Is an Intramedullary Nail a Valid Treatment for Limb-Length Discrepancy After Bone Tumor Resection? Case Descriptions

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ABSTRACT

One of the most frequent outcomes after resection of bone tumors in children is a limb-length discrepancy. An intramedullary nail is a valid method for lengthening the limb. We report our experience with four cases of limb-length discrepancy in the lower limbs several years after the primary treatment of bone tumor resection and subsequent reconstruction. Two femoral PRECICE® nails (NuVasive, Inc., San Diego, CA) were introduced retrograde and two were introduced in an anterograde manner. All four cases healed and showed a reduction of the limb-length discrepancy, early loading, and complete bone osteogenesis. In one case, a reduction of the joint ROM recovered after release of the iliotibial band and a quadriceps release according to Judet's arthrolysis.

INTRODUCTION

Limb-length discrepancy after resection of malignant bone tumors is a common outcome in children. A discrepancy of < 1 cm is acceptable because it is not noticeable and has no risk of complications. However, if the discrepancy is > 2cm, complications such as limping, scoliosis, osteoarthritis of the knee and hip, low back pain, and lower extremity stress fractures can develop.[1]

The closure of growth cartilage of the contralateral limb by epiphysiodesis may represent a possible means to reduce an excessive length discrepancy, but often this technique cannot guarantee an optimal compensation.

An extendible endoprosthesis is a valid alternative that allows a gradual and painless controlled lengthening using an electromagnetic device, but it requires sacrifice of the epiphysis and exposes the patient to the usual complications associated with a prosthesis, including infection and aseptic loosening.[2] Furthermore, it may only be used in patients immediately after resection, and enables a maximum lengthening of 5 cm; further lengthening requires substitution of the prosthesis.

External fixation has long been the standard for simultaneous surgical correction of length discrepancy and deformity, but it is uncomfortable and psychologically not well-accepted by patients or their families. The system exposes patients to complications such as pin-track infection and transfixion of the soft tissue.[3]

An intramedullary lengthening nail can be used as an alternative that is better accepted than external fixation in patients with limb-length discrepancy.[4]

The purpose of this report is to present our results obtained with the use of a PRECICE® nail (NuVasive, Inc., San Diego, CA) in four patients with limb-length discrepancy as a result of oncologic bone resection.

Case 1: 18-year-old female, treated in 2007 by extensive surgery for a high-grade soft tissue sarcoma in the right gluteal muscle. After excision, she developed a compartmental syndrome with a sciatic nerve deficit. The patient underwent radiotherapy and chemotherapy. Despite the surgery, compartmental syndrome and adjuvant therapy, she developed an unexpected

Figure 1. Case 1 - X-ray revealed a 3-cm residual length discrepancy.

Figure 2 a,b. Case 1 - Osteotomy and implant with an anterograde PRECICE® nail in the contralateral femur.

increase in the length of the treated limb compared to the contralateral healthy limb. In 2012, epiphysiodesis of the distal femur and proximal tibial was applied to block growth of the limb. The residual length discrepancy was 3 cm (Fig. 1). Osteotomy and implant with an anterograde PRECICE® nail in the contralateral femur was performed (Fig. 2a,b). A 3-cm increase in length was achieved during the initial postoperative months. When lengthening was complete, partial loading with the use of crutches was allowed. Follow-up with limb x-ray was performed every 30 days to highlight progressive lengthening of the femur and bone formation, with full healing at six months after surgery (Fig. 3a,b). The patient showed improved walking. The nail was removed 12 months after implantation. Currently, she walks without crutches and is aesthetically and psychologically satisfied.

Case 2: 29-year-old male, affected by osteosarcoma of the hip joint and treated in 1998 by en bloc resection of the acetabular region and proximal femur (Fig. 4a,b). Intercalary allograft fixed by a plate between the residual iliac bone and the femur was performed (Fig. 5a,b). In 2004, the patient underwent removal of the plate, allograft and screws after breakage. The residual length discrepancy was about 18 cm. In 2004, lengthening of 8 cm was achieved by external fixation (Ilizarov technique).

