

Distraction osteogenesis for bone repair in the 21st century: Lessons learned

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ARTICLE INFO

Article history:
Accepted 4 April 2011

Keywords:
Bone regeneration
Distraction osteogenesis
Osteotomy
Bone transport

ABSTRACT

Bone regeneration obtained by distraction osteogenesis is influenced by a series of factors. These include factors that are related to the mechanical stability of the system of distraction (internal or external devices), and to factors directly depending on the biology of the bone tissue, such as the method of bone interruption (osteotomy), the delay and rhythm of distraction, the anatomical site of the osteotomy, and the histological characteristics of the bone requiring reconstruction. The stability of the system of bone fixation depends on the rigidity of the frame, the connexion of the apparatus to the bone (wires, pins) and the intrinsic stability of the segment (length and level of maturation of bone regenerate). The radiological characteristics of bone regeneration (hypo- or hypertrophy) lead to the adaptation of the rhythm of distraction. Following more than 28 years of experience of application of the Ilizarov method for bone reconstruction, the authors describe the technique of frame assembly and the methods of evaluation and treatment of the complications of new bone formation.

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Introduction

The Ilizarov apparatus is a ring external fixator that is distinguishable from other monoaxial fixators because it has to be assembled by the surgeon for the type of treatment desired before it is applied, and the dimensions of the segment to be treated, and numerous other variables, have to be taken into consideration.^{1,3,4}

Many surgeons consider the Ilizarov fixator to be the only elastic and dynamic fixator, but elasticity and dynamics are intrinsic characteristics of all fixators and reflect the type of connexion between the bone and the fixator. For example, the monoaxial fixator, where the apparatus lies in a straight line, enables dynamic and elastic movement that corresponds to compression forces on the site of bone interruption, and to angular and rotational movements. Angulation and rotation are defined as "parasitic" in many studies, and can hinder the bone healing process.

As with all circular fixators, the real advantage of the Ilizarov apparatus is that it uses transosseous wires, which minimize "parasitic" movement (angulation and rotation) without eliminating the elasticity that appears favourable for bone healing, according to many biomechanical studies. Elasticity does not mean the fixator is weak, and dynamic does not mean to have few

connexions between the bone and the frame. Ilizarov constantly referred to the stability of the apparatus, particularly the bone-fixator connexion.

Evaluating the stability of circular fixators requires consideration of the following variables: (i) rigidity of the assembly; (ii) connexion of the apparatus to the bone and (iii) intrinsic (or internal) stability of the treated segment.

Rigidity of the assembly

The material from which the half rings are made has to be extremely rigid and enable the least bending when subjected to the stress of loading and to the tensioning of the wires.^{3,4} Steel is currently used at a thickness of 6 mm, which is considered optimal in terms of weight, rigidity and cost. Carbon fibre rings of 6 mm thick enable adequate rigidity to loading, but have a tendency to twist if subjected to the stress of wire tensioning. Increasing the thickness to 7–8 mm overcomes this problem. The same applies for aluminium rings.

The diameter of the ring is inversely proportional to the rigidity of the construct; therefore, the surgeon should select the smallest diameter considering the anatomical configuration of the limb. The distance between the soft tissues and the frame should be at least 2 cm, with a minimum of 3 cm in cases of significant oedema.

The number of rings is directly proportional to the stability of the system; therefore, frames with two rings per bone segment are preferable. The frame required for a leg-lengthening procedure, for example, has four rings (a block of two rings proximal and another block of two rings distal to the bone interruption), Fig. 1a and b.

The stability of the assembly also depends on the type of connexion between the two rings of each block. For example, a

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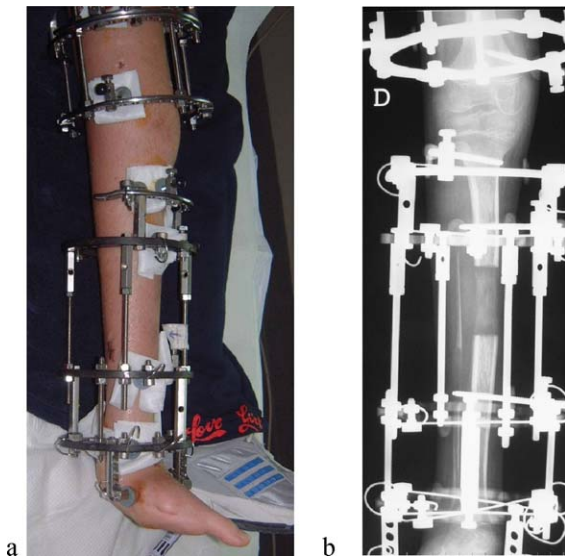


