Introduction

Distraction osteogenesis involves mechanical stretching of a low-energy osteotomy to encourage the formation of new bone in the gap created between the gradually distracted skeletal fragments. This method was introduced by Gavril Ilizarov[(1)].

Clinical applications include limb lengthening, deformity correction, and management of segmental bone defects[(2)].

New bone is generated and remodeled in the distracted gap through a balanced anabolic and catabolic response to biologic, chemical, and mechanical stimuli[(2)].

However, host and environmental factors may result in the formation of new bone that lacks sufficient mechanical strength to withstand physiologic loading[(2)].

Suboptimal new bone formation has several negative effects, including prolonged external fixation as well as bending or fracture of the regenerate following removal of the external fixator [(3)].

Several mechanical and biologic modalities have been developed to improve the rate, quality,and volume of new bone formation and thereby improve clinical outcome following limb reconstruction with DO, These modalities

include mechanical stimulation of the regenerate (i.e., new bone); exogenous application of low-intensity pulsed ultrasound (LIPU) or pulsed electromagnetic fields (PEMFs);local injection of bone morphogenetic protein (BMP), pluripotent stem cells, and plateletrich plasma (PRP). Anticatabolic agents, such as diphosphonates, and local bone marrow injection in the distraction gap [(4)].

Bone marrow contains a variety of osteoinductive growth factors that may play a role in the proliferation and differentiation of osteoprogenitor cells and thereby enhances new bone formation during DO [(5)].

A variety of BMPs in bone marrow aspirate play an active rolein osteogenesis, including recruitment of stem cells, cellular proliferation and differentiation, and bone formation [(5)].

Although the initial results of injection of bone marrow cells at the lengthening site seem encouraging, this treatment option requires additional visits to the operating room and special equipment [(6)].

Aim of the Work

The aim of the work is to see if bone marrow injection has a role in enhancement of healing of distraction callus and its role in shortening the time of application of the external fixator in the patient.

Overview on Bone Lengthening

BONE REGENERATION

Bone possesses the intrinsic capacity for regeneration as part of the repair process in response to injury, as well as during skeletal development or continuous remodelling throughout adult life [(7)].

Bone regeneration is comprised of a well-orchestrated series of biological events of bone induction and conduction, involving a number of cell types and intracellular and extracellular molecular-signalling pathways, with a definable temporal and spatial sequence, in an effort to optimize skeletal repair and restore skeletal function [(8)].

In the clinical setting, the most common form of bone regeneration is fracture healing, during which the pathway of normal fetal skeletogenesis, including intramembranous and endochondral ossification, is recapitulated [(9)].

Unlike in other tissues, the majority of bony injuries (fractures) heal without the formation of scar tissue, and bone is regenerated with its pre-existing properties largely restored, and with the newly formed bone being eventually indistinguishable from the adjacent uninjured bone [(8)].

However, there are cases of fracture healing in which bone regeneration is impaired, with, for example, up to 13% of fractures occurring in the tibia being associated with delayedunion or fracture non-union [(10)].

In addition, there are other conditions in orthopaedic surgery in which bone regeneration is required in large quantity (beyond the normal potential for self-healing), such as for skeletal reconstruction of large bone defects created by trauma, infection, tumour resection and skeletal abnormalities, or cases in which the regenerative process is compromised, including avascular necrosis and osteoporosis [(11)].

Bone Lengthening

Despite a lack of biomechanical data supporting a seemingly fundamental human anatomic principle, it is persistent orthopaedic common sense that thepelvis needs to be horizontal and the lumbar spine symmetrically loaded in a bipedal standing position and in the stance phase during gait [(12)].

Hence, acquired or congenital disparities ought to be restored, though the certain and historic 2-cm rule of acceptable leg length discrepancy is more enigma than science in light ofthe individual anatomic parameters such as pelvic width, absolute leg length, muscle force and proprioceptive capacity [(12)].

Preparation of the patient for a longstanding procedure:

The patient and his psychosocial, medico-economic, logistic and legal environment must be consented, educated and prepared for a potentially longlasting journey paved with hazards such as delayed consolidation, pseudarthrosis, malalignment, joint contractures and dislocations, pain, infection, prolonged inability to work and refrain from school and sports activities [(13)].

The basic principles of bone generation and moulding-gentle, periosteum-respecting osteotomy followed by incremental 1-mm/day fragment separation and consolidationare set [(14)].

All current methods of gradual leglengthening rely on distraction osteogenesis [14].

How to choose the proper technique for lengthening:

The concurring implants and techniques for mechanical bone guidance such as Taylor Spatial Frames (TSFs), traditional Ilizarov ring and wire constructs, various methods for unilateral external fixation and intramedullary mechanical or motor-driven nails offer space for individual application given by [15]:

- The skills and preferences of the surgeon.
- The affordability.
- The Patient's needs and wishes.
- The medical problem.
- The condition of the joint,muscle and soft tissue compound adjoining the segment to be corrected.

