



Mechanical solutions to salvage failed distraction osteogenesis in large bone defect management

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Received: 10 November 2017 / Accepted: 12 June 2018 / Published online: 23 June 2018
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Abstract

Introduction Ilizarov bone transport for large bone defect is challenging and may end in distraction osteogenesis failure.

Material and methods Ten forearm and seven tibial defect cases with failed regeneration due to ischaemia during bone transport were studied retrospectively. Mean forearm and tibial defects were 5.5 ± 0.8 and 7.6 ± 1 cm respectively, or 22.3 ± 3.6 and $20 \pm 2.3\%$ as compared with healthy segments. Most patients had numerous previous operations (2.6 ± 0.5 and 3.4 ± 0.8 per patient, respectively), extensive scars locally and post-traumatic neuropathy. There were seven infected defects. Mechanical solutions used were (1) additional osteotomy and transport of the fragment to compact the ischaemic regenerate (10 forearms, 4 tibias) and (2) compaction of the connective tissue layer in the tibial regenerate with either two 5-mm steps (two cases) or gradually (one case).

Results Bone integrity was restored in all the cases. Complete compensation of the defects was achieved in 12 patients with the first technique. Two patients with 8-cm ulna defects remained with residual discrepancy. In the forearm, mean compaction was 1.7 ± 0.4 cm. It took 25.7 ± 5.4 days followed by an average fixation period of 107.1 ± 11.8 days. In the tibia, mean longitudinal compaction by distraction measured 1.7 ± 0.8 cm. The second technique ended up with an acceptable shortening of 1 cm in two cases. Four centimeters were compressed in the third case gradually.

Conclusion The technical solutions used for mechanical effects on the ischaemic distraction regenerate resulted in its rescue and bone union in all the cases.

Keywords Bone defect · Bone fragment · Ilizarov transport · Distraction osteogenesis · Bone callus · Failed regeneration · Compression

Introduction

Transport of an osteotomized vascularized bone fragment within the soft tissues to reconstitute a missing long bone part by distraction osteogenesis (DO) with the Ilizarov method would be an ideal method of bone plasty if not for several known shortcomings and arising problems [1–5]. One of them is a possible bone regenerate insufficiency that may result in a

fracture at the distraction level after frame removal [6, 7]. The main reasons of fractures and deformities at this level are an early external fixator removal, lack of appropriate loading on the segment in the course of treatment, and hypoplastic bone regeneration [4, 7–9].

The issue of regeneration quality is especially important in large bone defect management when the defect size measures ≥ 6 cm [9, 10]. As reported, the DO process may be delayed or the compromised bone regenerate may acquire the shape of an hourglass, be concave, or have a big translucent intermediate layer [9–11]. Moreover, there are clinical situations when DO ceases to advance and complete regenerate insufficiency develops [4, 6]. Its arrest happens due to ischaemia or poor blood supply caused by different factors.

Prior studies have shown vascular formation locally within the regenerate and the association of angiogenesis and new bone mineralization [9, 12–16]. The volume of the mineralized tissue increases over time and correlates with the number

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of vessels in the bone regenerated [14]. It was shown that the formation of vascular tissue during DO occurs in both muscular and osseous compartments and the periods of intense osteogenesis and angiogenesis are concurrent [12, 14]. However, the middle regenerate layer consists of fibrous connective tissue that is poorly vascularized or avascular [13]. Therefore, there is a risk of ischaemia if this layer becomes large or prevails in the bone callus gap. It was shown that biopsies from failed DO sites revealed atrophic and ischaemic fibrous tissue [16]. We assume the validity of the term *ischaemic bone regeneration* and use it for cases of failed DO or its arrest. This pathological condition is bone tissue inability for further regeneration that may result in atrophic nonunion through the regenerate connective tissue layer that turns into cartilaginous fibrous tissue, mostly in large bone defect management or lengthening. Moreover, disturbed vascularity in the affected limb due to associated vascular lesions, previous multiple surgeries, and aggressive osteotomy may also have an impact on the regenerate formation [16].