In July 2015, a new lengthening of 8 cm was started after osteotomy and implantation of a retrograde femoral PRECICE® nail (Fig. 6). The progressive lengthening of 8 cm was performed over 5 months. Full healing with formation of bone was evident after 11 months (Fig. 7a,b). The patient developed stiffness of the knee with a reduction of knee flexion (0-40°). In July 2017, after about 24 months of treatment with the intramedullary nail, release of the ileotibial band and arthrolysis according to the Judet procedure (dissection of vastus medial muscles from the intermuscular septum from distal to proximal, release of vastus lateralis muscle from distal to proximal and rectus femoris muscle at the anterior inferior iliac spine) and explant of the nail was performed. The knee

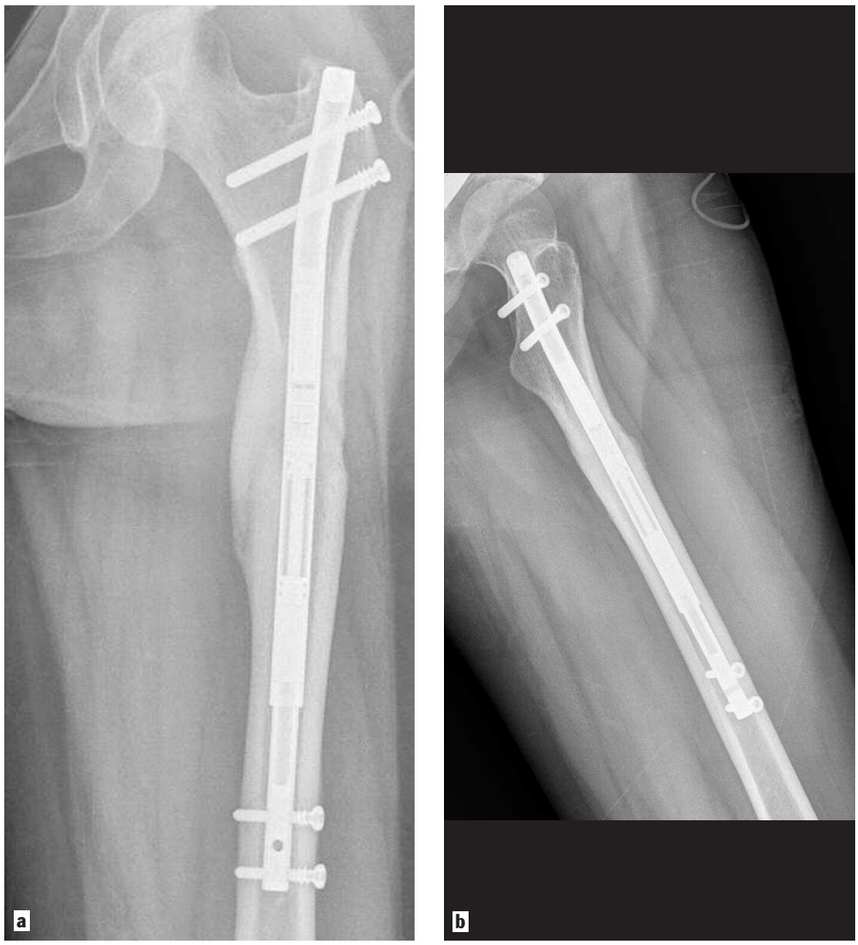

Figure 3 a,b. Case 1 - Bone formation with full healing at six months after surgery.

