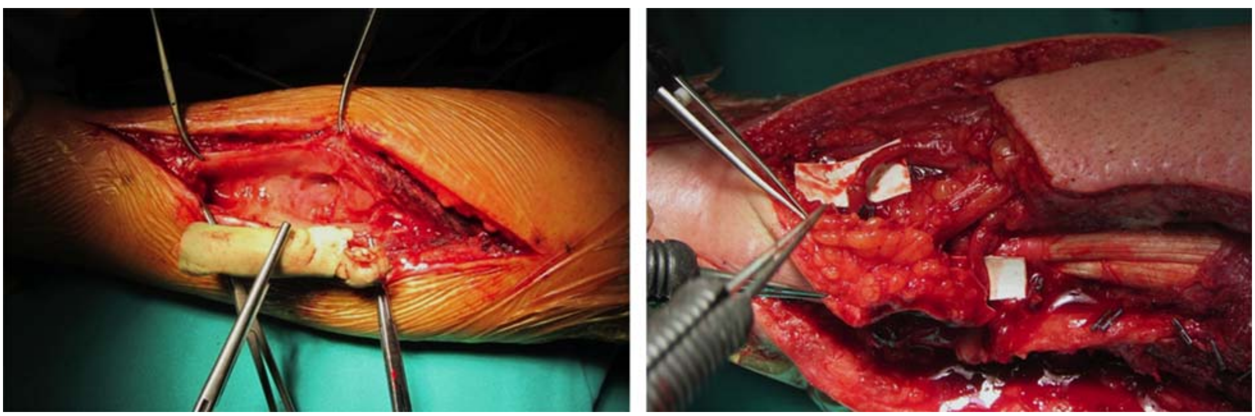

FIGURE 17. Intraoperative pictures showing the removal of the spacer from the radius with a good membrane formation (left) and the microvascular anastomosis of the autologous fibula to reconstruct the radial bone defect. full color online

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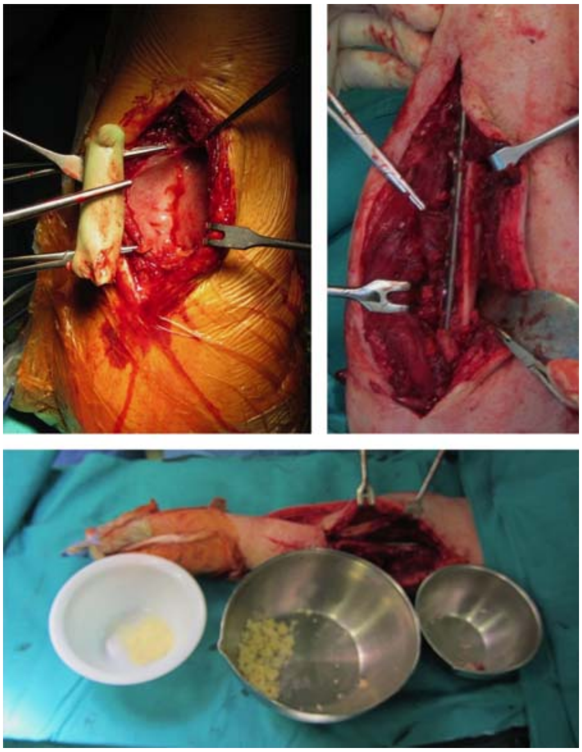

FIGURE 18. Intraoperative pictures showing the removal of the spacer from the ulna with its new formed membrane (left), the massive autologous fibular grafting (not vascularized) and the osteosynthesis with LCP plate to reconstruct the ulnar bone defect (right) and the application of rh-BMP-7 + homologous bone chips from the tissue bank. full color online

GRAFTING

In cases in which the loss of bone substance is not more than 3 cm we prefer to use autologous bone graft obtained from the iliac crest. For defects >3 cm we use the intramedullary canal of the femur (or tibia) to harvest autologous graft using the RIA (Reamer/Irrigator/Aspirator) device.[62–64]

The biological activity of the autologous bone graft can be further enhanced with the addition of osteoprogenitor cells (bone marrow aspirate harvested from the iliac crest) or with osteoinductive growth factors (commercially available BMPs).[65,66] These can be mixed with the autograft before filling the defect or they can be placed inside the medullary canal and in the bed of the defect, while the autograft can be inserted afterward for better containment.

Nowadays we prefer the bone harvesting with the RIA System as it possesses good biological properties and the volume of bone tissue harvested can be large (up to 80 mL) allowing reconstruction of quite large bone defects (Fig. 5).[67]

For defects >6 cm one can also consider the use of free vascularized fibula transplantation that can restore loss of substance even up to 10 cm.

OSTEOSYNTHESIS

Adequate mechanical stability must be provided, usually with an LCP plate and/or a locking plate. The plate can be placed either under the membrane or epiperiosteally for minimal disturbance of the periosteal blood supply and to assure firm closure of the membrane under the plate.