The versatility of the Ilizarov external fixator and its possible rearrangement enable to correct compromised bone regeneration by using mechanical effects such as compression, interchange of compression and distraction, or reduced distraction rates [17, 18]. The interchange of distraction and compression for delayed and poor callus formation has been widely used (the accordion maneuver) [18]. Moreover, a trifocal approach for large post-traumatic and post-resection defects to bridge the gap with two distraction areas was added to the arsenal of defect management [3, 5, 8, 10, 19]. However, an ischemic regeneration or complete regenerate insufficiency, being a rare situation, needs special attention and solutions.

The aim of our retrospective study was to show the mechanical means for solving the problem of ischemic bone regeneration during Ilizarov distraction osteogenesis used for large defect management.

Material and methods

We retrospectively studied 17 patients with bone defects and nonunion associated with limb length discrepancy (LLD) who developed ischemic bone regeneration and were treated in the period from 2000 to 2015 (Table 1). Six patients were referred to our clinic for ischaemic distraction gaps having the Ilizarov frames on their limbs, and 11 developed them at our clinic.

Ten patients had defects in the forearm bones (Table 1). Their mean age was 27.2 ± 4.1 years and their mean defect made 5.5 ± 0.8 cm. Mean bone deficit was $22.3 \pm 3.6\%$ as compared with the opposite segment. Tibial defects were seven cases (Table 1). Mean age of these patients was $31.3 \pm$ five years. Their mean defect was 7.6 ± 1 cm and bone deficit made $20 \pm 2.3\%$ as compared with the intact tibia.

Aetiology of the primary defect was mostly post-traumatic (13 cases). There were two benign tumour resections and two congenital cases. The number of previous operations per patient was 2.6 ± 0.5 in the forearm and 3.4 ± 0.8 in the tibia. Seven patients were diagnosed with post-traumatic neuropathy. All patients had extensive scars locally that were intimately adhered to bone fragments. There were seven infected cases in the remission stage by the time of regenerate compaction.

The ischemic type of the regenerate was detected by radiography during bone regeneration process monitoring in the late distraction or fixation periods. Sonography and CT were used in five cases to better visualize the regenerate condition.

Two technical solutions were used to compact the ischemic distraction regenerates.

1. Additional osteotomy (corticotomy) (Fig. 1a). An additional Ilizarov circular support with two or three crossed wires drilled into the bone fragment is mounted. Distraction is initiated on days five to seven after osteotomy with the rate of 0.5 to 1.00 mm a day. Distraction is stopped or reduced for some days in case of severe pain. Transport is directed towards an ischemic regenerate to produce its compaction until its bony parts contact each other. The contact is checked radiographically. This additional DO is also used for defect compensation.
2. Compaction of the regenerate intermediate connective tissue zone by applying step-wise compression with the same frame (consecutive two or three compression steps, 5 mm each, with an interval of two to three weeks between them) until the contact of the regenerate bony parts and compaction on the periphery occur (Fig. 1b). It results in acceptable segment shortening within 1 cm. Therefore, the intact fibula should be osteotomized or resected obliquely by 1 cm. Gradual compression is also applicable for cases of large ischemic regeneration (4–5 cm). Lengthening is planned as the second stage in such cases. The second technique is not applicable to the forearm as it foresees bone shortening.

The first technique was used in ten forearms (Fig. 2) and four tibias. The second technique was applied in three patients only: compression by steps was used in two of them (Fig. 3), and gradual compression (1 mm daily) was used to compact a 4-cm proximal ischemic regenerate in a 10-cm tibial defect (Table 1, case 15).

Methods of descriptive statistics were used in the study. Means and standard errors were calculated with Microsoft Excel 2010 software. The study was approved by the institutional ethic committee and was conducted in accordance with the ethical standards laid down in the Declaration of Helsinki. All the patients signed informed consents before the surgery.