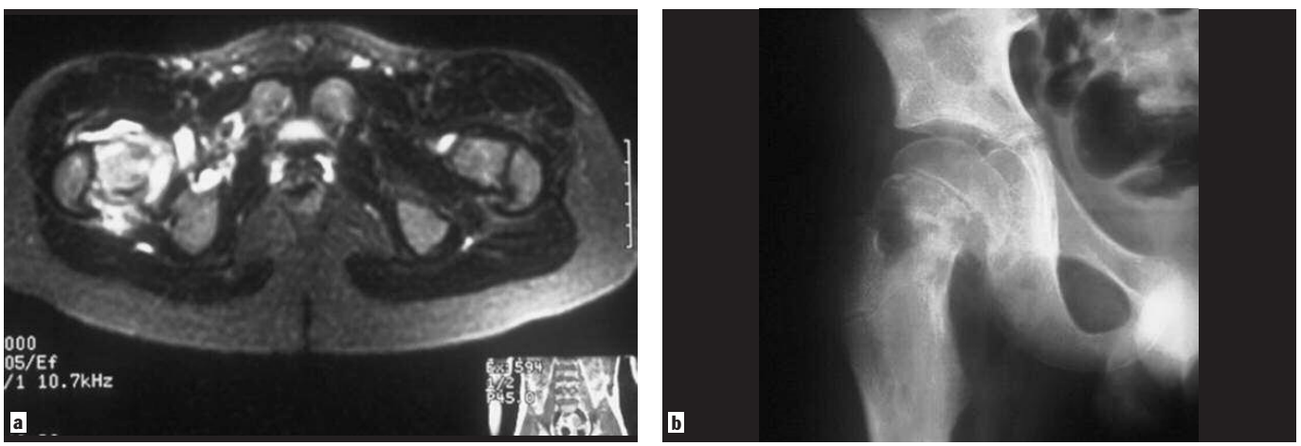

Figure 4 a,b. Case 2 - Osteosarcoma of the hip joint..

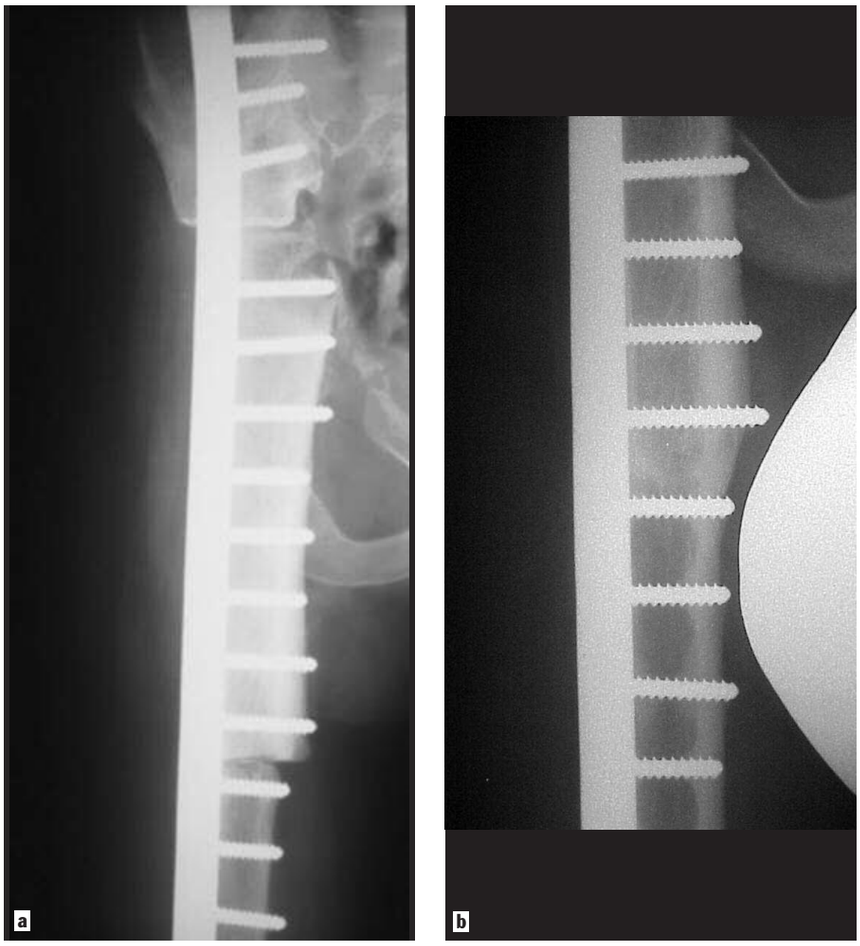

Figure 5 a,b. Case 2 - Reconstruction with an intercalary allograft fixed by a plate between the residual iliac bone and the femur.

was gradually flexed, and residual adhesions were addressed to achieve 90° of flexion. Currently, the patient has a residual length discrepancy of 2 cm, does not present pain and is functionally satisfied. He walks with a rise (insole) to compensate for the 2-cm length discrepancy.