Fig. 1. (a) and (b) The stable frame configuration has two rings per segment, for example, 4 rings for a lengthening.

block of two rings connected with hexagonal sockets is much more stable than a block that uses threaded rods or threaded rods with conical washers, which enable “parasitic” angular or rotational motion, Fig. 2.

The number of connexions (rods) between the two blocks of rings is also directly proportional to the assembly stability. At least four connexions are required for minimal stability, Fig. 3a and b. The length of the connexion between the two blocks also influences the stability of the frame. The progressive increase of this length in the major lengthening procedures decreases the stability of the system. In that case, the distance between the two blocks at the time of frame application must be minimized.

Connexion of the apparatus to the bone (original Ilizarov)

The diameter of the wire is directly proportional to the stability of the assembly: a larger diameter corresponds to greater stability.

The diameter of the wire is usually 1.8 mm for an adult, and 1.5 mm for a child, Fig. 4.

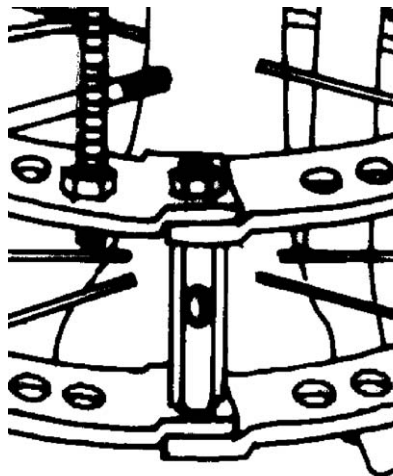


Fig. 2. The hexagonal socket increases the stability of a block of two rings.

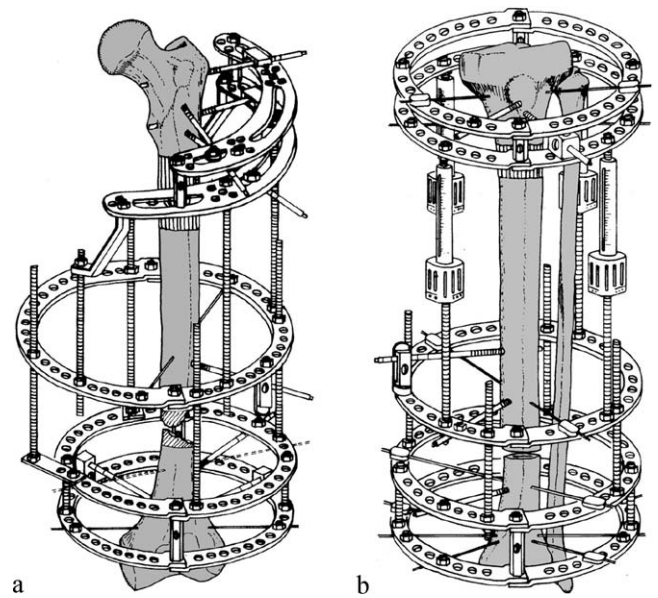


Fig. 3. (a) and (b) At least four connexions between rings are required for minimal stability.

The number of wires for each level (ring) is also directly proportional to the stability of the apparatus. The minimum number of wires is two per ring. The tension of the wire is directly proportional to the stability and is usually around 110 kg for a 1.8 mm diameter wire and 90 kg for a 1.5 mm diameter wire; less tension has to be applied to a half ring or to a five-eighths ring (max 50 kg), Fig. 5.

The best configuration for wire crossing is 90° between one wire and the other. The larger the angle of intersection, the greater the stability of the basic part (ring and two wires). The stability decreases as the angle is reduced, but is relatively sufficient at 45°. Below this angle, the stability decreases rapidly in the plane of the obtuse angle of crossing, and invariably motion can occur in the other plane, Fig. 6.