Table 1 Patients treated for ischaemic regeneration and their clinical findings

Patients (case number)	Age (years)	Sex	Bone	Defect aetiology	Number of previous surgeries	Defect cm (% from the intact side)	Ischaemic regeneration causes	Time elapsed since first osteotomy (days)	Distraction for defect compensation (days)	Amount of compaction (cm) and time (days)	Consolidation (days)	Bone length restoration cm (%)
First technique. Compaction by distraction												
Forearm												
1	46	f	Right ulna	Gunshot injury	2	4.5 (18.8)	High-energy injury, neuropathy, traumatic osteotomy, improper distraction rate,	47	93	1.5 (30)	105	4.5 (100)
2	10	m	Left ulna	Home accident	3	2.5 (12)	Multiple surgeries, foreign bodies (plate, nail), neuropathy, traumatic osteotomy,	61	47	0.5 (8)	92	2.5 (100)
3	9	f	Right ulna	Congenital deficiency	5	8 (44.4)	Very large defect, congenital anomaly traumatic osteotomy	37	70	0.6 (13)	61	6 (75)
4	34	m	Left ulna	Work accident (explosion)	5	8 (28.6)	Injury due to explosion, neuropathy, multiple surgeries, traumatic osteotomy, osteomyelitis	72	105	4 (61)	191	5 (62.5)
5	26	m	Right radius	Tumour resection (osteoclastoblastoma)	2	7 (28)	Traumatic osteotomy, improper distraction rate, post-tumour condition	155	170	1.5 (15)	77	7 (100)
6	40	m	Left radius	Gunshot injury	1	5 (17.2)	High-energy injury, neuropathy, traumatic osteotomy, osteomyelitis	66	97	0.5 (7)	117	5 (100)
7	30	m	Right radius	Road accident	2	2 (7.4)	High-energy injury, condition after plating, neuropathy	64	49	1.5 (26)	134	2 (100)
8	40	m	Right ulna	Road accident	4	3 (9.7)	Multiple plating, aggressive surgery	154	20	2 (20)	107	3 (100)
9	20	m	Right radius	Home accident	1	8.5 (31)	Very large defect	281	111	3.5 (42)	117	8.5 (100)
10	17	f	Right ulna	Home accident	1	6 (25.5)	Large defect, condition after screw fixation, improper distraction rate	36	35	1.7 (35)	70	6 (100)
Tibia												
11	35	m	Left tibia	Gunshot injury	7	5 (12.5)	High-energy injury, multiple surgeries, neuropathy, osteomyelitis, traumatic osteotomy,	223	69	1.5 (28)	376	5 (100)
12	28	m	Right tibia	Tumour resection (osteoclastoblastoma)	2	7.5 (17.9)	Large defect due to tumour resection	79	63	4 (63)	126	7.5 (100)
13	7	f	Right tibia	Congenital	3	5 (20)	Congenital bone deficiency	70	74	1.2 (17)	129	5 (100)
14	51	m	Right tibia	Gunshot injury	5	12.0 (29.3)		372	161	0 (26)	131	12 (100)

Table 1 (continued)

Patients (case number)	Age (years)	Sex	Bone	Defect aetiology	Number of previous surgeries	Defect cm (% from the intact side)	Ischaemic regeneration causes	Time elapsed since first osteotomy (days)	Distraction for defect compensation (days)	Amount of compaction (cm) and time (days)	Consolidation (days)	Bone length restoration cm (%)
Second technique. Compaction by compression												
Tibia												
15	32	m	Left tibia	Road accident	1	10 (25)	Large defect, peroneal nerve injury, osteomyelitis, improper distraction rate	87	40	4 (29)	280	0 (0)
16	38	f	Left tibia	Home accident	4	5 (12.7)	Improper distraction rate, osteomyelitis	330	104	1 (2)	45	4 (80)
17	28	m	Right tibia	Road accident	2	9 (22.5)	Multiple surgery (plating, nailing, external fixation), osteomyelitis	114	137	1 (2)	127	8 (88.9)
							Traumatic osteotomy, osteomyelitis					