Case 3: 19-year-old male treated with distal femur intercalary resection with epiphysis preservation for osteosarcoma at the age of 10 years in 2007. Reconstruction consisted of allograft + Vascularized Fibula Graft (VFG) + plate and screws (Fig. 8). Neoadjuvant and adjuvant chemotherapy were performed according to the national protocol, and ended in 2008. In 2009, he developed a valgus of the right ankle (donor site) and underwent surgery for tibio-fibular synostosis. In 2011, epiphysiodesis was performed for the right distal femur to block growth of the limb. Nevertheless, he developed a length discrepancy of 5 cm. In 2016, osteotomy was performed and an anterograde femoral PRECICE® nail was implanted after removal of a proximal screw of the plate. Full lengthening of 5 cm ended after 3 months (Fig. 9). At 16 months after surgery, the patient had good function of the hip and knee with preserved articular range. The nail was explanted after 24 months. He does not experience pain, walks without limping and without crutches, and is aesthetically satisfied.

Case 4: 19-year-old male treated in 2011 by right pelvic osteosarcoma resection and reconstruction with a hip prosthesis and cement spacer at another institute. After the reconstruction became infected, the patient was referred to us (June 2015) for removal of the spacer and prosthesis. Progressive growth of the contralateral femur led to the development of a length discrepancy of 14 cm (Fig. 10).

Once the infection was resolved by antibiotic therapy and normalization of inflammatory and clinical indices (September 2016), the patient was subjected to osteotomy and implantation of a retrograde femoral PRECICE® nail. The limb length has since increased by 8 cm, and the residual discrepancy is 6 cm (Fig. 11).

DISCUSSION

Thanks to systemic therapies and improvements in reconstructive methods, limb salvage has almost completely replaced amputation, and has greatly improved the functional, aesthetic and psychological results for patients suffering from bone tumors. The orthopedic surgeon must often face outcomes that occur many years after treatment of the tumor, including a limb-length discrepancy due to normal growth of the contralateral healthy limb.

Distraction osteogenesis or callus distraction (callotasis) uses the same mechanisms to initiate bone formation as in fracture repair after osteotomy.[5] The latency phase is biologically identical to fracture healing.[6] The local trauma of osteotomy induces an inflammatory response, which causes the release of cytokines, interleukins (IL-1, IL-6), which is accompanied by the recruitment, proliferation and differentiation of mesenchymal stem cells from bone marrow. These cells produce a variety of growth factors, such as BMP-2, BMP-4, BMP-6, TGF-β, PDGF and IGF-1.[5,7] The osteotomy gap and its immediate surroundings are inhabited by fibroblasts, chondroblasts and osteoblasts. The length of the latency chosen is usually from 3 to 10 days, depending on the age of the patient, the site (proximal tibial lengthening benefits from a longer latency period compared to that of the distal femur), diagnosis, local factors (infection, irradiation, poor soft tissue envelope), pharmacotherapy and smoking.[8]

The distraction phase of bone lengthening is performed in 1-mm increments (0.25 mm, 4 times per day). Collagen type I predominates, bone matrix proteins are secreted and mineral is incorporated to produce bone.[9] Parathyroid hormone (PTH) plays a central role in the process of mineralization.[10]

Secure fixation using an external fixator system or, in an older child or

Figure 6. Case 2 - Lengthening of 8 cm started after osteotomy and implant of a retrograde femoral PRECICE® nail.

