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Intramedullary Antibiotic Depot Does Not Preclude Successful Intramedullary Lengthening or Compression

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Summary: The challenging problem of long bone infection and limb length difference cannot be addressed using only an antibiotic-coated nonmagnetic static nail. The combined use of resorbable calcium sulfate and magnetic lengthening nails offers a possible solution to this dilemma, as well as for infected nonunions that require compression. We present a combined technique to treat or prevent infection using femoral or tibial intramedullary antibiotic delivery with an absorbable calcium sulfate depot and concomitant internal lengthening or compression using a nail. Adequate débridement is required in cases of established infection and is a prerequisite for this technique.

Key Words: intramedullary lengthening, intramedullary compression, antibiotic-impregnated calcium sulfate, internal lengthening nail, infection, resorbable calcium sulfate antibiotic depot

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INTRODUCTION

Modern internal lengthening nails provide limb reconstruction surgeons with the advantages of distraction and compression of long bones without the challenges associated with prolonged external fixation.[1–4] Intramedullary (IM) lengthening nails operate using a ratcheting mechanism or rotating magnet to move a telescoping portion of the nail.[5,6] These nails are useful for treating limb length inequality via distraction osteogenesis, although the technology may also be applied to treat a variety of long bone conditions where external fixation has been used previously such as compression and distraction of nonunions.[7–10] Insertion of lengthening nails requires techniques requisite for any IM nail placement.

When a long bone canal is infected, has a history of osteomyelitis, or is at risk of osteomyelitis (eg, prior external fixation), IM instrumentation may not be the first choice, as infection is difficult to eradicate when colonized implants are present.[11–15] Resection of osteomyelitis and posttraumatic infectious bone loss can result in limb length inequality.[16–20] Long bone delayed union or nonunion is also associated with infection.[11,21–23] Even though internal lengthening nails may be useful to correct limb length difference in postinfectious bone loss or to distract or compress infected nonunions, there remains the risk of placing an IM nail into an infected canal. In the orthopaedic trauma literature, antibiotic-coated nonmagnetic static nails are described to mitigate this very concern by using the nails to achieve boney stabilization plus IM antibiotic delivery.[22,24–29]

The combined problem of long bone infection and limb length difference is not addressed by an antibiotic-coated nonmagnetic static nail. A combined approach of local antibiotic delivery to the IM space and internal lengthening nail would be ideal for these challenging limb reconstruction problems. McNalley et al[30] described the use of intramedullary injection of a combination of calcium sulfate and tricalcium phosphate before the insertion of nonmagnetic static nails, allowing passage of the nails through the antibiotic cement. However, the method of IM antibiotic delivery would also have to allow the telescoping nail to still distract or compress despite the antibiotic depot occupying space in the intramedullary canal or around the osteotomy. We present a technique of IM lengthening or compression using a nail plus IM antibiotic delivery with an absorbable calcium sulfate depot. The authors propose that the 2 combined technologies are a feasible approach to antibiotic delivery and IM lengthening/compression.

Operative Technique

Standard IM start point was identified using fluoroscopy, and an entry reamer was used to open the canal. All tibial nails in this series were placed using an infrapatellar

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start point. Although a suprapatellar start point is also compatible with the technique, the surgeon must evaluate whether a long enough cement gun nozzle is available to successfully inject the absorbable calcium sulfate depot into the distal segment.

For nonunion or infection cases, open débridement was performed, and deep culture biopsies were obtained. For lengthening cases, a percutaneous osteotomy was marked with multiple drill holes before reaming. The IM canal was reamed sequentially using standard flexible reamers to 1.5–2 mm greater than the anticipated IM nail diameter. The intramedullary nail was assembled and ready to pass before preparation of the antibiotic cement. Antibiotic-loaded cement spacer (ALCS) was mixed to include 2–5 packs of STIMULAN (Biocomposites Inc, Wilmington, NC) mixed with vancomycin (2–6 g), tobramycin (1.2 g), and/or daptomycin (1 g).[30] The liquid element was added, and several drops of sterile water were titrated to decrease the viscosity of the paste as needed.