During 1986, the original Ilizarov apparatus (rings and wires) was modified for the femoral configuration,⁵ with the introduction of smaller dimension arches, fixed to the bone with half pins of 5–6 mm diameter, Fig. 7. The same modification was applied in the humerus (1987) the tibia (1989), and forearm (1990). In the pin

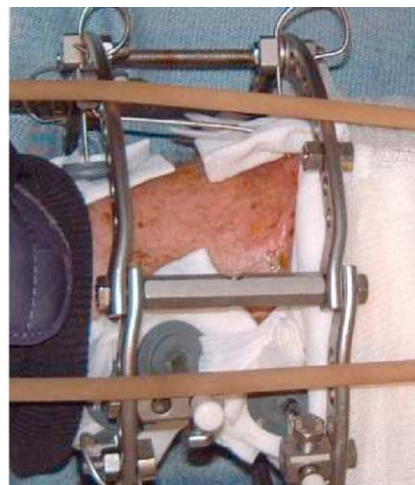




Fig. 4. Kirschner wires with bayonet tip with 1.8 mm diameter (for adults) and 1.5 mm diameter (for children).



Fig. 5. Wire tensioner.

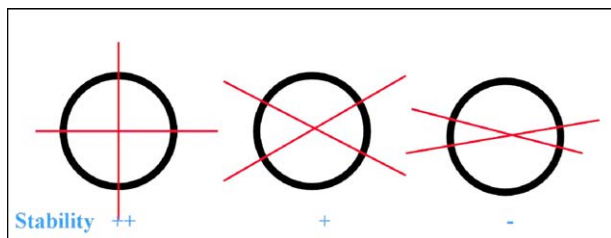


Fig. 6. The larger the angle of intersection, the greater the stability.

configuration, as described by Catagni-Cattaneo, there is better stability with pins crossing at 30–90°, the so-called delta pattern. This configuration is the fruit of observation of another fixator (Hoffman-Vidal)¹⁰ and of the clinical experience of the developer of the assembly.

A further consideration regarding the connexion between the fixator and the bone is the centralization of the bone axis with respect to the central axis of the apparatus. The closer the longitudinal axis of the bone is to the central aspect of the frame,

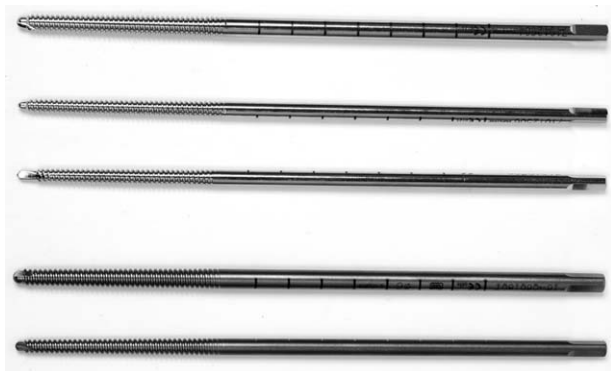


Fig. 7. Half pins: 5–6 mm diameter, available in stainless steel or in titanium with hydroxiapatitis coating.

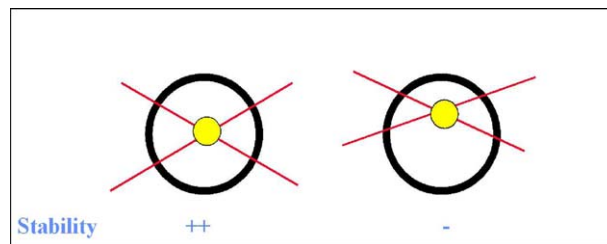


Fig. 8. The centralization of the bone axis with respect to the central axis of the apparatus increases the stability.

the more stable the apparatus, Fig. 8. Unfortunately for anatomic reasons (soft tissues), this ideal configuration is difficult to achieve in the tibia, but is more easily obtained in the femur, humerus, or forearm.