Figure 7a,b Case 2 - Full healing with formation of bone was evident after 11 months.

Figure 8. Case 3 - Intercalary resection in the distal femur with epiphysis preservation and reconstruction with allograft + Vascularized Fibula Graft (VFG) + plate and screws.

Figure 9. Case 3 - Full lengthening of 5 cm ended after 3 months.

Figure 10. Case 4 - After the reconstruction developed infection, we removed the spacer and prosthesis. Progressive elongation of the femur led to the development of a 14-cm length discrepancy.

Figure 11. Case 4 - Implantation of a retrograde femoral PRECICE® nail led to an increase in limb length of 8 cm.

adult, an intramedullary lengthening device, should ensure an optimal local environment for the initial healing response.[8]

The final stage of fracture healing involves consolidation of the fracture and remodeling of the callus. Active weight-bearing also has a positive effect during the distraction phase, and serves to minimize the loss of bone mineral in the native bone being lengthened.[11]

An external fixator is historically the most commonly used system to achieve limb-lengthening, as well as corrections of the axis in different planes. In the 1950s, Ilizarov [12,13] developed a circular external skeletal fixation system attached to bone with tensioned wires. De Bastiani and co-workers used these principles with a mono-lateral frame fixed with half-pins.[14] Their latency period was longer than that of Ilizarov (14 days vs 5–7 days) to allow callus formation before distraction, and was called callotasis. However, external fixation is not only inconvenient for patients, but also increases the risk of pin loosening, superficial pin-tract infections, and deep bone infections.

In addition, cancer patients, who are presumed to have undergone chemotherapy and radiotherapy, are more prone to complications. Radiotherapy used in the treatment of bone sarcomas (more commonly in Ewing's sarcoma) can create adverse effects even after many years, such as increased infections, muscle contracture, ankylosis, joint contracture, osteitis, tendon adhesion, nonunion, pathological fracture, and radiation-induced sarcoma.[15,16] These effects may occur in up to 74% of patients.[17-19]

Therefore, it is likely that distraction osteogenesis is negatively affected by radiation. In a rabbit tibia model, Tsuchiya et al. demonstrated that the quantity and quality of both regeneration and angiogenesis during distraction osteogenesis are decreased by exposure to radiation.[20] Osteotomy should be performed in healthy non-irradiated bone with intact periosteal, where the vascularization and surrounding soft tissues are viable.

Psychological considerations are important in patients who have undergone repeated chemotherapy treatments. Treatment with an external fixator is generally not welcomed by the patient, and this attitude could contribute to poor compliance with the normal daily activities required with an external fixator, such as hygiene and the normal lengthening phases, which could increase the risk of infections that could slow or prevent bone formation.

An intramedullary lengthening nail is a valid alternative to external fixation in selected cases. Instead of requiring months of postoperative external fixation, patients can now undergo limb-lengthening with a completely internal device. Patients who undergo intramedullary limb-lengthening experience less pain, maintain better ROM, and have a lower incidence of infections than those with external fixation.[21]

An intramedullary lengthening nail can be advantageous because it maintains the alignment of the bone segment, eliminates soft tissue scarring from pins or wires, eliminates the risk of pin-tract infection, and yields a better cosmetic result. After the prolongation phase is complete, the nail should be left in place until maturation of the callus.

The initial devices used ratchet mechanisms with rotation of the bone fragments to achieve lengthening (Bliskunov, Albizzia and ISKD). More accurate control of lengthening and a reduction in pain, resulting from manual rotation of the leg required for ratchet progression, was achieved by the use of a transcutaneous electrical conduit powered by external high-frequency electrical energy (Fitbone®, Wittenstein intens GmbH, Igersheim, Germany).[22]

PRECICE® (NuVasive, Inc., San Diego, CA) is a magnet-operated telescopic internal lengthening device with an outer casing of titanium alloy (Ti-6Al–4 V).[23] A generic rare earth magnet is connected to a gear box and screw shaft assembly within the nail. An external remote controller (ERC) contains 2 rotating magnets. When the patient places the ERC on the skin over the magnet within the nail, the rotating magnets cause rotation of its internal magnet, which induces progressive lengthening of the nail. The lengthening capacity is 8 cm.