The ALCS was then loaded into the supplied cement gun. To ensure adequate passage of the ALCS throughout the intramedullary space, the long nozzle attachment of the cement gun was used. The nozzle was inserted over the guidewire into the distal aspect of the bone from the reamed start hole (Figs. 1 and 2). The guidewire was then removed, and the cement gun was attached to the nozzle. The ALCS was injected while withdrawing the nozzle to ensure placement along the entire canal. Alternatively, a chest tube and Toomey syringe can be used to inject the ALCS. After insertion of the ALCS, the nail was immediately inserted into the canal to minimize the risk of cement hardening, which can limit passage of the nail.

For each case, the magnetic internal lengthening nail (MILN) used was the PRECICE system (NuVasive, San Diego, CA).[1,6] For lengthening cases, the percutaneous osteotomy was completed, and the nail was inserted into the IM canal. For compression cases, the nail was predistracted 13 mm and then passed into the IM canal. As the MILN was inserted into the IM canal, the ALCS was pushed out through the insertion site and through the osteotomy/nonunion site (Fig. 3). Anesthesia was alerted to the potential of fat emboli and O_2 desaturation. Locking of the nail was routine, and blocking screws were used as needed. Per individual surgeon's routine, the MILN was tested using fluoroscopy before skin closure to assure functioning of the magnetic gears (see **Figure**, **Supplemental Digital Content 1**, http://links.lww.com/JOT/B332, which shows testing of the magnetic lengthening device after rod insertion).

Case Series

Case logs of 4 limb reconstruction surgeons at 3 tertiary referral centers were surveyed. Eleven patients were identified as undergoing intramedullary or osteotomy site treatment with antibiotic-loaded resorbable calcium sulfate and placement of IM lengthening or compression nail. Seven patients underwent lengthening, and 4 underwent compression of recalcitrant nonunions. Three patients had known active intramedullary canal infection, 4 had history of osteomyelitis, and 4 had a risk of intramedullary infection (eg, previous external fixation with pin infection, recalcitrant nonunion). In 9 cases, the nail passed without antibiotic depot impeding nail placement. Two cases required repeated reaming, which was followed by successful depot delivery and nail passage. In all 11 cases, the intramedullary telescoping nail functioned as