Intrinsic (or internal) stability of the treated segment

Internal stability is also very important for the stability of the system. For a fracture or non-union, it is necessary to evaluate the surface area of contact at the site of bone interruption: the larger the surface area, the better the stability and, therefore, the greater the possibility of granting weight bearing. The length, diameter and maturation of new bone formation also influence intrinsic stability. The shorter the bone formation, the smaller the diameter and the more mature the bone the better in terms of stability. The quality and amount of soft tissues surrounding the bone on treatment are also important for internal stability. Another important consideration is the length of the treated segment: the longer the treated segment, the less stable is the whole system.

In summary

(a) Variables directly proportional to the stability of the system:

- Rigidity of the ring material
- Number of rings
- Rigidity of the connexion between the rings
- Number of connexions between the rings
- Diameter of the wires
- Number of wires
- Tension of the wires
- Crossing angle of the wires
- Diameter and angle of crossing of the half pins
- Centralization of the apparatus
- Surface area of contact of bone ends
- Diameter of the regenerate and its maturation

(b) Variables inversely proportional to the stability of the system:

- Length of the connexion between the rings
- Length of the regenerate
- Length of the treated segment

(c) Variables under the control of the surgeon:

- Construction of a stable apparatus, with enough rings (at least two levels of fixation per bone segment).
- Enough wires and half pins per basic part (ring or arch) (two wires per ring or one wire and one half pin or one wire and two half pins).
- Good reduction of the fracture and adequate surface contact of the non-union for internal stability, with open surgery to reduce the fracture well or to remodel the bone ends in the non-union.

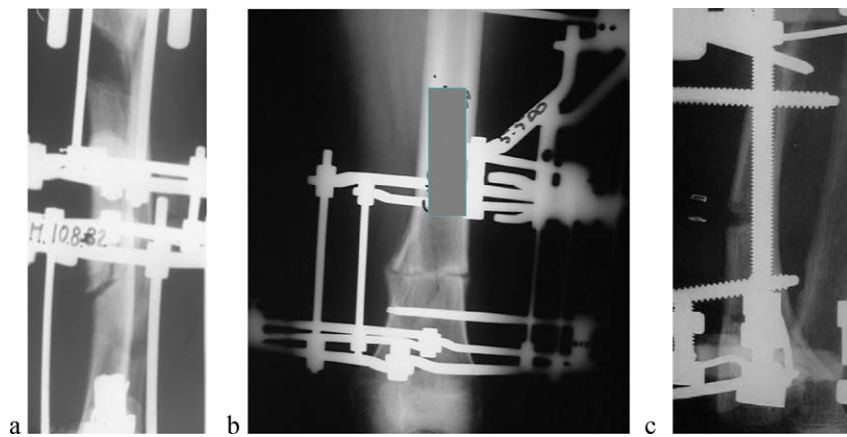


Fig. 9. Spiroid osteotomy (a), osteotomy through the pins (b), and incomplete osteotomy (c).

- The diameter of the regenerate depends on the level of the osteotomy, it needs to be in the metaphyseal region where the bone has a larger surface area.
- For a good regenerate, the osteotomy needs to be accurate without damaging the periosteum¹⁴ and without traumatizing the bone, avoiding the use of an oscillating saw or aggressive manipulation.
- The maturation of the regenerate can be guided by careful observation and applying a rhythm of elongation that respects the biology of the patient; eventually the surgeon can intervene with an accordion manoeuvre or, in extreme cases of atrophic regenerates, apply bone graft.

In conclusion, for stable construction of a circular frame the following should be considered:

- Selection of an appropriate diameter ring.
- At least four connexions between each two rings.
- Minimum distance between the level of the rings and the point of bone instability.
- Two levels of fixation for each injured bone segment.
- Frequent monitoring of the stability of the parts of the fixator, changing during treatment as indicated.
- Osteotomy at low energy, subperiosteal, percutaneous, in the metaphyseal region.
- Close observation of the regenerate bone with ultrasound and X-ray.

The original method of bony interruption introduced by Ilizarov, called “Corticotomy”, is based on the possibility to interrupt the cortex of the long bone with the total respect of the medullar vascularity. This procedure used to be conducted using an osteotome and was associated with a great risk of inducing a comminuted fracture and displacement, and was found to be a very difficult procedure in small bone segments, Fig. 9a–c.

