7

External Fixators for Limb Lengthening

Roberto C. Hernández-Irizarry
and Stephen M. Quinnan

General Principles

Distraction osteogenesis (DO) refers to the process of forming new bone at the site of a corticotomy/osteotomy undergoing gradual distraction [1]. The new bone that forms during the process of DO is termed "regenerate." Regenerate formation begins as bony fracture callus at the site of the cut in the bone and, with the application of gradual distraction, forms a column of new bone extending from this site primarily through a process of intramembranous ossification [2, 3]. When DO is used to make new bone to treat a segment of bone loss, it is called bone transport. When DO is used to lengthen an extremity, it is often termed limb lengthening or distraction histogenesis. The term distraction histogenesis is preferred in this scenario because it emphasizes that in addition to new bone formation there is also generation of vascular, nerve, and other soft tissue structures.

DO is most often performed with external fixation. The process begins with application of the external fixator. An Ilizarov circular external fixator is the most classic method, but many types of external fixators can be used, including other varieties of circular fixation, monolateral rails, hexapods, and cable constructs. The chosen construct is then used to achieve angular correction, lengthening of the limb, and/or transportation of the bone. Once the external fixator is applied, the next step is to cut the bone with either a corticotomy or osteotomy. Following completion of the operation, DO progresses through three phases; latency, distraction, and consolidation. The latency period is usually 3–7 days during which early bony callus forms and neovascularization of the bone at the corticotomy site occurs. The distraction phase then begins, usually at a rate of 1 mm per day, until the desired length and angular correction is obtained. The consolidation phase follows during which calcification and maturation of the regenerate bone occur.

Applying an external fixation construct that is mechanically sound and stable throughout the process of DO and performing an appropriate bone cut are critical to the success of the procedure. Early descriptions of DO paid a great deal of attention to the concept of a corticotomy in which the periosteum and endosteal bone along with their blood supply were preserved in their entirety [4]. This method therefore aimed to cut just the bony cortex whether performed with a drill, osteotome, or Gigli saw. The importance of the true corticotomy has been challenged over time as being both impractical and unnecessary

R. C. Hernández-Irizarry
Department of Orthopaedic Surgery, Jackson Memorial Hospital, University of Miami Miller School of Medicine, Miami, FL, USA

S. M. Quinnan (✉)
Department of Clinical Orthopaedics, University of Miami Miller School of Medicine, Miami, FL, USA
e-mail: squinnan@med.miami.edu

© Springer Nature Switzerland AG 2020
B. D. Crist et al. (eds.), *Essential Biomechanics for Orthopedic Trauma*,
https://doi.org/10.1007/978-3-030-36990-3_7

to achieve a successful result. It has been demonstrated that an osteotomy in which the cancellous bone is also cut and the periosteum separated can also form excellent regenerate. However, the core concept embodied in the original description of a corticotomy—that performing a low-energy bone cut preserves local vascularity and minimizes damage to the periosteum—remains essential to a successful result. The modern concept of a corticotomy/osteotomy is thus focused primarily on the critical aspects of minimal energy, minimizing damage to local blood supply and preventing thermal injury. There are a number of methods that have been shown to achieve this successfully, including a multiple drill hole osteotomy completed with methods such as rotational osteoclasis, inserting an osteotome at the corticotomy site and rotating it 90°, or using a Gigli saw [5]. Although no human studies are available, animal models show delayed consolidation when using higher-energy techniques more prone to burning the bone (such as an oscillating saw) to perform the osteotomy, and therefore this technique is highly discouraged [6]. The metaphyseal region is an ideal site to perform a corticotomy because of the large trabecular surface and robust vasculature that often leads to a large amount of regenerate, although other regions of the bone can also be used when necessary [7].

Prior to starting the distraction phase, a postoperative latency period is advocated [4]. This is usually 3–7 days during which early callus formation and local neovascularization occur. The exact length of the latency period should be individualized for each patient based on physiologic factors. Once begun, distraction at the osteotomy site typically proceeds at 1 mm/day. This rate was established by the work of Ilizarov, who found that in dog studies 0.5 mm/day of distraction can result in premature consolidation, while 2.0 mm/day produced poor regenerate [7]. Although 1 mm is most common, the rate may need to be altered due to patient factors. For example, young children may require a faster rate to prevent premature consolidation. In contrast, patients with multiple comorbidities such as diabetes and smoking may require a slower rate to allow for good regenerate formation that does not outpace the neovascularization occurring at the scene of the regenerate.

In addition to rate, rhythm is also an important aspect. Ilizarov demonstrated that more frequent and shorter distance distractions lead to improved regenerate formation. However, dividing the distraction into a large number of separate distractions is impractical, and so the recommendation is made to use a rhythm of four separate one-fourth millimeter turns per day, which is practical and also achieves excellent bone formation. It is notable that comparisons between regenerate formed using Taylor Spatial Frame (TSF) (Smith & Nephew, London, UK) distraction at 1 mm/day in one increment and that with an Ilizarov at one-fourth mm 4 × per day have failed to demonstrate a difference in quality of regenerate bone formation. This is encouraging when it is necessary to use the less frequent protocol, but it is best to respect the more scientifically rigorous data from the basic science studies and use the more frequent rhythm when feasible. Following completion of distraction, the new bone calcifies and remodels to form a cortex and medullary canal [8–10].

Distraction also induces morphologic changes in surrounding soft tissues. Muscle tissue undergoes hypertrophy and hyperplasia. Neoangiogenesis occurs in the direction of the tension vector. Nerves to innervate the growing and new tissue develop as well. Different tissues have different biologic compositions, and thus the "optimal" distraction rate is different for each tissue than it is for the bone. This difference is one reason for nerve palsies and joint contractures, which will be discussed later.

Biology of Distraction

The classic experiments done by Ilizarov provide helpful insight into the biochemical, mechanical, and biophysical processes that are involved in DO. After corticotomy, a local inflammatory response facilitates new bone formation during the latency period. This response is multifactorial but primarily consists of migration of pluripotential cells and the secretion of cytokines and growth factors to guide osteogenesis. During distraction, regenerate has a characteristic histologic appearance with five zones that resemble a growth plate [11]. The central portion is a growth zone, with fibroblast-like cells that secrete collagen. These collagen fibers align parallel to the distraction force being applied. This zone is bordered on either side by a mineralization front, with osteoblasts producing osteoid in a manner that resembles intramembranous ossification. This occurs without any endochondral ossification when a stable, rigid construct is used. If there is some instability, the process is slowed and more closely resembles endochondral ossification or even pseudoarthrosis if gross instability is present [7]. Between the mineralization front and the surface of the native corticotomized bone lies a zone of microcolumn formation. Primary bone is mineralized in this zone, which later in the consolidation phase continues to cross-link and remodel all zones of the regenerate. By this mechanism, the distraction gap is replaced by mature, remodeled bone with distinct medullary canal and cortices, in accordance with Wolff's law [11].