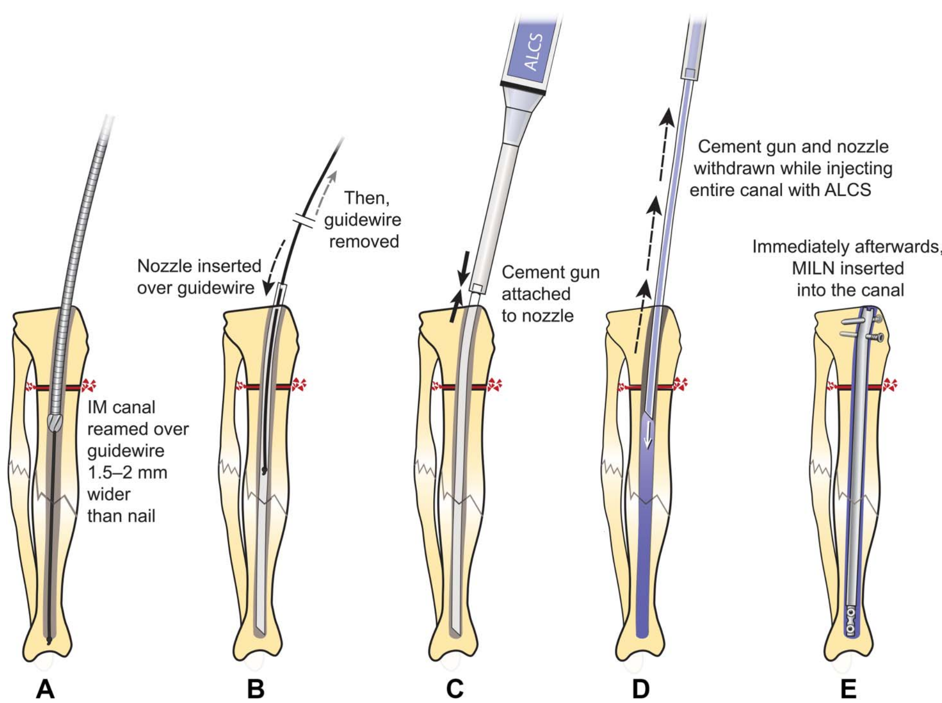

FIGURE 1. A, Guidewire inserted and IM canal reamed over the guidewire 1.5- to 2-mm wider than the selected magnetic internal lengthening nail. B, Cement gun nozzle was inserted over guidewire into the distal aspect of the bone so that it was well past the osteotomy/nonunion. Then, the guidewire was removed. C, Cement gun was filled with ALCS and attached to the exposed end of the nozzle. D, As the nozzle was slowly withdrawn, ALCS was injected along the length of the entire intramedullary canal. E, MILN immediately inserted into the IM canal. Copyright 2020, Rubin Institute for Advanced Orthopedics, Sinai Hospital of Baltimore.

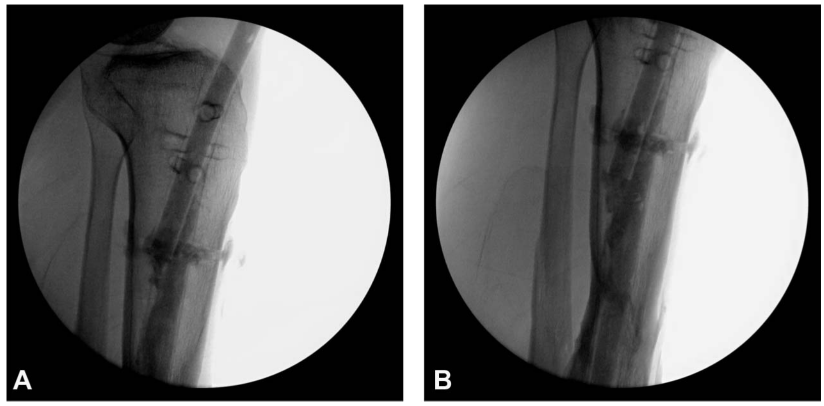

FIGURE 2. A, Cement injection tube in proximal tibia after injecting antibiotic-loaded cement spacer paste into the distal two-thirds of the tibia. B, Continued withdrawal is done to ensure canal fill during cementing. Used with permission from the Rubin Institute for Advanced Orthopedics, Sinai Hospital of Baltimore.

desired with targeted length achieved. Average healing index was 1.36 mo/cm (range, 0.89–2.4 mo/cm).

Patient characteristics are presented in Table 1. Eight patients were diagnosed with nonunion, and 3 patients had posttraumatic and/or postinfectious bone loss resulting in a limb length difference. Three patients had known active infection in the IM canal, 4 had a history of osteomyelitis, and 4 had a risk of or concern for IM infection due to prior external fixation or recalcitrant nonunion. In all cases, the resorbable calcium sulfate consisted of 2–5 packs of STIMULAN mixed with vancomycin (2–6 g), tobramycin (1.2 g), and/or daptomycin (1 g).

In all cases, the PRECICE system was used as the IM lengthening or compression nail. Seven patients required lengthening with the nail, and 4 were treated with the nail for compression at the nonunion site. Nail placement proceeded without difficulty through the STIMULAN in 9 cases (Table 2). The nail placement was impeded in 2 cases where the STIMULAN hardened, requiring rereaming. In both cases, the STIMULAN was noted to have hardened before nail placement. The ALCS remains workable for only a few minutes after mixing, and it has variable setting times depending on the room's temperature and antibiotic content. Repeat reaming was performed to remove the hardened material up to but not exceeding the diameter of the previous reaming. STIMULAN was reinjected with more liquid included in the mixture, resulting in successful passage of the nail. No patients experienced intraoperative drop in oxygen saturation or perioperative pulmonary complication. One patient experienced a perioperative seroma, but no wound complications required treatment beyond observation.