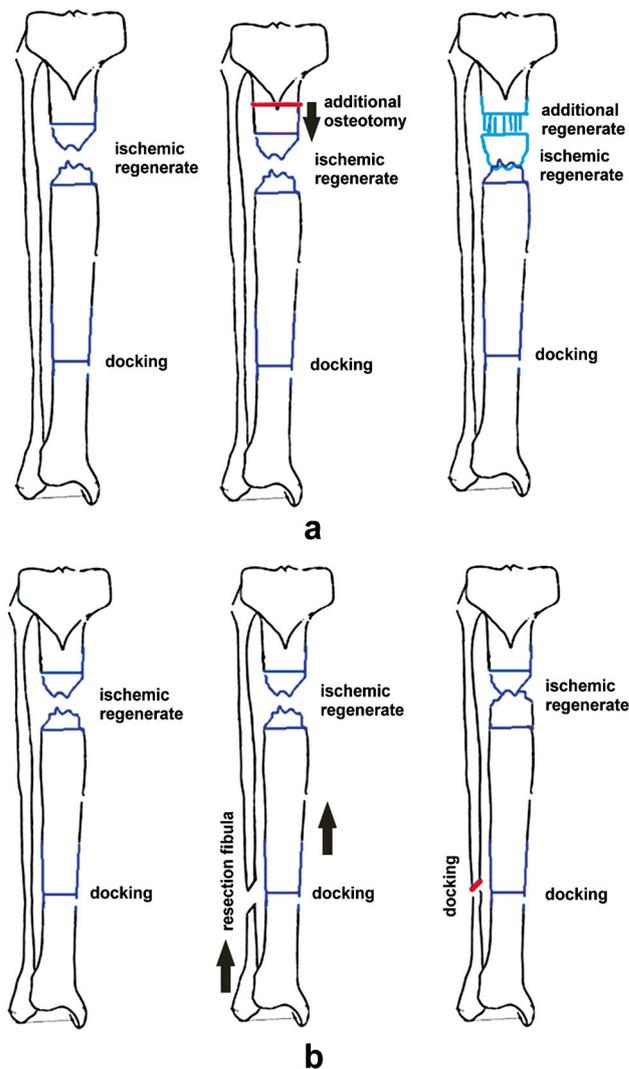


Fig. 1 Techniques used for ischemic regenerate compaction. Diagram of the first technique (a). Diagram of the second technique (b)

Results

Complete compensation of the defects was achieved in 12 patients with the first technique (Table 1). Distraction for defect compensation continued 79.7 ± 14.1 days on average in the forearm cases. The mean defect size bridged was 4.95 ± 0.6 cm ($93.8 \pm 4.3\%$). Compaction of the mean length of 1.7 ± 0.4 cm took 25.7 ± 5.4 days and was followed by an average fixation period of 107.1 ± 11.8 days. Two patients with ulna defects, 8 cm each, remained with LLD (Table 1, case 3 and case 4) and had lengthening at the second stage. Additional osteotomy helped to bridge the mean defect size of 7.4 ± 1.7 cm in tibial defect patients. Distraction for tibial defect compensation continued 91.8 ± 23.2 days. Compaction took 33.5 ± 10.1 days and fixation continued 190.5 ± 61.8 days on average. Mean longitudinal compaction measured 1.7 ± 0.8 cm. It was possible to compact two ischemic regeneration

Fig. 2 Case 5 of post-resection defect due to benign tumour managed previously by iliac crest autograft and plating that resulted in graft lysis after plate removal, 7-cm right radius discrepancy (28%), radial club hand (40°), palmar flexion (35°), ulnar head dislocation and radial deviation of 145°(a). Ischemic distraction regenerate with bone fragment endplates after 81 days of distraction with a daily rate of 0.5–1 mm following radial bone osteotomy (b). Additional osteotomy in the middle third of the radius followed by 89 days of distraction (including 15 days needed for the compromised regenerate compaction) that resulted in two regeneration areas of 3.0 and 4.0 cm (c, d). Condition of regenerates, restored length, and corrected club hand after 77 days of fixation in the frame and 2 months of plaster cast fixation (e)