Several signaling molecules have been identified to play an important role in the process of DO. They are categorized as (1) pro-inflammatory cytokines, (2) transforming growth factor-β (TGF-β) and bone morphogenetic family of proteins, and (3) angiogenic factors [12]. Pro-inflammatory cytokines initiate the repair cascade after corticotomy. Interleukin-1 (IL-1), tumor necrosis factor-α (TNF-α), and IL-6 are elevated in the latency and distraction phases and play a significant role in the process of intramembranous bone formation and remodeling [13, 14]. Insulin growth factor-1 (IGF-1) is elevated early in the distraction phase, and levels decrease once distraction stops, suggesting a key role in osteogenesis [15]. TGF-β has been found to support new bone formation, and its levels are elevated during the early distraction phase [16, 17]. Bone morphogenetic proteins (BMPs) are also upregulated, and high levels are maintained throughout the distraction phase [18–20]. BMP-2 has been shown to accelerate the rate of bone formation in rabbits [20]. Vascular endothelial growth factor (VEGF) is recognized as an important stimulator for angiogenesis, and levels are increased during the distraction phase. Angiogenesis facilitates the diffusion of signaling molecules during DO.

Mechanotransduction plays an important role in osteogenesis by triggering cell signaling and gene expression [21, 22]. Integrins are key in cell signaling and are the primary pathway by which mechanotransduction induces stem cell differentiation [23, 24]. Mechanical load by the distractor also stimulates the osteoblastic production of extracellular matrix proteins, such as collagen type I and osteocalcin [17].

Finally, the fluid flow theory helps to explain how mechanical load translates into bone remodeling. The theory proposes that load forces interstitial fluid to flow around the bone microarchitecture, creating shear strain. This initiates the downstream cascade of cell signaling, mainly through the activity of nitric oxide (NO), prostaglandins, and Wnt [25, 26]. Wnt is upregulated by shear stress, which leads to osteoblastic bone formation and inhibition of osteoclast formation [27, 28].

External Fixator Construction

The goals of using external fixation in bone transport are to maintain stable bone alignment and to allow adequate compression of bone at the docking site to encourage healing [1, 29]. The construct should be stable enough to permit weight-bearing and to allow as normal as possible functioning of the limb and adjacent joints. Weight-bearing and limb use help support local neovascularity and facilitate bone healing [30]. Stability of the construct is multifactorial [30, 31], and general concepts of the biomechanics of external fixator constructions and fixation block composition are discussed in earlier chapters. These concepts apply equally when DO is being performed, but in this circumstance, there are a number of additional considerations relevant to creating a construct that will achieve the reconstructive goals. DO can be used for limb lengthening, bone transport, or a combination of both with osteotomies proximal, distal, or both. The construct employed depends primarily on the goals of the procedure in terms of the location of malangulation, bone defect, planned lengthening, and planned osteotomy(s).

There are many external fixator configurations capable of achieving stable fixation and successful DO for limb lengthening. Circular fixators are most often used because they are mechanically the soundest and allow great flexibility in obtaining and maintaining stability. Ilizarov discovered DO and pioneered the use of ring fixation to apply this method. He used a frame constructed of threaded rods attached to stainless steel or carbon fiber rings. These rings were fixed to the bone with high-tension wires both proximal and distal to the zone of injury and/or osteotomy site (Fig. 7.1a). Limb lengthening can be performed at the site of an osteotomy by distracting the rings using telescopic rods such as seen in Fig. 7.1a, b.

Another circular fixation construct well suited to performing limb lengthening is a hexapod fixator such as seen in Fig. 7.1c. This construct uses six struts instead of four threaded rods to stabilize across the distraction site. The advantage of this method is that it allows for a simple method of deformity correction and/or correction of angulation that develops during lengthening caused by either an imperfectly mounted fixator or a drift of the transport segment away from its original alignment during transport caused by instability of the transport segment fixation and/or uneven soft tissue tensions. Hexapods use a computer program generated from information about the frame and osteotomy that informs the patient about which struts to turn and how often. Hexpods

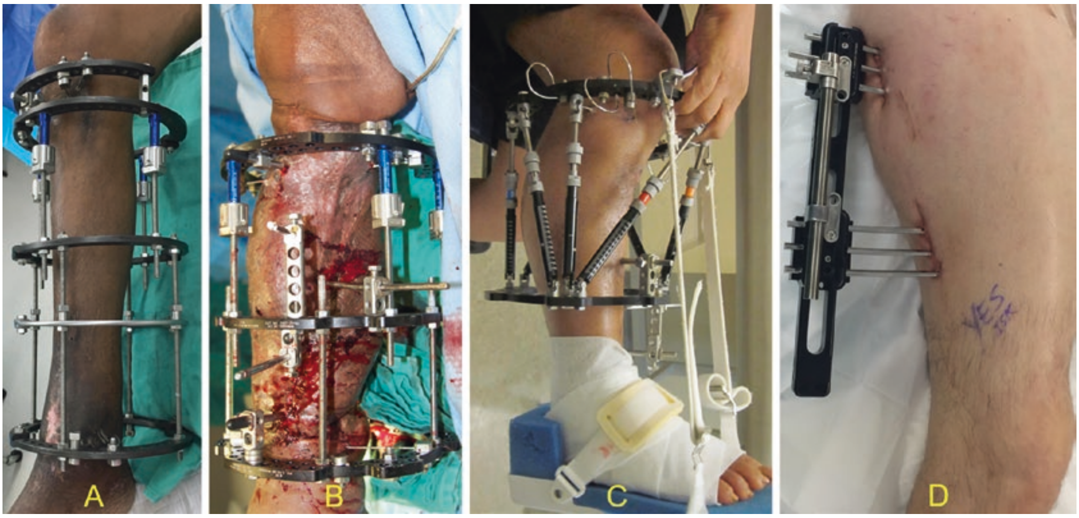

Fig. 7.1 Frame constructs used for lengthening. (**a**) Ilizarov external fixator constructed as both a lengthening and bone transport frame. Fixation rings are carbon fiber and the transport ring is stainless steel. The rings are fixed to the bone with high tension wires and hydroxyapatite-coated half pins. Lengthening is motored by the telescopic rods (often referred to as "clickers"). The clickers are designed to motor the lengthening with the patient making turns in one-fourth mm increments. (**b**) Ilizarov-type external fixator with stable block of two rings distally connected by threaded rods and connection of top two rings with telescopic rods. Distraction occurs between the proximal and middle rings driven by the telescopic rods. (**c**) Hexapod external fixator (specifically, a Taylor Spatial Frame (TSF) in this example) being used as a lengthening construct. There are proximal and distal fixation blocks each built off of a single ring with fixation widely spread. Distraction is motored by the TSF struts between the rings. The struts move in 1 mm increments when turned by the patient. This construct allows for simultaneous correction of malalignment while performing limb lengthening. (**d**) Monolateral rail external fixator construct. Limb lengthening is driven by the distraction rod placed between the two stable bases. The distraction rod turns in one-fourth mm increments when turned by the patient using a special wrench. This construct is mechanically disadvantageous because the pins are all in the same plane, but is much better tolerated in the femur than ring fixation