For the 7 patients who underwent lengthening, the mean lengthening goal was 3.9 cm (range, 1.6–6 cm) and lengthening achieved was within 0.2 cm of the goal for 2 of 7 patients and at goal for 5 of 7 patients. Average healing index was 1.36 months per centimeter (range, 0.89–2.4 mo/cm). The compression goals were achieved for all 4 patients requiring nonunion compression (mean, 0.75 cm; range, 0.4–0.9 cm). In all 11 cases, the PRECICE nail functioned without impediment by the STIMULAN. Within the periods of available follow-up, no exacerbation or recurrence of intramedullary infection was recorded.

DISCUSSION

Patients underwent successful limb reconstruction with local antibiotic delivery using calcium sulfate and intramedullary lengthening/compression. For each case, the PRECICE nail that was used to lengthen or compress was able to function without impediment by the STIMULAN calcium sulfate. Although 2 cases required rereaming, the STIMULAN and PRECICE nail combination was still

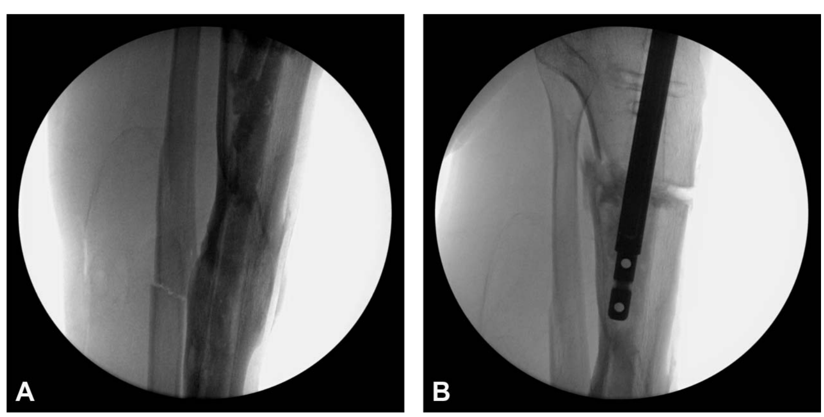

FIGURE 3. A, B, Proximal tibia during nail insertion through the antibiotic-filled injectable bone cement. Care must be taken to proceed quickly to avoid hardening and difficulty with insertion. Used with permission from the Rubin Institute for Advanced Orthopedics, Sinai Hospital of Baltimore.

TABLE 1. Patient Characteristics

Patient	Sex	Age, yr	Diagnosis	Bone Operated	Indication for Antibiotic	Nail Use
1	M	24	Posttraumatic LLD	Tibia	Prior external fixation	Lengthening
2	M	24	Infected nonunion	Femur	Active infection	Lengthening
3	M	30	Postinfectious LLD	Tibia	History of infection	Lengthening
4	M	34	Nonunion	Tibia	History of infection	Lengthening
5	M	41	Nonunion	Tibia	Prior external fixation	Compression
6	M	51	Infected nonunion	Tibia	Active infection	Lengthening
7	F	56	Nonunion	Femur	Concern for infection	Compression
8	M	61	Postinfectious LLD	Tibia	History of infection	Lengthening
9	F	71	Nonunion, radiated bone	Femur	History of infection	Lengthening
10	M	71	Infected nonunion	Tibia	Active infection	Compression
11	F	82	Nonunion	Femur	Concern for infection	Compression

F, female; LLD, leg length discrepancy; M, male.

successfully applied in concert. No patients experienced intra- or perioperative pulmonary complications from the canal instrumentation.