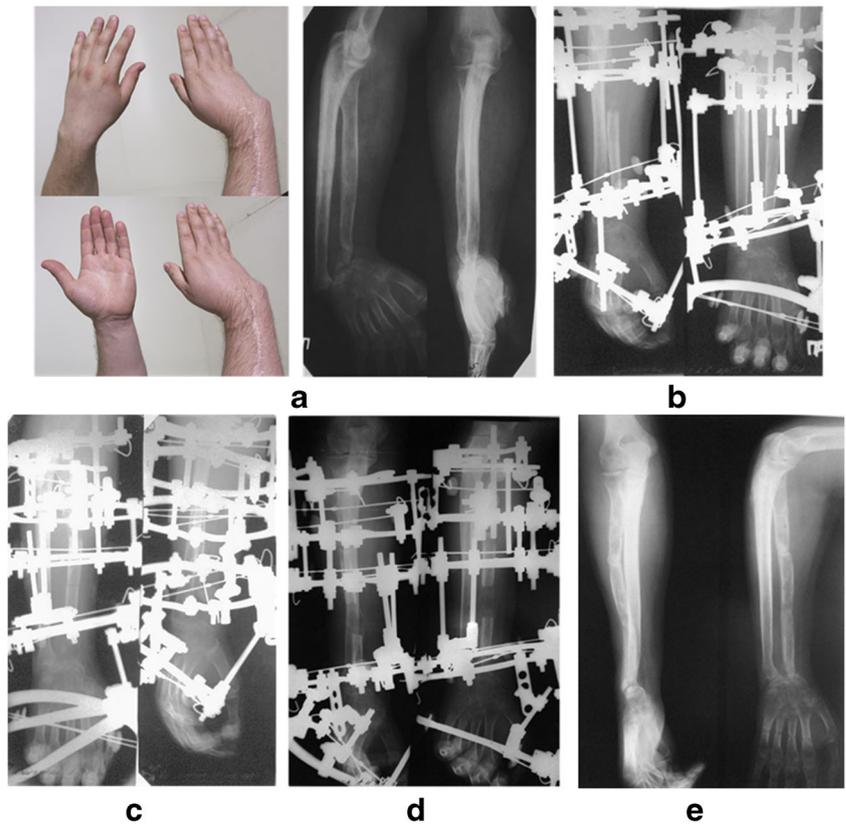
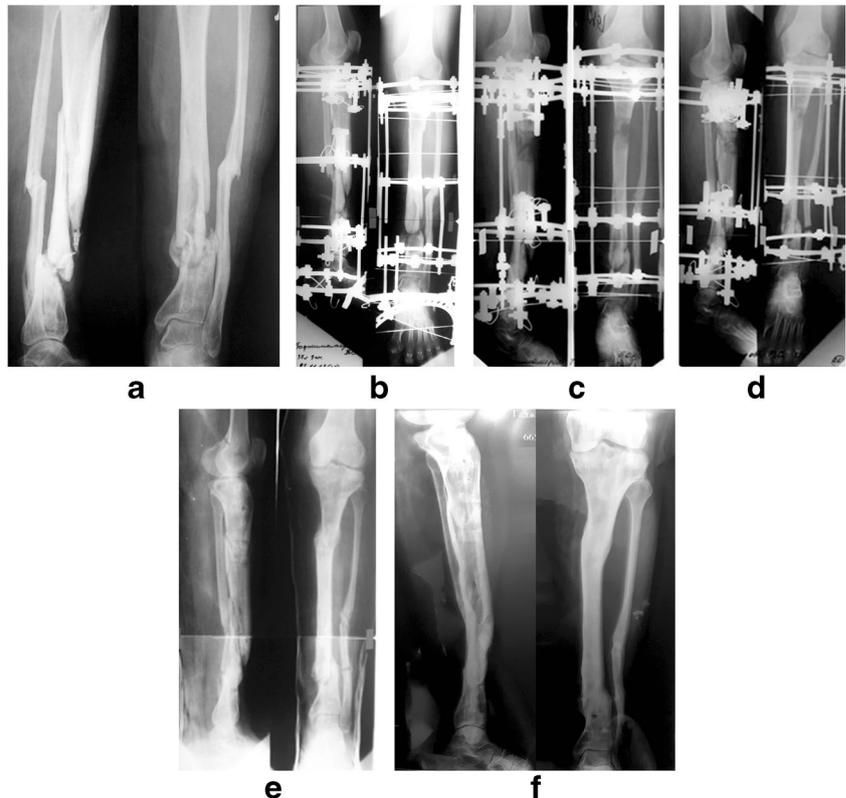


Fig. 3 Case 16 with chronic post-traumatic osteomyelitis in the left tibia after multiple operations at other clinics (plating, nailing, external fixation) (a). Proximal corticotomy 2 weeks after distal surgical debridement (b). Distal tibial resection defect management by lengthening of the proximal fragment that resulted in a 5-cm ischemic distraction regenerate after 104 days of bone transport with the rate 0.5–1.00 mm (c). Intraoperative ischemic regenerate compression by 5.00 mm and 1 cm resection of the fibula followed by 5-mm compression of the regenerate postoperatively after 18 days (d). Distraction regenerate consolidation after 45 days of fixation and apparatus removal; 1-cm residual LLD with acceptable angulation (e). 3-year follow-up (f)



areas in case 12 (Fig. 4). One patient was treated by longitudinal fibular osteotomy to produce a split for partial tibialization using transverse distraction (Fig. 5). Bone integrity was restored in all tibial cases.