Following on from the original osteotomy, we introduced the multiple drill osteotomy in the early 1980s. This procedure requires only a small incision, is much more precise than the “Corticotomy” and is an easier method to use in small bone segments. Such osteotomy is similar at the bony interruption as that applied by the Verona group,⁸ but is conducted percutaneously. With this method, the vascularity of the marrow is partially damaged, but many studies demonstrated that the new bone formation starts from the periosteum.^{11,14} Although the medullar vascularity is mechanically destroyed, it recovers in a few days. Subperiosteal Gigli saw osteotomy was introduced in the early 1990s. Many years of experience, and comparison between the different osteotomies in the same adult patient treated bilaterally for lengthening, indicate that new bone formation is more rapid with the original “Corticotomy” and multiple drill osteotomy than the Gigli saw if the latency period between the day of the osteotomy and the day of lengthening is the same (7 days). If the latency period is longer (15 days) in the Gigli osteotomy, the new bone formation is more evident and homogeneous, Fig. 10.

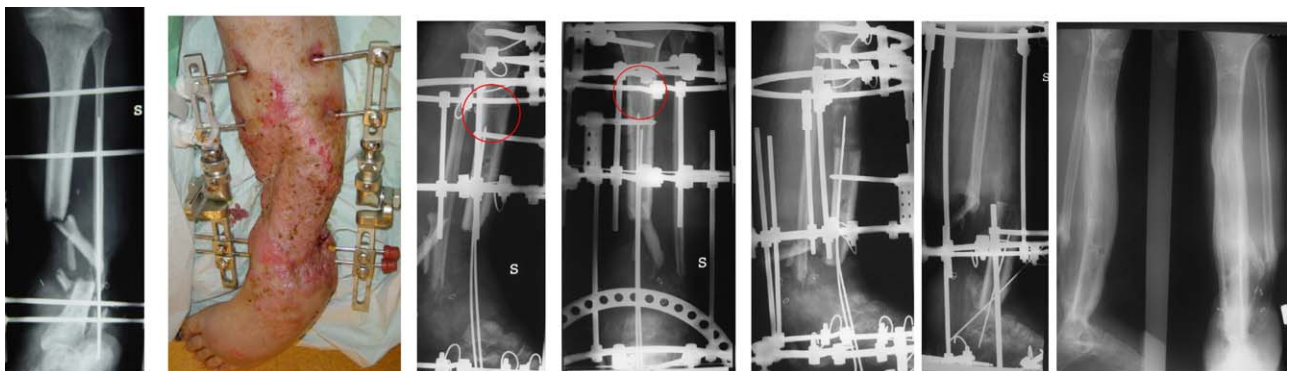


Fig. 10. Homogeneous new bone formation with Gigli saw osteotomy.

In conclusion, the original “Corticotomy” is not recommended for perfect and well localized bone interruption in case of bone transport where the segments are short and fragile.

For evaluation of new bone formation, the following parameters should be considered:

1. Time interval
2. Radiographic appearance
3. Mechanical quality

Using these parameters it is possible to distinguish normal, hyper- and hypotrophic new bone formation in the adult.⁶ Normal new bone is defined as that which is normally present radiographically within 30 days following osteotomy, where lengthening of 0.25 mm every 8 h is the goal. Distraction usually begins within 7–15 days of surgery (depending on the type of osteotomy performed). Thus, new bone is evident after approximately 1.5 cm of lengthening. This bone is characterized radiographically by a constant diameter in both the anteroposterior and lateral planes that is the same as the width of the normal bone at the site of osteotomy. There is a slow but progressive increase of radiodensity with time, Fig. 11.

During the period of fixation, there is a progressive remodelling of the new bone leading to the formation of new peripheral cortex. This appearance emulates that of normal bone. The time of fixation varies from three to seven months depending on the absolute amount of lengthening. At the end of this period, the new bone has acquired the mechanical qualities essential for weight bearing in the lower extremity, or functional loading in the upper extremity, as well as appearing radiographically near to normal.