The antibiotic depot STIMULAN is a pharmaceutical grade calcium sulfate that dissolves with time. Compared with polymethylmethacrylate (PMMA), calcium sulfate depots elute antibiotics from surface degradation, allowing for a more consistent level of drug and decreased opportunity for low levels of the drug to support drug-resistant organisms.[31] Calcium sulfate delivered antibiotics have been shown to eradicate osteomyelitis in animal infection models and reduce immature biofilm formation in vitro.[32–35] Studies have also demonstrated orthopaedic infection treatment success as part of local antibiotic therapy and dead space management.[30,32,36–42] Resorbable calcium sulfate is advantageous compared with PMMA because it does not require an additional surgery to remove.[35] Purported disadvantages compared with PMMA are that calcium sulfate depots are not good structural supports. However, in combined limb lengthening and infection cases as presented here, the superior antibiotic delivery properties are desired while structural support is not required. In fact, the resorbable properties of the calcium sulfate are likely what permits the use of a lengthening nail without nail interference or malfunction.

The MILN used in each of these cases is an intramedullary nail with a telescopic segment driven by a rotating magnet. Several nails have been designed for internal lengthening using internal motors or ratcheting mechanisms.[43–45] Approved by the Food and Drug Administration in 2011, the PRECICE nail is driven by a magnet connected through a series of gears to a piston. The magnet is activated by an externally applied controller that is held in place by the patient for a prescribed time and at prescribed intervals.[46] One advantage of the magnetically driven nail is the ability to compress or distract with the same implant. In this series, 7 patients used the PRECICE for distraction, whereas 4 patients underwent compression, demonstrating the advantage of bidirectional capability.

The risk of intramedullary infection with an internal nail may influence some surgeons to opt for external fixation; however, the combined intramedullary nail with intramedullary antibiotic depot could mitigate the risk of internal implants so that the patient and surgeon do not have to accept the risk of prolonged external fixation. Although this report focused on the technical feasibility of combining an internal lengthening nail and resorbable antibiotic depot, recurrent infection was not diagnosed during the period of available follow-up. Additional follow-up and cases are

TABLE 2. Procedure Outcomes

Patient	Challenge Passing Nail	Intraoperative O_2 Drop	Wound Complication	Length/Comp Goal (cm)	Bone Healed at Goal	Postoperative Infection
1	No	No	No	3	Yes	No
2	No	No	No	4.5	Yes	No
3	Yes	No	No	1.6	Yes	No
4	No	No	No	3.2	Yes	No
5	Yes	No	No	0.4	Yes	No
6	No	No	No	5	Yes	No
7	No	No	No	0.9	Yes	No
8	No	No	Yes	6	Yes	No
9	No	No	No	4	Yes	No
10	No	No	No	0.9	Yes	No
11	No	No	No	0.8	Yes	No

necessary to draw conclusions on the control of infection with this approach; however, prolonged external fixation does have an established record of infection risk. The slightly increased healing index noted in these cases is within a reasonable range given the complexity of cases presented.[3,4,9,47–49] We did not experience any postoperative limitations to bone distraction in our series, indicating no negative effect on distraction by the absorbable antibiotic cement.[1] Because there were no recurrent infections, we feel that the potential risk of healing delay is justified by the potential benefit of infection control. Of note, in our series, we did not observe delayed union beyond what has been seen in similar populations.

CONCLUSION

Long bone infection and bone loss are challenging problems that often present together. External fixation is useful in these clinical settings but comes with known disadvantages. Use of internal devices coated with traditional antibiotic-loaded PMMA cement is feasible but does not allow for concomitant lengthening treatment. The combined use of internal lengthening nails with an antibiotic delivery that does not impede the nails telescoping mechanism is an attractive option to avoid the disadvantages of prolonged external fixation while addressing the infectious and length pathologies. This technique is a promising option for successful internal lengthening or compression nail function in the presence of calcium sulfate.

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