HOMOLOGOUS BONE IMPLANTATION

As already mentioned the forearm is subject to strong torsional forces. Therefore, the osteosynthesis must be extremely stable to prevent future failures. For this reason, in this anatomic region, in addition to the fixation with the LCP plate and in cases of large defects with poor bone stock, we prefer to provide additional stability of the defect with a fibula allograft (Fig. 6). The fibula "stick" allograft suitably prepared is applied on the opposite side of the plate, thus increasing the spectrum of stability of the implant. The defect then between the plate and the fibula can be filled in with the autologous graft material. During the subsequent months the fibula allograft will be incorporated to the host by cripping substitution (Fig. 6).

CLOSURE

The membrane must be closed to ensure that the graft material is contained into the "chamber" (bone defect area). Good soft tissue coverage is essential and free tissue transfer may be required. Wound closure must not be under tension (Fig. 7). Two case examples are demonstrated in Figures 8–12 (case 1) and Figures 13–21 (case 2).

DISCUSSION

There are some published studies focusing in the treatment of forearm nonunions.

In 1997, Moroni et al[68] conducted a study on 24 patients; 24 isolated radius and ulna nonunions with segmental bone loss were surgically treated. The surgical technique consisted of removal of the necrotic bone, filling of the bone defect with an intercalary bone graft, and internal fixation with a cortical bone graft fixed opposite to a plate. In 23 cases union was achieved; in particular, radiographic union was noted at a mean time of 13.9 ± 3.9 weeks. Functional results were classed as excellent in 10 patients, satisfactory in 6, unsatisfactory in 7, and failure in 1.

Smith and colleagues reported their experience using distraction osteogenesis in the treatment of traumatic bone loss in the forearm. Eleven consecutive patients with traumatic forearm atrophic nonunion with bone loss were treated with Ilizarov ring fixation. Records were reviewed retrospectively. The union rate with Ilizarov treatment alone was 64%; 36% of the patients developed a hypertrophic nonunion and underwent compression plating. The overall rate of union was raised to 100%.[69]

Baldy and colleagues performed a study that involved 31 patients with a diagnosis of nonunion of the forearm; surgical revision was performed by restoring the length by autologous bone grafting of the resected nonunion from the iliac crest and compression plating using a 3.5 mm dynamic compression plate or limited contact DCP. Radiologic bony union was achieved in 30/31 patients within a mean time of 3.5 months of revision surgery. Clinically, 29/31 patients showed a good functional outcome and 26/31 patients were able to resume their previous work.[70]

Kloen and colleagues published a retrospective study that involved 47 patients with 51 nonunions of the ulna and/or radius. All nonunions were managed following the AO-principles of compression plate fixation and autologous bone grafting if needed. All nonunions healed within a median of 7 months. According to the system of Anderson et al, 29 patients

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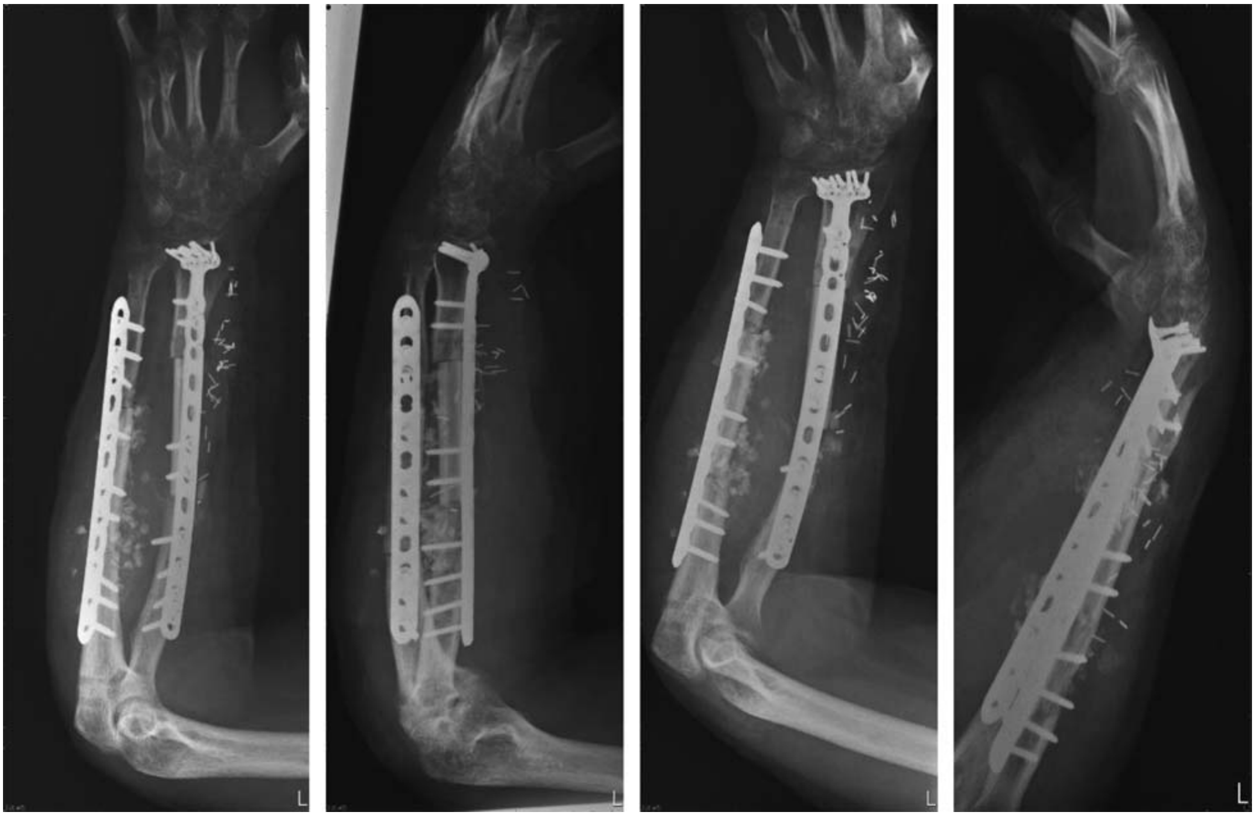