can be highly advantageous in certain circumstances, but it is especially important to assure sound biomechanics when using these devices.

Another type of external fixator that is commonly used for limb lengthening is a monolateral rail (Fig. 7.1d). Rails have the mechanical disadvantage that all pins are parallel and in the same plane and are therefore a less stable construct than a multiplanar construct. In addition, because all of the fixation is performed with half pins, there is a cantilever effect with a tendency toward deformity away from the pins (e.g., tendency toward varus in the femur as lateral pins bow apart). However, the pins and frame are manufactured to be especially robust in order to help prevent this. This tendency of the monolateral rail frames having been recognized, many of these systems have the ability to angulate either at the beginning or at the end of distraction to compensate for this tendency. The major advantage of a monolateral rail is that it is much easier for the patient to tolerate than a complete ring around the limb, especially in the femur [32–34].

DO for bone transport or lengthening combined with bone transport requires additional consideration in regard to frame construct [35]. Transport with a traditional Ilizarov fixator occurs at an intermediate ring, traditionally stainless steel, with distraction driven by square nuts such as seen in Fig. 7.2a. The intermediate ring moves along the threaded rods "rails" and drags the transport segment with it. A column of new regenerate bone forms behind the transport segment, and eventually the transport segment crosses the defect to meet the opposite bone end. Half pins can also be used to fix the transport segment to the bone and have the advantages of traversing less soft tissue and application with greater crossing angles than wires (Fig. 7.2b). However, half pins have larger dimensions and cut a larger path through soft tissue during transport and are therefore less soft-tissue-friendly in this circumstance.

Many types of rings are available with variable thicknesses and made of differing materials. These rings can be connected to threaded rods and function the same as an Ilizarov fixator. For this reason, the author refers to a construct of rings connected with threaded rods as an Ilizarov-type construct and then names the type of rings, for example, "Ilizarov-type construct with Taylor Spatial Frame rings" (Fig. 7.2c). Transport using an Ilizarov-type construct with hexapod rings is straightforward with progression along the threaded rods, but there is a big advantage in that the threaded rod segments crossing the docking site can be changed to struts at the time of docking. The struts then allow for easy adjustment of bone end alignment at the docking site without the need for strut adjustments or changes during transport.

An alternative construct that allows for bone transport and limb lengthening is the bifocal frame. Fundamentally, a bifocal transport frame distracts an osteotomy at one location and compresses the gap to bring bone ends together at another site. The lengthening is typically motored by either telescopic rods or square nuts, and compression is performed with either square nuts or struts (Fig. 7.2d). The bifocal frame with telescopic rods at the distraction site and struts at the docking site is convenient because it allows for biologically friendly distraction with flexibility to adjust docking site alignment without frame modification at the time of docking. This is a powerful construct but requires many adjustments at two levels by the patient and surgeon during the reconstruction.

A special type of bifocal frame is the "double-stacked" hexapod (Fig. 7.2e). The double-stacked frame is advantageous because there is maximum adjustability of both the regenerate bone segment and the docking site. However, this method of transport requires the greatest number of adjustments by the patient and strut changes by the surgeon, is by far the most expensive, has the most hardware obscuring radiographic evaluation, and is mechanically less rigid. For these reasons, the authors generally reserve this construct for special situations that require additional flexibility in alignment such as soft tissue coverage, deformity correction with multiple CORAs (center of rotation of angulation), or malalignment between the segments across regenerate column at the end of transport. An alternate construct is the cable transport frame. Figure 7.2f shows an example of


A
B
C
D
E
F

Fig. 7.2 Ilizarov frame variations for lengthening and transport. (**a**) Traditional Ilizarov external fixator frame with rings attached along long threaded rods that run the full length of the construct. Note the transport ring is stainless steel even when the fixation rings are carbon fiber. Square nuts are used as motors. Typically, there would be two carbon fiber rings distally or the addition of a foot plate. A foot plate was originally attached but was removed in clinic 6 weeks after transport docking. The patient has a typical dorsiflexion splint attached to the frame. (**b**) Ilizarov transport with half pins fixing the bone to the transport ring with square nuts as the motor. Distal fixation with metaphyseal wire cluster after staged foot plate removal in clinic. (**c**) Ilizarov-style transport frame with long threaded rods attached to the rings. This construct uses Taylor Spatial Frame (TSF) hexapod rings instead of Ilizarov rings. This construct allows for adjustability at the end of transport because the threaded rods can be cut and struts applied across the docking segment. (**d**) Bifocal transport frame with telescopic rods "clickers" proximal and hexapod TSF struts distally. This allows for biologically optimal cadence of 4 × 0.25 mm movements per day but great flexibility in controlling alignment at docking. This construct allows for adjustability without revising frame components but requires many more daily adjustments than in (**c**). (**e**) Double-stacked hexapod with TSF struts. Maximizes adjustability of alignment for both transport and docking segments. (**f**) Balanced cable transport external fixator frame. Allows bone transport with no pins or wires dragging through the skin. TSF struts with the shoulder bolt removed are used as motors in this example

a balanced cable transport frame with internal cables pulling the transport segment [36]. Note the absence of pins and wires in the transport segment and the attachment to a strut proximally used to motor the transport. The chosen construct for any given patient should be tailored to the specifics of the bone available for fixation, soft tissue constraints, where the osteotomy is planned, and whether lengthening and/or transport is planned.