The second technique gained 1-cm regenerate compaction with two compressive steps, 0.5 cm each, in two patients that remained with acceptable LLD of 1 cm. LLD due to gradual compression of 4.00 cm in the third case required lengthening which was completed at the second stage after a year. Bone union was achieved in all three cases, and plaster cast immobilization was not required after Ilizarov frame removal.

Both procedures ran without bone grafting. Bone infection or its recurrence was not observed. Wire tract problems were local and were treated by antibacterial dressings or wire removal. No fractures of the regenerate were reported at long-term follow-ups (range 2–15 years). It was impossible to correct the deformity in case 16 (Fig. 3) as it was risky to osteotomize the bone due to poor quality. Incomplete remodeling of DO and at docking site in case 12 required protection with an orthotic device after the removal of the apparatus (Fig. 4).

Discussion

Induction of new bone formation through DO has a widespread clinical application in the treatment of bone defects, limb lengthening, deformity correction, and nonunion [1–11]. However, complications such as fractures or nonunion at the distraction level may happen in cases of large lengthening and defects [4, 6–9, 12].

It was long established that the distraction bone callus has three distinct zones which are two bony zones formed by fine cancellous vascularized bone tissue and a central zone that is radiolucent in the images and histologically consists of longitudinally arranged fibrous tissue that is poorly vascularized or

avascular [12, 20–23]. It was shown that if the radiographic appearance of the regenerate contains a central radiolucent zone greater than 8–10 mm, then the distraction may be too fast, and conversely, if it is less than 2 mm, then the distraction is too slow [23]. Thus, if this fibrous tissue layer prevails in the distraction gap, there is a risk of regeneration incompleteness and, finally, of nonunion [12, 24, 25].

Vascular formation within the regenerate is intimately associated with bone formation during DO [12–16]. Although the spatial increase in limb blood flow during DO was proven, vascularity in post-traumatic or post-resection bone defects is impaired initially before osteotomy, what is not characteristic for pure lengthening [8, 12]. To our knowledge, there is no experimental evidence on the association of disturbed angiogenesis in the limb and ischemic bone regenerate. Nevertheless, as far as both muscular and osseous compartments play role in the regenerate vascularity, local blood supply to the distraction area could be also affected by scar tissue and neuropathies that were present in the majority of our cases [13–16]. Lack of a large bone marrow portion that is so crucial for vascularity and bone regeneration is characteristic for large congenital deficiencies, bone loss due to tumor resection or aggressive high-energy trauma. Therefore, impaired blood supply in the soft tissues adjacent to DO area and intraosseous dysvascularity or poor vascularity will surely have a negative impact on the process of regenerate mineralization.

From the mechanobiological point of view, poor osteotomy performance, frame instability, and high distraction rate may disturb angiogenesis and blood supply to regenerating tissues and cause delay in DO [16, 17, 23]. Moreover, multiple previous surgery on the affected limb, extensive scars, rheological and neurological disorders, poor bone callus monitoring, or associated vascular pathology or injury will contribute to the development of regenerate insufficiency. Most frequently,