A standard protocol involves a latency period, after a pre-drilled corticotomy and graduated lengthening of between 0.66 and 1 mm per day. The femoral canal is over-reamed 1.5–2 mm larger than the nail that is inserted. Patients are instructed to be non-weight bearing and physiotherapy is directed at maintaining joint range of motion. Full weight-bearing is allowed after regenerate consolidation has occurred in 3 of 4 cortices.

Calder et al. reported that a small number of nails failed to lengthen immediately following implantation, breakage occurred prior to adequate regeneration, patients have fallen and premature consolidation was observed.[22]

Patient selection is important, since, in patients with a BMI > 35, the ERC may be too far away from the nail to function normally. The manufacturer suggests a weight cut-off of 114 kg (250 lbs) and a maximum distance of 51 mm between the ERC and the nail.[23]

Kirane et al. described 5 patients who required bone grafting due to poor regeneration.[4] Two patients required release of the iliotibial band [20,21] and 2 required gastrocnemius recession following tibial lengthening.[4] During lengthening, Kirane et al. observed a tendency for varus-procurvatum misalignment in proximal femur osteotomies and valgus-procurvatum in proximal tibial osteotomies. This trend was more prevalent in tibial cases. The use of blocking screws (Poller) can help maintain nail alignment;[24] Laubscher et al. reported excellent functional outcomes with fewer complications and greater patient satisfaction, with significantly less pain and better cosmetic results.[25]

In our series, two cases increased the desired length, 3 cm and 5 cm, respectively. In the other two cases, the maximum expected length of 8 cm was reached, leaving a residue of about 2 cm in one patient treated for resection of the hip joint and about 6 cm in the other patient treated for resection of the pelvis with consequent ascent of the femur. We did not observe any breakage or failure of the nails, and the nail was removed in 3 cases. In one case we observed a reduction of ROM from about 110° to about 40° postoperatively at the end of 8 cm of lengthening. In the same patient, an increase in pain in the limb due to compression by the femur against the neo-acetabular area during lengthening was observed. Release of the ileotibial band and release according to Judet led to pain resolution and increased knee ROM from 40 to 90°. In this patient, muscle and tendon components had been altered since the last external fixator lengthening. The advantages of joint recovery and the preservation of articulation are seen in postoperative rehabilitation.

In addition, after bone healing with an intramedullary nail, patients enjoy full loading without the need for external crutches. This is mainly related to protection of the regenerated bone from deformation during healing. Furthermore, the smooth axial distraction produced by a PRECICE® nail creates excellent regenerated bone despite a loss of bone contact at the beginning of the procedure (after osteotomy).[25,27]

None of our patients required bone grafting, bone marrow aspirate injection, bone stimulators, or any other type of augmentation to achieve full healing of the regenerated bone. While Mahboubian et al. observed a low incidence of delayed union,[26] Kirane et al. reported a high percentage of delayed union in tibia lengthening with a PRECICE® nail.[4] Karakoyun, Horn and their respective co-workers described rapid healing with the use of retrograde femoral intramedullary lengthening nails for the correction of acute deformity.[28,29] Use of a percutaneous osteotomy with minimal periosteal stripping and a predrilled osteotomy ensures deposition of the reamings at the lengthening site, which may contribute to healing.[28,29]

CONCLUSION

Limb-length discrepancy is a real and frequent outcome many years after limb salvage and oncologic reconstruction. Our limited experience confirms that gradual lengthening can be achieved using a retrograde femoral PRECICE® nail. PRECICE® nail allows progressive and complete loading after the distraction phase. Moreover, this system is better accepted by patients who have undergone oncological treatment such as chemotherapy, thanks to the greater ease of postoperative management. STI

AUTHORS' DISCLOSURES

The authors have no conflicts of interest to disclose.

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