Mechanical Modulation to Encourage Bone Formation

Altering the mechanical load on the affected limb can modulate the regenerate. Early weight-bearing has been a mainstay for encouraging better bone formation and remains a cornerstone of treatment. As discussed earlier, increasing the frequency of distraction while decreasing the amount of lengthening at each interval may shorten the external fixation index [31, 37]. However, currently available methods make greater than four incremental turns per day impractical and have not been clinically demonstrated to be of significant benefit to justify the added difficulty. Techniques such as compression after over-distraction, "pumping the regenerate," have been described but have not demonstrated clear benefit in increasing the rate of regenerate healing. In contrast, "pumping of the regenerate" can be a useful method of salvage when poor regenerate is formed early in the distraction phase. In this scenario, the transport segment is compressed back to or near its original position and then gradually distracted again. This can often encourage a greatly improved regenerate to salvage a poor start.

Dynamization, as classically described, has been used since the original descriptions by Ilizarov in order to encourage fracture healing and regenerate consolidation. In its original form, dynamization meant that the nuts holding the stable ring on one side of the fracture or regenerate were made loose and backed up by a small amount (~2 mm). This had the effect of loosening the frame and allowing a small amount of dynamic compression at the fracture site. Dynamization was performed to encourage additional callus formation or as a final stage prior to fixator removal. The process also acted as a clinical test to see how the patient felt with an unstable fixator. If they could walk without pain, then it likely meant it was safe to remove the fixator. This method is still commonly used today as is a process of dynamization where frame components are gradually removed in order to shift weight-bearing forces from the fixator to the bone. The introduction of the TSF as the first hexapod complicated the ability to dynamize the external fixator. It was no longer possible to back up and stabilize the nuts as had been possible with an Ilizarov-type fixator. However, *dynamization* continued to be a highly employed concept but with a new method of application. The hexapod could by dynamized by either removing fixation components to provide more flexibility or by unlocking the struts, which completely destabilizes the fixator across the fracture site. *Dynamization* performed by unlocking the struts is a good test of fracture and regenerate healing but is not helpful for encouraging bone formation during the consolidation process. To address this problem, there are reports of special shoulder bolts designed to allow a true axial dynamization of hexapod external fixators in the same manner that an Ilizarov frame could be dynamized, but to date these are not widely available [31]. Consequently, the exact meaning of the word *dynamization* has become somewhat confused, as the same word is used to describe very different mechanical processes. However, the principle of fixator destabilization late in the reconstruction process remains a common element of the treatment process.

More recently, there has been compelling basic science evidence that challenges the usefulness of dynamization as a method to encourage final healing. This evidence supports a new paradigm called “reverse dynamization” [38, 39]. Reverse dynamization relies on the principle that early on in fracture healing there is a soft and flexible hematoma that is converted to a cartilaginous callus. Callus formation during these early stages is encouraged by fracture micromotion, and larger amounts of relative motion of the bone ends are well tolerated. Later stages of fracture healing occur as softer bone is replaced by more rigid organized mature bone formation. This stage is sensitive to relative motion of the bone ends and is harmed by larger amounts of motion and is thus aided by greater construct stability. The reverse dynamization concept therefore advocates for making the fixator construct more stable during the consolidation phase and after the end of the initial phases of callus formation in order to optimize the speed of bony healing. Therefore, instead of removing components in late healing, the surgeon would add threaded rods or attach additional points of fixation after the initial healing stages in order to encourage final healing. Reverse dynamization is a relatively new concept and is awaiting validation from clinical data but has shown anecdotal success in the authors’ experience.

The use of noninvasive physical modalities has become a popular adjuvant to encourage bone healing. One such intervention is the use of low-intensity pulsed ultrasound (US). US is theorized to modulate signal transduction at the cellular level by inducing a pressure wave [40]. US has been shown to increase callus formation during fracture healing [41]. This potential has led researchers to investigate its use during DO. A recent meta-analysis suggests that US could possibly reduce the healing index of DO by 15 days/cm in tibia defects, and it is more effective when used during distraction and early consolidation phases [42]. However, a more recent study did not show a statistical difference in reduction in treatment time, radiographic or histologic fill length, or bone density increase [43]. The limitation in interpreting efficacy of US results from the heterogeneity of patients reported, publication and selection bias, and other confounding factors.

Biological Adjuvants

The role of BMPs in osteogenesis has been previously described. Recombinant BMP-2 and BMP-7 have been used in adults as adjuvants or substitutes for bone graft. Although not approved by the US Food and Drug Administration (FDA) for DO, off-label applications have been reported for patients with poor regenerate and persistent nonunion [44].

Platelet-rich plasma (PRP) contains osteoinductive growth factors and has been investigated in combination with bone marrow grafting for bone formation in DO [45, 46]. The results of these investigations showed increased cellular activity in rats, but there was no difference in osteoblast activity. There are also no clinical data to support the use of PRP as an adjunct to improve regenerate bone formation. Anticatabolic agents (i.e., calcitonin, diphosphonates) have also been used in off-label cases in pediatric patients with poor-quality regenerate with eventual healing [47, 48]. However, there are limited data to support the efficacy of these agents, and in fact the use of an agent that retards bone turnover seems counterproductive given that callus and regenerate maturation rely on bone turnover as part of the natural healing process.

Augmentation with bone marrow aspirate concentrate (BMAC) has also been proposed. Percutaneous insertion of marrow cells has been shown to be a safe and effective approach and to accelerate bone regeneration during DO [49, 50]. This technique has also been used as an adjuvant to treat segmental long-bone defects [51]. Another study reported the use of BMAC in femur and tibia lengthening, with faster femoral than tibial healing, with no difference in the number of cells present in the concentrate. These results suggest that the effect of BMAC on the bone regenerate may be multifactorial and probably related to the local milieu at the transplanted site and not the actual number of cells. However, more studies are needed to optimize this technique.

Complications

DO with external fixation provides a reliable tool for lengthening of an extremity and treating even large bone defects [52]. However, there are significant challenges to consider. The related problems of superficial cellulitis, deep pin infection, and loosening have improved with hydroxyapatite-coated (HA) pins but remain the most common problem for both surgeon and patient [53, 54]. Pin site cellulitis causes increased pain and the need for additional clinic visits and infrequently may require hospital admission for IV antibiotics or pin removal/exchange. Most cases of pin site cellulitis are successfully treated with a short course of oral antibiotics and do not compromise the final outcome of reconstruction, but the short-term burden for both patient and surgeon is significant. Apart from cellulitis, HA half pins can mature to be painless, but discomfort around wire sites generally persists to some degree until their removal. This discomfort can lead to greater pain medication use during treatment [55].