Hypertrophic new bone is defined as the precocious appearance of new bone that has a greater diameter than the normal bone at the site of osteotomy and proceeds to consolidation earlier than anticipated. The three factors that seem to contribute to the formation of hypertrophic new bone are: (a) a young patient, (b) high level of physical activity whilst in the fixator and (c) the anatomic site of the osteotomy.

Precocious consolidation of hypertrophic new bone occurs most commonly in the proximal humerus and the distal femur. This bone, unlike the tibia, is surrounded by well-vascularized muscle tissue. In addition to these factors, there is substantial patient-to-patient biologic variability in new bone formation following osteotomy.

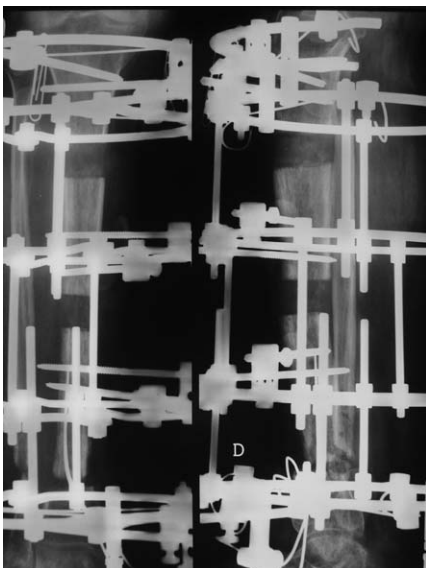


Fig. 11. The radiographic aspect of normal new bone.

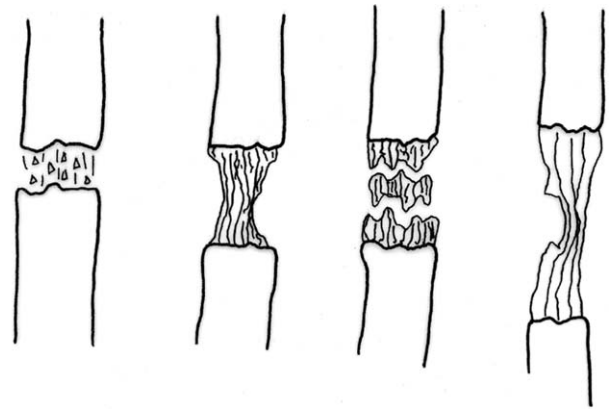


Fig. 12. Hypotrophic new bone.

If, despite adherence to careful surgical technique and postoperative care, new bone does not appear on X-ray or does not progressively acquire the radiographic morphology and mechanical characteristics of normal bone, it must be considered to be hypotrophic, Fig. 12. There are various reasons for slow formation of new bone. Prior surgery or severe trauma, with the resultant poor vascularity and inflammation of soft tissue and muscle, can significantly retard new bone formation. The presence of inelastic soft tissues surrounding the bone may interfere with bone nutrition and vascularity, which results in the formation of new bone with a decreased diameter relative to the normal bone. Too rapid a rate of lengthening with respect to the biologic repair capacity of the individual patient may lead to an hourglass shape or transverse areas of radiolucency within the new bone suggestive of ischaemia. Inadequate functional activity by the patient, particularly weight bearing, may delay the rate of corticalization by as much as 30–50%.

The classification of new bone formation being either hypertrophic or hypotrophic should be used as a guide for surgeons undertaking limb reconstruction using the Ilizarov technique. The postoperative management should vary with the rate and type of new bone formation to avoid complications of early or delayed consolidation.

Adjustments should be made when it is noted that the bone formation during lengthening or transport is not normal. Hypertrophic new bone formation is generally encountered in distal femoral and proximal humeral lengthening, particularly in achondroplasia. It is necessary to X-ray these patients every 7–10 days during the initial stages of lengthening to identify hypertrophic bone formation prior to early consolidation. The solution is to increase the rate and to decrease the frequency of lengthening. For example, if a patient is lengthening 0.25 mm every 6 h, or 1 mm per day, this rate and rhythm should be changed to 0.5 mm every 8 h for a total of 1.5 mm per day. Merely increasing the frequency (for example, 0.25 mm every 4 h) can lead to even more rapid bone formation and consolidation. This was demonstrated experimentally by Ilizarov, who showed that the higher the frequency, the more rapid the consolidation. Conversely, by increasing the extent and decreasing the frequency of lengthening, new bone formation is less rapid. Following such a change in the rate of lengthening, new X-rays must be obtained to ensure that there are no hypotrophic ischaemic changes in the new bone.