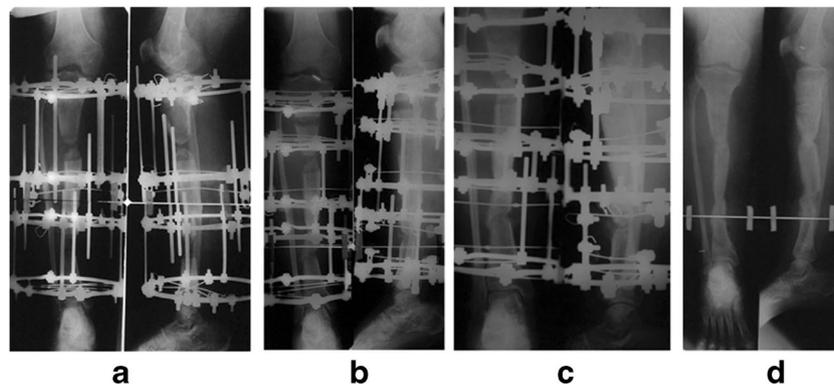
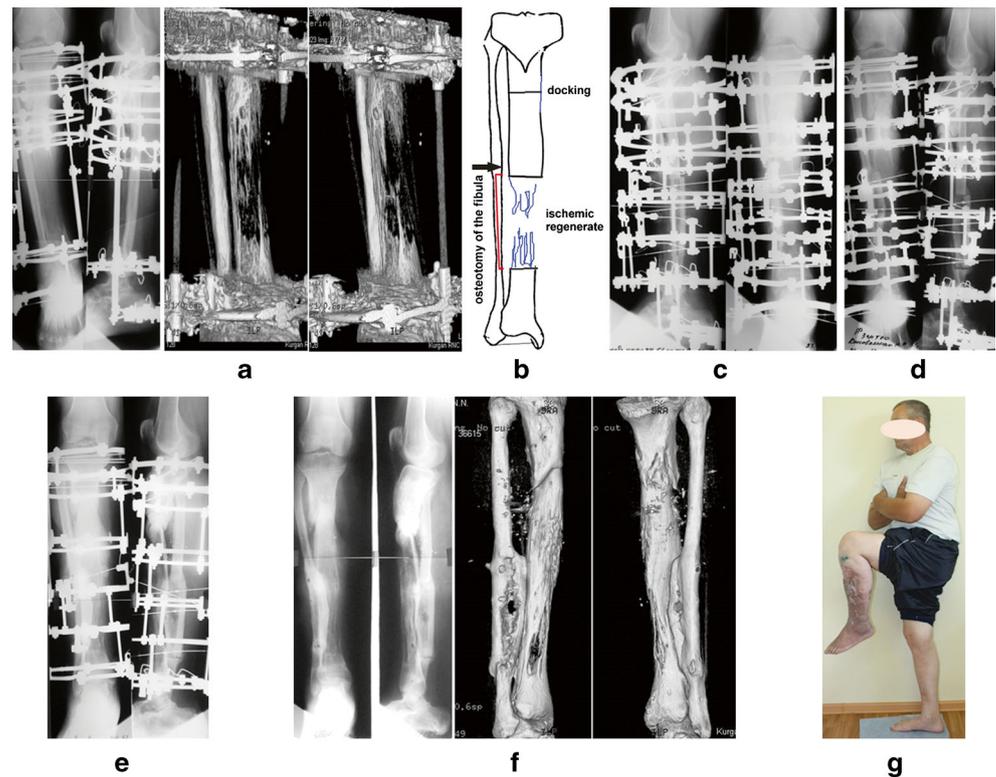


Fig. 4 Case 12 of post-resection defect due to benign tumor in the right tibia and 1.2-year fixation after double level transport to fill in a 9-cm gap that ended with two ischemic regenerates (a). Additional osteotomy of the proximal fragment and reassembly of the Ilizarov frame to compact the ischemic regeneration areas by distraction (0.25 mm \times 3 times a day) and compression of both ischemic regenerates with the same rate alternatively

in the upper and lower thirds (b). Six-centimetre additional regenerate after 63 days of distraction and a 4-cm compaction of the ischemic regenerates gained (c). Consolidation after 126 days of fixation (d) (orthotic device was used 1.5 months after frame removal for protection and transition to full weight-bearing)

Fig. 5 Case 14 of a 12-cm infected tibial defect after failed management with a fibular graft treated by open coaptation of bone ends and distal fragment distraction that resulted in ischemic regenerate formed by day 372 after the first osteotomy (in VRT images metal rods changed for carbon ones) (a). Diagram of additional longitudinal osteotomy of the fibula (b). Fibular split for transverse distraction with the rate of $0.25\text{ mm} \times 2\text{--}3$ times a day for 26 days (c). Start of fixation (d) and its end (e). Regenerate condition after frame removal (f). Patient's knee function after treatment (g)



several factors are involved into the process of DO incompleteness [26].