Indications for Bone Lengthening

History:

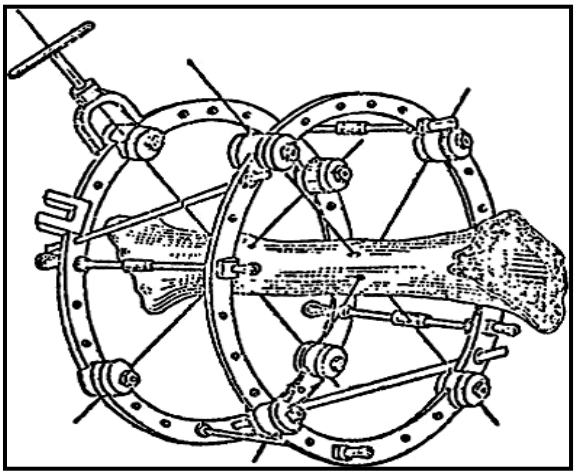

Figure (1): Diagram of the apparatus for fracture repair (Ilizarovapplication for invention dated 9 June 1952, courtesy of the Centre's museum.

The first successful attempt at therapeutic human bone regeneration in humans was reported by Codivilla in 1905 [(16)].

As part of a strategy to lengthen shortened limbs, he created an osteotomy through the cortex of the femur and the tibia and induced tractional forces with the use of a calcaneal pin [(16)].

In 1908, successful human femoral lengthening was reported, which was achieved by creating a median longitudinal step-cut osteotomy [(17)].

The proximal segment was fixed, and the distal segment was attached to a pulley-weight system that accomplished 2- to 3-inch lengthenings in 5 minutes [(17)].

Once the desired length and alignment had been achieved, the fragments were fixed with screws [(17)].

External fixator appearance:

In 1913, Ombredanne was the first to use an external fixator for limb lengthening, but unfortunately complications of skin necrosis and infection arose [(18)].

It was not until 1927 that Abbott introduced theconcept of a latency period to promote formation of bone prior to distraction [(18)].

Figure (2): Distraction osteogenesis with ext. fixator

Current thinking suggests that the latency period provides

Time for the initial phases of bone repair to take place at the osteotomy site, resulting in a mechanically compliant callus, restoration of the blood supply by means of revascularization, and initiation of the bone regeneration sequence [(18)].

Ilizarov:

The procedure of distraction osteogenesis for bone regeneration was refined by Ilizarov.

Perhaps more than any other development in medical history, the Ilizarov method shows how bone regenerationis possible in humans[(18)].

The so called low-energy osteotomy of the cortex was suggested by Ilizarov to be critical to the success of the procedure.

Although it is possible to perform the osteotomy at any site, the metaphysis is ideal, in that it offers good stability because of the thin cortex and large trabecular surfaceand is endowed with excellent blood flow from an extensive system of collateral vessels[(18)].

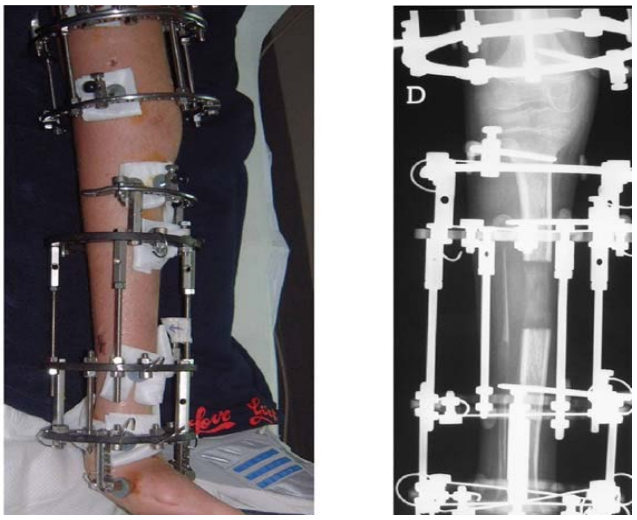

Figure (3): Use of ilizarov in distraction osteogenesis

An innovative method for the treatment of **segmentaldefects** caused by **trauma, infection, or tumor resection** was also devised by Ilizarov[19].

Change of indications over years:

Over the last 100yrs, indications have shifted

from

- Leg length discrepancies.
- deformities due to poliomyelitis, war wounds, osteomyelitis and malunited fractures

to:

- Congenital problems such as femoral deficiencies, simple femoral hypoplasia, fibular hemimelia and tibial aplasia, hemihyper- and hemihypotrophy[20].

And a long list of acquired problems, such as:

- Post-traumatic growth arrest.
- Post-infectious issues.
- Avascular necrosis.
- Perthes' disease.
- Blount's disease.
- Skeletal dysplasia.
- Rickets, syndromes.
- Ollier's disease.
- Enchondromatosis etc[21].