Precocious consolidation may be mimicked radiographically by an incomplete osteotomy. In this situation, the bone ends will distract unevenly resulting in an angular deformity. With partial bony continuity, the tension unloads on the wires without an increase in lengthening. If an X-ray is obtained in an oblique position, the incomplete osteotomy can be missed and be confused with hypertrophic new bone. The obvious solution in this case is

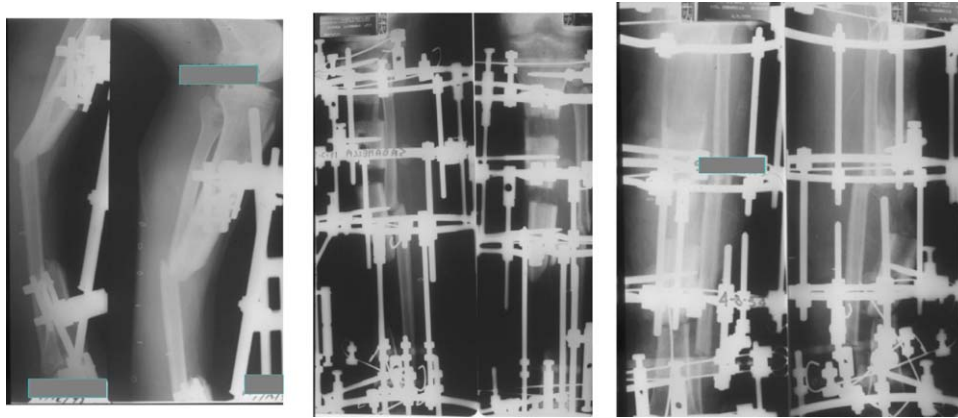


Fig. 13. Small fragment transport.

not an increase in lengthening rate, but rather to repeat the osteotomy.

The appearance of hypertrophic new bone is an ominous sign to both the patient and surgeon. This is most often seen in bone that has undergone prior surgical intervention, irradiation, or fracture.

In these circumstances, the rate of lengthening should be decreased to 0.25 or 0.5 mm daily and not started until a minimum of 15 days after osteotomy. If new bone formation is still delayed, it is absolutely necessary to compress or shorten the new bone for 3 days (1 mm 3 times daily), followed by a stop for 10 days, followed by lengthening 0.25 mm twice a day; in 18 days the previous length is regained. This manoeuvre is called the “accordion” procedure. It can be repeated until good new bone can be demonstrated radiographically. If the bone is still atrophic despite multiple manipulations, the solution is the application of growth factors. The more useful and cheap option is bone grafting with bone harvested from the iliac crest. It is also possible to inject inside the new bone 15–10 cm³ of marrow aspirated from the pelvis. Recently we have started to use concentrated bone marrow aspirate by injecting 5 cm³ of mesenchymal stem cells obtained from 60 cm³ of marrow blood.^{7,13} Another solution is the application of BMP,¹² but the literature regarding this option is obscure.

Regarding the length of the transported fragment, our experience indicates that one segment of 2 cm is sufficient for transport and the new bone formation is independent from the size of the bone, Fig. 13.⁹ The bone resected has to be alive at the site of the osteotomy, but it is not necessary to resect all the sclerotic bone if it is not infected. In fact, during the transport the vasculature of the new bone “invades” the transported segment and, in the majority of cases, the transported bone appears soft and well vascularized at the time of revision at the docking site.