FIGURE 19. Postoperative X-ray showing the reconstruction of the radius and ulna.

(62%) had an excellent result, 8 (17%) had a satisfactory result, and 10 (10%) had an unsatisfactory result.[71]

Faldini and colleagues published their clinical experience about the use of homologous bone graft in the treatment of aseptic forearm nonunion; they reviewed 14 patients treated by surgical technique included a homologous bone graft in combination with a plate. At last follow-up, all forearm bones had remodeled (mean, 5 y; range, 2 to 13 y).[72]

Soucacos et al[73] retrospectively reviewed 18 patients affected by large skeletal defects of the upper extremity treated with free vascularized fibular graft (15 forearm nonunion) with an overall success rate of 92%.

Recently, Calori and colleagues performed a study on 52 patients with 52 forearms nonunions classified according to the NUSS score. A group of patients was treated according to the principles of "monotherapy" (33 patients) and another group of patients was treated according to the principles of "polytherapy" (19 patients).The results were encouraging. In the monotherapy group 21/33 nonunions (63.64%) went on to develop radiographic and clinical union within a period of 12 months, and the calculated DASH score showed a mean value of 55.15 points. In the polytherapy group 17/19 (89.47%) of the cases progressed to osseous healing within 12 months, and the average DASH score showed a mean value of 45.47 points.[28]

Liu and colleagues retrospectively reviewed a consecutive series of 21 patients who were treated for their forearm infected nonunion by bone transport with external fixator after debridement. The mean amount of bone defect was 3.1 cm (range, 1.8 to 4.6 cm) as measured on plain radiographs. All patients achieved bony union and were satisfied with the functional and cosmetic outcome.[43]

Noaman et al[46] reviewed 16 patients affected by upper limb bone defect treated with free vascularized osteoseptocutaneous fibular bone graft and he showed bone union in 15/16 patients with an average follow-up of 84 months.

Zhang and colleagues retrospectively reviewed 16 patients with infected forearm nonunion treated by bone transport. The average length of the bone defects after radical debridement was 3.81 cm (range, 2.2 to 7.5 cm). The mean follow-up after removal of the frame was 39.63 months (range, 26 to 55 mo). All the patients progressed to bone union and no recurrence of infection was observed.[53]

CONCLUSIONS

In conclusion, the concept of the induced membrane is another alternative technique for reconstruction of bone defects of the forearm secondary to traumatic bone loss, posttraumatic septic or aseptic nonunions, chronic osteomyelitis, and tumor excision.[58]

The advantages of this method are that the induced membrane maintains the bone graft, it prevents its resorption at the early stages, and it plays an important role in revascularization and bone formation facilitating the regeneration process.

In cases in which difficulties of bone repair are anticipated (NUSS > 50 points) the graft can be augment with cells, growth factors, allograft, or other bone substitutes depending on the patient characteristics and the local environment requirements.

One disadvantage of the induced membrane technique is that it is a staged procedure, requiring 2 different interventions lengthening the time of healing. But it is common practice that

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FIGURE 20. X-ray and computed tomography scan after 12 months showing the healing of both bones.

FIGURE 21. Pictures showing the clinical and functional outcome and the skin aspect after plastic surgery. full color online

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the management of cases needing extensive bone reconstruction, especially in the presence of infection, requires 2 surgical steps in any case, firstly, to remove the infected and necrotic tissue minimizing the risk of recurrence of the infection and, secondly, the delivery of a power osteogenic stimulus promoting a successful bone repair response.

The selection of patients for reconstruction of bone defects and the type of method to be used including the Masquelet technique is important for the final outcome. For this reason we suggest the NUSS classification to identify the patients who could benefit from escalation of a biological-based therapy.

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