Indications as concern the defect:

Leg length discrepancy of more than 2cm is regarded as an indication for therapeutic measures, 2-4cmand enough growth in an individual above the 50thpercentilefor height an indication for growth modulation (epiphysiodesis) and discrepancies of more than 4cm anindication for callotasis[22].

Which technique of lengthening is indicated:

The average amount of lengthening ranges between 2. min. 2cm to max. 17.4cm for Ilizarov ring fixators (IRF) and intramedullary nails and around min. 8mm to max. 80mm for TSF [23].

The IRF is mostly indicated for complex three-dimensional problems, where the shortness is not the most prominent issue[23].

Though callotasis and complex deformity correction is predominantly a paediatric orthopaedic field, the age of patients ranges from as young as 2yrs up to 70yrs[24].

Concerning young age groups. Patients treated with ring fixators and unilateral external fixators have usually an average age of around 12-16yrs**fig (4)**, whereas by solid nails constitute young adults around the age of 18-25yrs[25].

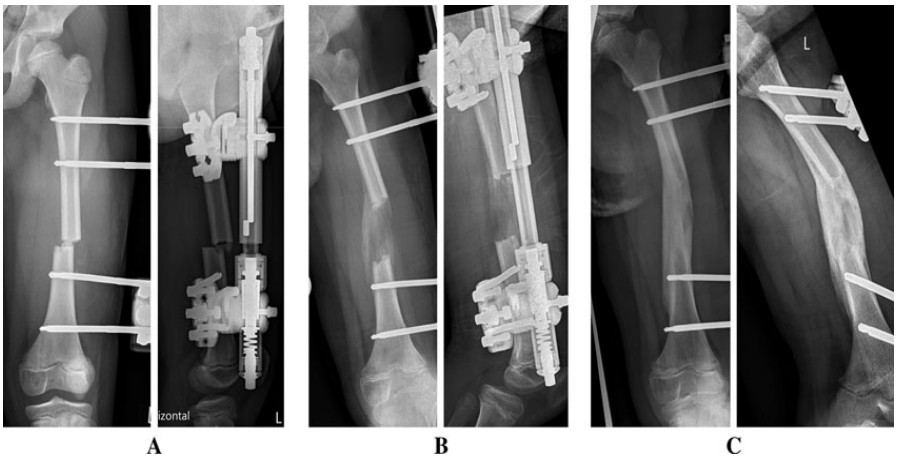

Figure (4): An 12-year-old girl with 4 cm congenital left femoral shortening (Pappas type IX). a Day 1 after diaphyseal drill hole osteotomy.Normal alignment, 50 % lateral translation. b 7.5 weeks after theindex procedure, 6 weeks of distraction. Secondary 10_ varusdeformity. Timely callus formation and ossification. c Four monthsfollow-up prior to hardware removal. Anteroposterior and slightoblique view to prevent bone–fixator overlap in order to provide afree projection of the femur. Three of four cortices are consolidated.

Baseline diagnostics in bone lengthening:

It is of utmost importance that the diagnostic algorithmdoes not only focus on the bony defect but creates a

bigger picture including the patient's physical and mental status, as well as the local biology[26].

This allows to gauge the level of difficulty and risk and to inform and educate the patient by weighing out all the potential hazards:

- Jointinstabilities ranging from mild laxity to fixed subluxation or even dislocation, fixed flexion deformities and decreased range of motion of the knee, osteoarthritic changes, poorbone.Soft tissue quality, previous infections and general medical issues like smoking, diabetes and regenerate-inhibiting medication[27],[28].
- Psychological assessment (intelligence, compliance, and social environment) to determine if the patient and family is suitable for the proposed procedure and contact with other patients might be wise in order to define the expectations [29].

Osteotomy techniques:

The fundament of successful iatrogenic new bone formation is an adequate osteotomy technique: prevention of thermal damage, careful bone separation, creation of vascular bone surfaces, respecting the periosteal sleeve andaftera latency period of several daysgraduallypulling the two bony segments apart are the biological cornerstones for good callus formation[30].

Corticotomy vs osteotomy:

- Preservation of periosteum as the main source of bloodsupply is critical[31].
- Its disruption significantly decelerates bone formation[32].
- Ilizarov and others firmly recommended corticotomies to preserve medullary blood flow [33].
- However, this is difficult to perform and experimental work revealed that complete bone separation (osteotomy) is equally effective[34].

Dual-energy X-ray absorptiometry (DEXA) and histomorphometrical studies showed that the periosteum produces up to five-fold more callus than bone marrow duringlengthening[35].

Hence, most surgeons nowadays perform percutaneous formal osteotomies varying in technical details depending on personal preferences, site of osteotomy and type of implant used[35].