In a patient with Neurofibromatosis-1 where it is necessary to reconstruct the continuity of the tibia, any kind of osteotomy performed would carry a great risk of delaying new bone formation, transforming into atrophic non-union. The solution in young patients is to perform a physal distraction.² The procedure can be conducted in young patients before they are 10 years old, with no risk to future natural growth in the growing plate. The rhythm of distraction, after manipulation in the operating room (gentle distraction in the ring closed at the cartilage), is 0.25 mm, starting 3 days after surgery. The new bone formation is exuberant and homogeneous (Fig. 14), and the amount of lengthening has to be increased several times to 1 or 1.5 mm per day. At the end of lengthening, the consolidation is quick and the growth plate remains active for further natural growing. The procedure can be repeated in the same segment and still the growth plate remains active. If the procedure is applied in older patients (11–12 years



Fig. 14. Physal distraction in congenital atrophic pseudoarthrosis (Neurofibromatosis-1).

old), new, good quality, bone is present, but the cartilage is closing definitively.

There are several factors to consider when planning removal of an apparatus following lengthening. There are both radiologic and clinical considerations with respect to new bone formation. Therefore, consider: (a) homogeneity (presence of absence of defects), (b) density, (c) cross-sectional area and (d) neocorticalization. When these are present radiologically, the connecting rods can be removed and the bone stressed carefully. If there is no apparent motion, the nuts can be left loose or a little shortening can be made, and the patient asked to use the extremity normally for one week. If there is no pain or increase in oedema, it is likely that the new bone can be freed from the apparatus. Finally, if the patient is large or heavy, or has had significant inadequate new bone formation, it is reasonable to use a period of functional casting or bracing.

Conflict of interest statement

The authors disclose any financial and personal relationships with other people or organizations that could inappropriately influence his work. Neither them nor a member of their immediate family received from a commercial entity in support of the research for the preparation of this work any outside funding, payments or other benefits or a commitment or agreement to provide such benefits.

References

1. A.S.A.M.I. Group. *Operative principles of Ilizarov*. Milano, Italy: Medi Surgical Video, Medicalplastic Srl; 1991.
2. Boero S, Catagni MA, Donzelli O, et al. Congenital pseudarthrosis of the tibia associated with neurofibromatosis-1: treatment with Ilizarov's device. *J Pediatr Orthop* 1997;17(5):675–84.
3. Catagni MA, Malzev V, Kirienko A. *Advances in Ilizarov apparatus assembly*. Milano, Italy: Medicalplastic Srl; 1994.
4. Catagni MA. *Treatment of fractures, nonunions and bone loss of the tibia with the Ilizarov method*. Milano, Italy: Medi Surgical Video, Medicalplastic Srl; 1998.
5. Catagni MA. *Atlas for the insertion of transosseous wires and half pins*. Milano, Italy: Medi Surgical Video, Medicalplastic Srl; 2002.
6. Catagni MA, Cattaneo R. Osteogenesis in distrazione nei grandi allungamenti degli arti. *Atti 1° Congresso Nazionale A.S.A.M.I.*. 1986.
7. Connolly JF. Injectable bone marrow preparations to stimulate osteogenic repair. *Clin Orthop Relat Res* 1995;313:8–18.
8. De Bastiani G, Aldegheri R, Renzi Brivio L, Trivella G. Limb lengthening by callus distraction (callotaxis). *J Pediatr Orthop* 1987;7:129–34.
9. Guerreschi F, Azzam W, Camagni M, et al. Tetra focal bone transport of the tibia with circular external fixation. A case report. *J Bone Joint Surg Am* 2010;92:190–5.
10. Hoffmann R. Osteotaxis. Ostéosynthèse externe par fiches e rotules. *Acta Chir Scand* 1954;107:72–88.
11. Kojimoto H, Yasui N, Goto T, et al. Bone Lengthening in rabbits by callus distraction. *J Bone Joint Surg Br* 1988;70-B:543–9.
12. Mizumoto Y, Moseley T, Drews M, et al. Acceleration of regenerate ossification during distraction osteogenesis with recombinant human bone morphogenetic protein 7. *J Bone Joint Surg Am* 2003;85:124–30.
13. Muschler GF, Boem C, Easley K. Aspiration to obtain osteoblast progenitor cells from human bone marrow: the influence of aspiration volume. *J Bone Joint Surg Am* 1997;79:1699–709.
14. Yasui N, Kojimoto H, Shimizu H, Shimomura Y. The effect of distraction upon bone, muscle and periosteum. *Orthop Clin North Am* 1991;22(4):563–7.