A related concern is that irritation from points of fixation may lead to discomfort that discourages joint range of motion and may lead to joint contractures [56]. Joint contracture can also occur because of the pull on muscle-tendon units and the translocation of muscular origins that can occur during the process of DO. Joint contracture can be one of the most difficult problems to deal with during limb lengthening and bone transport. In fact, loss of motion and joint stiffness are the most likely cause for long-term problems following DO. Great care must be taken during treatment to encourage range of motion and physical therapy. In addition, early recognition and intervention for a developing contracture is an important part of the treatment.

The weight of the external fixator can be a challenge for some patients, such as the elderly, with limited strength reserve. Therefore, the weight of the external fixator construct should be considered carefully in this patient population and construct choice modified as needed.

Shortening and angulation of the regenerate is a significant complication. This occurs when the fixator is removed prior to complete consolidation of the regenerate. When this occurs, it is almost always impossible to acutely correct without an osteotomy, as the regenerate tends to rapidly consolidate in this scenario. Correction requires a return to the operating room for an osteotomy and surgical correction of angulation. This is best prevented by assuring adequate regenerate healing prior to frame removal by obtaining radiographic confirmation of healing, waiting an adequate and expected time for healing (generally no less than 1.5 months/cm in an adult), and testing with frame dynamization prior to removal.

Nonunion of the regenerate typically occurs when there has been poor compliance with the distraction process. This can be treated with bone grafting and other methods described above. Another alternative is to consider conversion to internal fixation, but it should be emphasized that this must be undertaken with great care and respect for contaminated pin and wire sites. Multiple means such as a pin holiday and antibiotic cement-coated implants can be used to help moderate this risk when this approach is necessary. However, generally speaking, conversion to internal fixation at the conclusion of limb lengthening or bone transport should be considered a salvage procedure with significant attendant risks. The exception to this is when the initial construct was applied to avoid contamination from the fixator components in the path of the staged internal fixation, in which case routine conversion has been shown to carry low risks.

Integrated Techniques

To address some of the challenges of DO with external fixation alone, methods that integrate the use of internal fixation have been proposed. Techniques include lengthening over an intramedullary nail (LON) [57–60], lengthening and then nailing (LATN) [61], transport and then nailing (TATN) [36], and lengthening over a plate (LOP). LOP has had mixed results and is generally not preferred. LON, LATN, and TATN have all proven to significantly decrease external fixation index or days in ex-fix/cm new bone (EFI). LATN and TATN have also substantially decreased the bone healing index or months/cm new bone (BHI). Disadvantages of using internal hardware include the potential for deep infection, increased surgical time, blood loss, added cost, and the added technical difficulty.

Lengthening Over a Nail (LON)

With this technique, an intramedullary nail is inserted after the corticotomy is performed. A frame is then applied after the nail is inserted with care taken to keep fixation points remote from the deep hardware. The external fixator is used to lengthen over the nail (Fig. 7.3). When the desired length is achieved, the nail is locked,

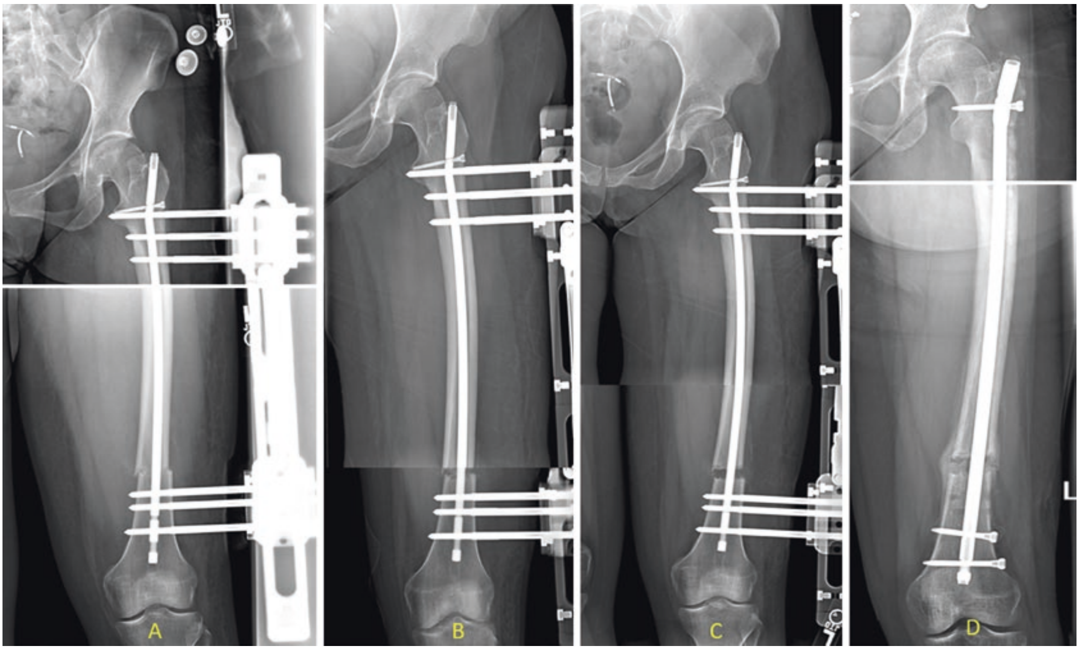

Fig. 7.3 This is an example of lengthening over a nail. This patient had residual limb length discrepancy after being treated for Perthes as a child. She had failed orthotic treatment and had persistent back pain and a limp. (**a–d**) An antegrade nail was placed in the femur with a distal corticotomy in the diaphyseal-metaphyseal junction. The limb was subsequently lengthened with a monolateral frame

and the fixator removed [57, 59, 60, 62]. EFI is decreased while providing the regenerated bone support in the consolidation phase, although the BHI is not significantly different than the classic Ilizarov technique [60, 63]. The deep infection risk must be considered, as the rate has been reported to be 14%. Another disadvantage is the need to use smaller-diameter nails to allow sliding of the bone and to allow concomitant placement of an external fixator. This may lead to suboptimal stability. Any deformity must be corrected acutely with this technique, which may compromise bone healing.

Lengthening and Then Nailing (LATN) and Transport and Then Nailing (TATN)

LATN is the technique of using a ring fixator to perform limb lengthening followed by placement of an intramedullary nail at the conclusion of the distraction phase with removal of the external fixator. The initial external fixator is constructed in such a manner that it avoids placing contaminated pins and wires in the path of the intramedullary nail that is placed later on. The regenerated bone is supported by the nail during the consolidation phase. The EFI is decreased from 45–60 days to approximately 14 days/cm, and the BHI is decreased from 1.5–2.0 to 0.9. The time in frame is therefore 75% less, with healing in 50% less time. Both LATN (Fig. 7.4) and TATN (Fig. 7.5) have shown identical results in terms of effect on EFI and BHI. One concern of using an intramedullary device after prolonged time in external fixation is the risk of deep infection. This risk, however, has been reported to be lower than 5% and as low as 0% in some studies [36, 61, 64]. This technique can be used for pure lengthening, transport, or combined cases.