Up to date, there is no unified classification of a possible DO course. The most known is the classification developed by Ru Li et al. on a large material (6000 radiographs and 125 segments taken in 92 patients that underwent lower limb lengthening) [20]. The classification identified 10 types of distraction bone callus density. However, these types could not explain our notion of the ischemic regenerate. The same paper presents five distraction regenerate shapes. Shapes 3 (hourglass-like) and 5 (thin central cylinder) of the callus may develop into ischemic ones if their translucent middle zone becomes big during distraction. The preservation of the periosteum is essential for DO success. Otherwise, the participation of the endosteal bone structures will result in the formation of a risky cylindrical regenerate (shape 5) [20, 21]. The regenerate shape 4 that features a marginal defect and bone formation hypoplasia could not be referred to ischaemic regeneration as it usually happens after a traumatic osteotomy and in DO procedure that runs with a formation of an angular deformity. A typical example is the defect of a newly formed bone within the distraction gap in the upper third of the anterior tibia when lengthening runs with antecurvatum deformity of the fragments. Other studies of callus patterns also conclude that the regenerate concave shape and lucent types showed poor outcomes and should guide the surgeon in planning some additional procedure or intervention if necessary [11, 22].

We would like to note that hypoplastic and ischaemic regeneration are different clinical conditions. A hypoplastic type of the distraction bone callus presents an insufficient regeneration that can still be improved and will develop cortical layers in the fixation phase. Ischaemic regeneration happens when the regenerate hypoplasia has not been timely corrected, and no cortical layers to bridge the middle regenerate zone in the phase of fixation can be expected. A hypoplastic type of callus with at least three cortices regenerated is judged to be sufficient for fixator removal but is not ischaemic. As for large defects, it was advocated that the fourth cortex should be fully formed before removing the external fixator in the cases with more than 10 cm of lengthening magnitude or more than 50% of the original length to exclude the regenerate fracture or nonunion [26].

Ischaemic regeneration would feature the following radiographic manifestations: (a) regenerate connective tissue layer area prevails over the area of distraction gap bony parts, (b) extensive hourglass regenerate shape, and (c) endplates at the regenerate bony edges that are separated by a connective tissue layer (the so called regenerate growth zone). CT and ultrasound studies assist in its detection and are essential in doubtful cases. Ischaemic regeneration will result in atrophic nonunion and fracture if not treated. It is obvious that its management should be timely. Otherwise, the patient would need re-operation and even amputation [4].

Therefore, several factors are involved into the development of ischaemic regeneration:

1. High-energy trauma followed by multiple surgery and long-term bone defect treatment that failed
2. Aggressive osteotomy
3. Improper distraction rate
4. Poor bone regeneration monitoring during distraction phase
5. Pathological anatomical and functional disorders (large bone defect, extensive scars, neuropathies, trophic disorders)
6. Associated pathology that affects blood flow or may have an impact on DO, such as poor bone quality in congenital bone defects

The technical solutions for mechanical stimulation of the ischemic DO type used in our retrospective study resulted in its salvage and bone union. The two solutions have different indications.

Indications to the first technique are as follows:

1. Condition when the defect size has not been yet fully compensated but the regenerate connective tissue layer is big
2. Radiographic monitoring shows no progress and it is pointless to continue distraction or fixation of the regenerated area
3. When compression only is inappropriate or impossible due to segment anatomy (forearm)

The second technique can be used for ischaemic regenerate which connective tissue layer measures up to 4–5 cm, and (1) there is a possibility to produce either an acceptable 1–1.5-cm shortening, or (2) compress to a greater amount gradually and plan limb lengthening at the next stage, or (3) poor bone quality does not allow for additional osteotomy performance. This technique is not used for the forearm as each of its bones should be united and both have equal length to exclude deformity.

Our study is a retrospective retrieval of exceptional cases to present salvage means for severely compromised regeneration. It has its limitations for statistical analysis as its sample size is small, especially with the use of the second technique. Unfortunately, we could not present functional results as not all data were available. It is also evident that the tibial and forearm groups cannot be compared. Despite that both techniques include additional procedures and require surgeon's proficiency as well as may end with some LLD, we consider them as a rescue means in a risky DO course which could have had an unpredictable outcome.

Conclusion

The Ilizarov method mechanical means of bone distraction and compression are viable methods to salvage failed distraction osteogenesis that is caused by ischemia in extensive bone defect management. Their application for ischaemic regeneration helps exclude nonunion and amputation.

Acknowledgements The authors would like to thank Tatiana Malkova from the medical information service of our institute for her contribution to the literature review and English language interpretation.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent For this type of study formal consent is not required.

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