Meta-analysis of the results of bone defect management indicates that integrated methods appear to be the most effective treatment for bone loss and limb length discrepancy, with LATN and TATN having significant advantages over all other methods. Because there are far more data on traditional methods, additional data on integrated methods are necessary before any solid conclusions can be reached.

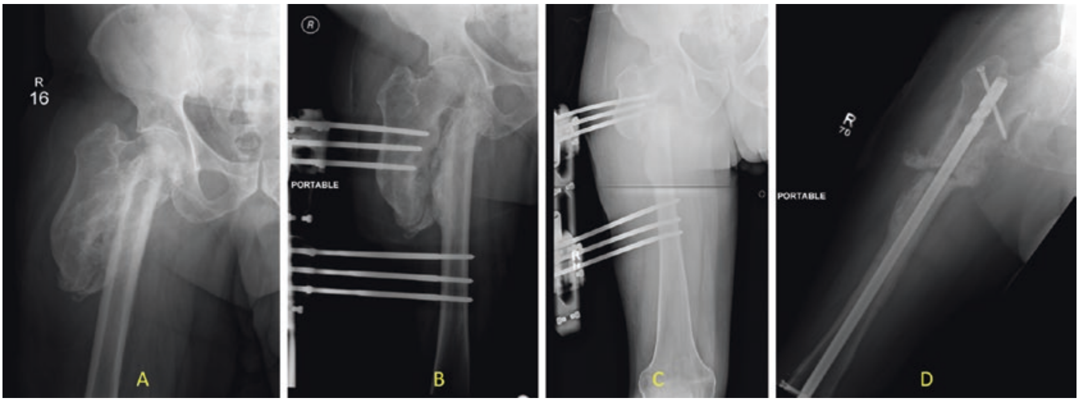

Fig. 7.4 This patient had suffered a right femur fracture treated without surgery in another country (**a**). The length of the femur was re-established using a monolateral external fixator (**b**, **c**). After length was restored, the frame was removed, and an intramedullary nail was placed (**d**)

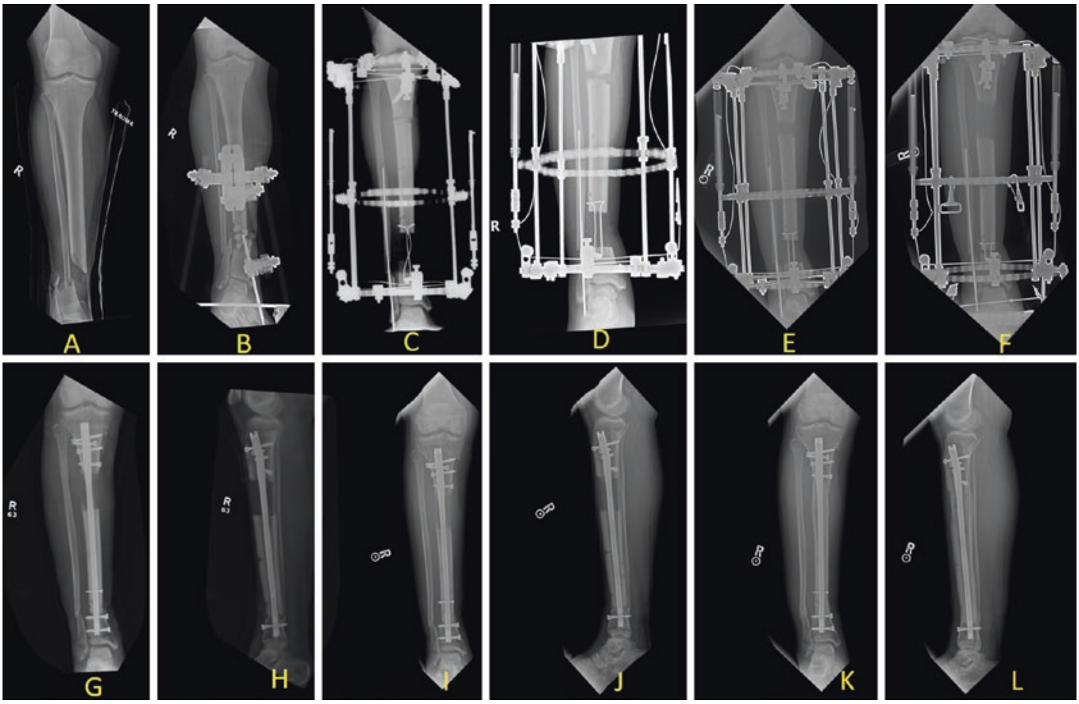

Fig. 7.5 This patient sustained a high-energy grade III B tibia fracture that underwent serial debridement (**a**, **b**). After soft tissue stabilization, a complex transport using a cable frame was used to reconstruct the residual segmental defect of the bone (**c**, **d**, **e**). After the transport segment reached the docking site (**f**), docking with placement of an intramedullary antibiotic cement-coated nail was performed, and the frame removed (**g**, **h**). Consolidation occured rapidly as seen at one month (**i**, **j**) and with final healing at 3 months after frame removal (**k**, **l**)

References

1. Aronson J, Harrison BH, Stewart CL, Harp JH Jr. The histology of distraction osteogenesis using different external fixators. Clin Orthop Relat Res. 1989;241:106–16.
2. Kojimoto H, Yasui N, Goto T, Matsuda S, Shimomura Y. Bone lengthening in rabbits by callus distraction. The role of periosteum and endosteum. J Bone Joint Surg Br. 1988;70(4):543–9.
3. Kusec V, Jelic M, Borovecki F, Kos J, Vukicevic S, Korzinek K. Distraction osteogenesis by Ilizarov and unilateral external fixators in a canine model. Int Orthop. 2003;27(1):47–52.
4. De Bastiani G, Aldegheri R, Renzi-Brivio L, Trivella G. Limb lengthening by callus distraction (callotasis). J Pediatr Orthop. 1987;7(2):129–34.
5. Dabis J, Templeton-Ward O, Lacey AE, Narayan B, Trompeter A. The history, evolution and basic science of osteotomy techniques. Strategies Trauma Limb Reconstr. 2017;12(3):169–80.
6. Yasui N, Kojimoto H, Sasaki K, Kitada A, Shimizu H, Shimomura Y. Factors affecting callus distraction in limb lengthening. Clin Orthop Relat Res. 1993;293:55–60.
7. Ilizarov GA. The tension-stress effect on the genesis and growth of tissues. Part I. The influence of stability of fixation and soft-tissue preservation. Clin Orthop Relat Res. 1989;238:249–81.
8. Codivilla A. On the means of lengthening, in the lower limbs, the muscles and tissues which are shortened through deformity. Clin Orthop Relat Res. 1904;1994(301):4–9.
9. Monticelli G, Spinelli R, Bonucci E. Distraction epiphysiolysis as a method of limb lengthening. II. Morphologic investigations. Clin Orthop Relat Res. 1981;154:262–73.
10. De Bastiani G, Aldegheri R, Renzi Brivio L, Trivella G. Limb lengthening by distraction of the epiphyseal plate. A comparison of two techniques in the rabbit. J Bone Joint Surg Br. 1986;68(4):545–9.
11. Fischgrund J, Paley D, Suter C. Variables affecting time to bone healing during limb lengthening. Clin Orthop Relat Res. 1994;301:31–7.
12. Dimitriou R, Tsiridis E, Giannoudis PV. Current concepts of molecular aspects of bone healing. Injury. 2005;36(12):1392–404.
13. Cho TJ, Kim JA, Chung CY, Yoo WJ, Gerstenfeld LC, Einhorn TA, et al. Expression and role of interleukin-6 in distraction osteogenesis. Calcif Tissue Int. 2007;80(3):192–200.

14. Kon T, Cho TJ, Aizawa T, Yamazaki M, Nooh N, Graves D, et al. Expression of osteoprotegerin, receptor activator of NF-kappaB ligand (osteoprotegerin ligand) and related proinflammatory cytokines during fracture healing. J Bone Miner Res. 2001;16(6):1004–14.
15. Liu Z, Luyten FP, Lammens J, Dequeker J. Molecular signaling in bone fracture healing and distraction osteogenesis. Histol Histopathol. 1999;14(2):587–95.
16. Farhadieh RD, Dickinson R, Yu Y, Gianoutsos MP, Walsh WR. The role of transforming growth factor-beta, insulin-like growth factor I, and basic fibroblast growth factor in distraction osteogenesis of the mandible. J Craniofac Surg. 1999;10(1):80–6.
17. Mehrara BJ, Rowe NM, Steinbrech DS, Dudziak ME, Saadeh PB, McCarthy JG, et al. Rat mandibular distraction osteogenesis: II. Molecular analysis of transforming growth factor beta-1 and osteocalcin gene expression. Plast Reconstr Surg. 1999;103(2):536–47.
18. Onishi T, Ishidou Y, Nagamine T, Yone K, Imamura T, Kato M, et al. Distinct and overlapping patterns of localization of bone morphogenetic protein (BMP) family members and a BMP type II receptor during fracture healing in rats. Bone. 1998;22(6):605–12.
19. Weiss S, Baumgart R, Jochum M, Strasburger CJ, Bidlingmaier M. Systemic regulation of distraction osteogenesis: a cascade of biochemical factors. J Bone Miner Res. 2002;17(7):1280–9.
20. Yonezawa H, Harada K, Ikebe T, Shinohara M, Enomoto S. Effect of recombinant human bone morphogenetic protein-2 (rhBMP-2) on bone consolidation on distraction osteogenesis: a preliminary study in rabbit mandibles. J Craniomaxillofac Surg. 2006;34(5):270–6.
21. Carter DR, Beaupre GS, Giori NJ, Helms JA. Mechanobiology of skeletal regeneration. Clin Orthop Relat Res. 1998;(355 Suppl):S41–55.
22. Pavalko FM, Norvell SM, Burr DB, Turner CH, Duncan RL, Bidwell JP. A model for mechanotransduction in bone cells: the load-bearing mechanosomes. J Cell Biochem. 2003;88(1):104–12.
23. D'Angelo F, Tiribuzi R, Armentano I, Kenny JM, Martino S, Orlacchio A. Mechanotransduction: tuning stem cells fate. J Funct Biomater. 2011;2(2):67–87.
24. Gjorevski N, Nelson CM. Bidirectional extracellular matrix signaling during tissue morphogenesis. Cytokine Growth Factor Rev. 2009;20(5-6):459–65.
25. Burger EH, Klein-Nulen J. Responses of bone cells to biomechanical forces in vitro. Adv Dent Res. 1999;13:93–8.
26. Klein-Nulend J, Bakker AD, Bacabac RG, Vatsa A, Weinbaum S. Mechanosensation and transduction in osteocytes. Bone. 2013;54(2):182–90.
27. Tan SD, de Vries TJ, Kuijpers-Jagtman AM, Semeins CM, Everts V, Klein-Nulend J. Osteocytes subjected to fluid flow inhibit osteoclast formation and bone resorption. Bone. 2007;41(5):745–51.
28. Vezeridis PS, Semeins CM, Chen Q, Klein-Nulend J. Osteocytes subjected to pulsating fluid flow regulate osteoblast proliferation and differentiation. Biochem Biophys Res Commun. 2006;348(3):1082–8.
29. Aronson J, Johnson E, Harp JH. Local bone transportation for treatment of intercalary defects by the Ilizarov technique. Biomechanical and clinical considerations. Clin Orthop Relat Res. 1989;243:71–9.
30. Ilizarov GA. Clinical application of the tension-stress effect for limb lengthening. Clin Orthop Relat Res. 1990;250:8–26.
31. Ilizarov GA. The tension-stress effect on the genesis and growth of tissues: part II. The influence of the rate and frequency of distraction. Clin Orthop Relat Res. 1989;239:263–85.
32. Prince DE, Herzenberg JE, Standard SC, Paley D. Lengthening with external fixation is effective in congenital femoral deficiency. Clin Orthop Relat Res. 2015;473(10):3261–71.
33. Szymczuk VL, Hammouda AI, Gesheff MG, Standard SC, Herzenberg JE. Lengthening with monolateral external fixation versus magnetically motorized intramedullary nail in congenital femoral deficiency. J Pediatr Orthop. 2019;39(9):458–65.
34. Arora S, Batra S, Gupta V, Goyal A. Distraction osteogenesis using a monolateral external fixator for infected non-union of the femur with bone loss. J Orthop Surg (Hong Kong). 2012;20(2):185–90.
35. Quinnan SM. Segmental bone loss reconstruction using ring fixation. J Orthop Trauma. 2017;31(Suppl 5):S42–S6.
36. Quinnan SM, Lawrie C. Optimizing bone defect reconstruction-balanced cable transport with circular external fixation. J Orthop Trauma. 2017;31(10):e347–e55.
37. Mizuta H, Nakamura E, Kudo S, Maeda T, Takagi K. Greater frequency of distraction accelerates bone formation in open-wedge proximal tibial osteotomy with hemicallotasis. Acta Orthop Scand. 2004;75(5):588–93.
38. Glatt V, Tepic S, Evans C. Reverse dynamization: a novel approach to bone healing. J Am Acad Orthop Surg. 2016;24(7):e60–1.
39. Glatt V, Evans CH, Tetsworth K. A concert between biology and biomechanics: the influence of the mechanical environment on bone healing. Front Physiol. 2016;7:678.
40. Harrison A, Lin S, Pounder N, Mikuni-Takagaki Y. Mode & mechanism of low intensity pulsed ultrasound (LIPUS) in fracture repair. Ultrasonics. 2016;70:45–52.
41. Claes L, Willie B. The enhancement of bone regeneration by ultrasound. Prog Biophys Mol Biol. 2007;93(1-3):384–98.
42. Raza H, Saltaji H, Kaur H, Flores-Mir C, El-Bialy T. Effect of low-intensity pulsed ultrasound on distraction osteogenesis treatment time: a meta-analysis of randomized clinical trials. J Ultrasound Med. 2016;35(2):349–58.
43. Lou S, Lv H, Li Z, Tang P, Wang Y. Effect of low-intensity pulsed ultrasound on distraction osteogenesis: a systematic review and meta-analysis of

randomized controlled trials. J Orthop Surg Res. 2018;13(1):205.

44. Burkhart KJ, Rommens PM. Intramedullary application of bone morphogenetic protein in the management of a major bone defect after an Ilizarov procedure. J Bone Joint Surg Br. 2008;90(6):806–9.
45. Kawasumi M, Kitoh H, Siwicka KA, Ishiguro N. The effect of the platelet concentration in platelet-rich plasma gel on the regeneration of bone. J Bone Joint Surg Br. 2008;90(7):966–72.
46. Kitoh H, Kitakoji T, Tsuchiya H, Mitsuyama H, Nakamura H, Katoh M, et al. Transplantation of marrow-derived mesenchymal stem cells and platelet-rich plasma during distraction osteogenesis--a preliminary result of three cases. Bone. 2004;35(4):892–8.
47. Kiely P, Ward K, Bellemore CM, Briody J, Cowell CT, Little DG. Bisphosphonate rescue in distraction osteogenesis: a case series. J Pediatr Orthop. 2007;27(4):467–71.
48. Kokoroghiannis C, Papaioannou N, Lyritis G, Katsiri M, Kalogera P. Calcitonin administration in a rabbit distraction osteogenesis model. Clin Orthop Relat Res. 2003;415:286–92.
49. Kitoh H, Kawasumi M, Kaneko H, Ishiguro N. Differential effects of culture-expanded bone marrow cells on the regeneration of bone between the femoral and the tibial lengthenings. J Pediatr Orthop. 2009;29(6):643–9.
50. Gessmann J, Koller M, Godry H, Schildhauer TA, Seybold D. Regenerate augmentation with bone marrow concentrate after traumatic bone loss. Orthop Rev (Pavia). 2012;4(1):e14.
51. Petri M, Namazian A, Wilke F, Ettinger M, Stubig T, Brand S, et al. Repair of segmental long-bone defects by stem cell concentrate augmented scaffolds: a clinical and positron emission tomography--computed tomography analysis. Int Orthop. 2013;37(11):2231–7.
52. Kadhim M, Holmes L Jr, Gesheff MG, Conway JD. Treatment options for nonunion with segmental bone defects: systematic review and quantitative evidence synthesis. J Orthop Trauma. 2017;31(2):111–9.
53. Moroni A, Faldini C, Marchetti S, Manca M, Consoli V, Giannini S. Improvement of the bone-pin interface strength in osteoporotic bone with use of hydroxyapatite-coated tapered external-fixation pins. A prospective, randomized clinical study of wrist fractures. J Bone Joint Surg Am. 2001;83-A(5):717–21.
54. Moroni A, Orienti L, Stea S, Visentin M. Improvement of the bone-pin interface with hydroxyapatite coating: an in vivo long-term experimental study. J Orthop Trauma. 1996;10(4):236–42.
55. Quinnan SM. Definitive management of distal tibia and simple plafond fractures with circular external fixation. J Orthop Trauma. 2016;30(Suppl 4):S26–32.
56. Pettine KA, Chao EY, Kelly PJ. Analysis of the external fixator pin-bone interface. Clin Orthop Relat Res. 1993;293:18–27.
57. Kocaoglu M, Eralp L, Kilicoglu O, Burc H, Cakmak M. Complications encountered during lengthening over an intramedullary nail. J Bone Joint Surg Am. 2004;86-A(11):2406–11.
58. Kristiansen LP, Steen H. Lengthening of the tibia over an intramedullary nail, using the Ilizarov external fixator. Major complications and slow consolidation in 9 lengthenings. Acta Orthop Scand. 1999;70(3):271–4.
59. Paley D, Herzenberg JE, Paremain G, Bhave A. Femoral lengthening over an intramedullary nail. A matched-case comparison with Ilizarov femoral lengthening. J Bone Joint Surg Am. 1997;79(10):1464–80.
60. Watanabe K, Tsuchiya H, Sakurakichi K, Yamamoto N, Kabata T, Tomita K. Tibial lengthening over an intramedullary nail. J Orthop Sci. 2005;10(5):480–5.
61. Rozbruch SR, Kleinman D, Fragomen AT, Ilizarov S. Limb lengthening and then insertion of an intramedullary nail: a case-matched comparison. Clin Orthop Relat Res. 2008;466(12):2923–32.
62. Song HR, Oh CW, Mattoo R, Park BC, Kim SJ, Park IH, et al. Femoral lengthening over an intramedullary nail using the external fixator: risk of infection and knee problems in 22 patients with a follow-up of 2 years or more. Acta Orthop. 2005;76(2):245–52.
63. Alrabai HM, Gesheff MG, Conway JD. Use of internal lengthening nails in post-traumatic sequelae. Int Orthop. 2017;41(9):1915–23.
64. Siebenrock KA, Schillig B, Jakob RP. Treatment of complex tibial shaft fractures. Arguments for early secondary intramedullary nailing. Clin Orthop Relat Res. 1993;290:269–74.