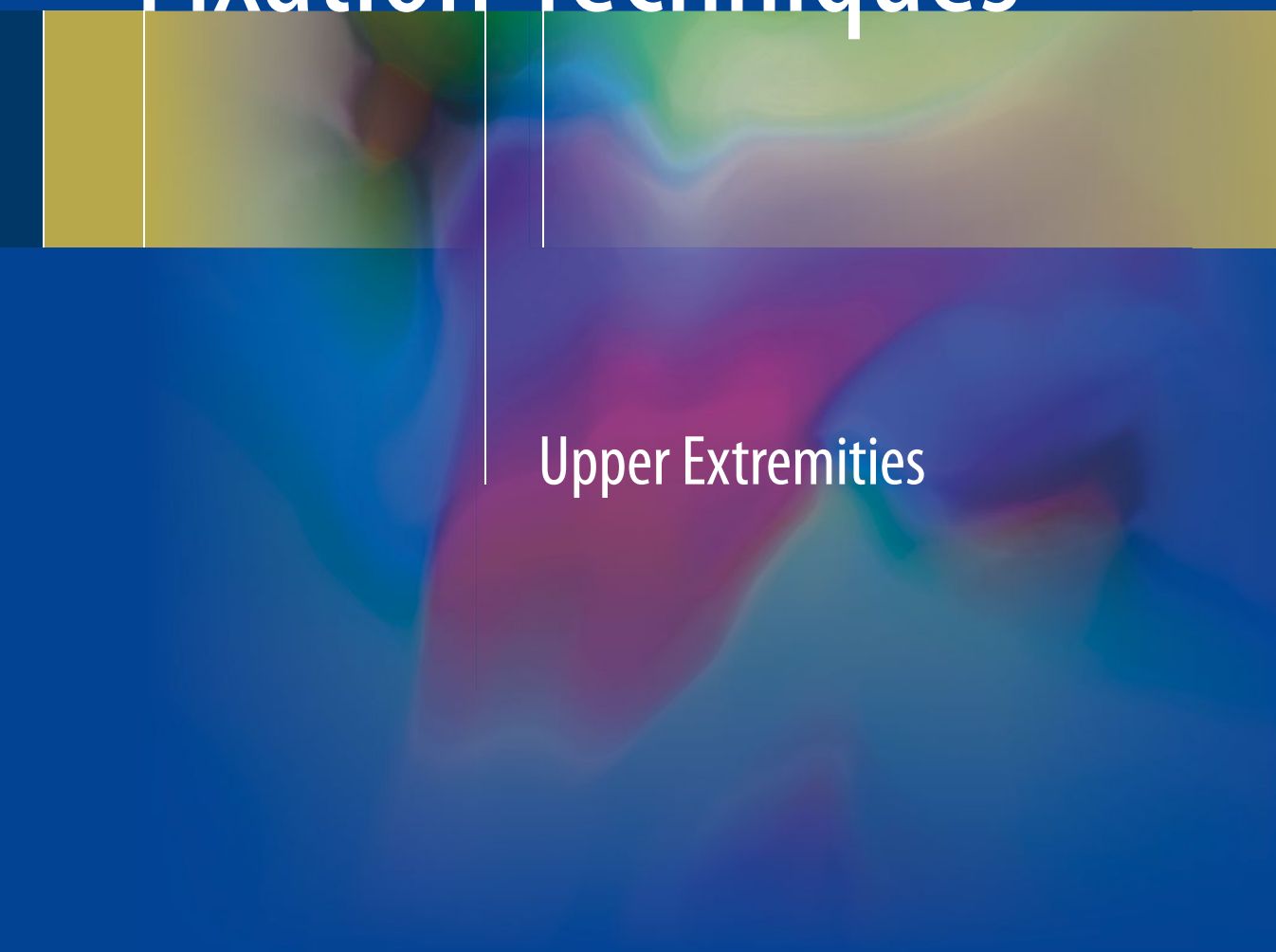
Peter V. Giannoudis
Editor

Fracture Reduction and Fixation Techniques

Upper Extremities



Springer

Fracture Reduction and Fixation Techniques

Peter V. Giannoudis
Editor

Fracture Reduction and Fixation Techniques

Upper Extremities

Springer

Editor
Peter V. Giannoudis
School of Medicine
University of Leeds
Leeds
Yorkshire
United Kingdom

ISBN 978-3-319-68627-1 ISBN 978-3-319-68628-8 (eBook)
https://doi.org/10.1007/978-3-319-68628-8

Library of Congress Control Number: 2018930258

Printed on acid-free paper

This Springer imprint is published by Springer Nature
The registered company is Springer International Publishing AG
The registered company address is: Gewerbestrasse 11, 6330 Cham, Switzerland

Preface

Fracture fixation techniques have continued to evolve since their introduction in the 1950s by the AO Group in Switzerland. Advances made in metallurgy, implant design, targeting devices, surgical instruments, radiology and functional anatomy and the better understanding of fracture healing led to the modern practising techniques. Preoperative planning became a routine step of every fixation case. Moreover, it was recognised that optimal fracture reduction prior to fixation is a key element facilitating bone repair and a satisfactory anatomical and functional outcome. There is plenty of scientific evidence available that suboptimal fracture reduction is often associated with complications such as implant failure, impaired healing, malunion and early onset of osteoarthritis, amongst others.

This highly illustrated textbook is written by a panel of experts in the upper limb, who share tips and tricks that will aid in achieving an optimal reduction and fixation of different fracture types whilst avoiding common pitfalls.

Each technique is clearly demonstrated using a stepwise approach with real-time intraoperative photographs, improving the understanding and ensuring the production of an easy-to-read, memorable textbook.

Each chapter in this book includes an outline of useful techniques for fracture reduction. Its objective is to provide orthopaedic surgeons and especially those still in training with a quick reference to common reduction techniques becoming an essential guide to their practice. The ultimate goal is to improve the standards of care of our patients.

Leeds, UK — Peter Giannoudis

Contents

Part I

General Considerations

Fracture Healing: Back to Basics and Latest Advances

1

Ippokratis Pountos and Peter V. Giannoudis

The research on bone biology and healing over the last decades has been intense. The reason for this high research output can be attributed to two elements: firstly, the discovery of mesenchymal stem cells (MSCs), a population of multipotent stem cells found to reside in bone marrow (and in many other tissues within the body), which opened new avenues in tissue engineering approaches for bone regeneration, and secondly, the discovery and commercialization of molecules that can upregulate bone repair mechanisms. The aim of this chapter is to present the key aspects of bone healing biology, factors that can influence it adversely, and key strategies found to enhance the healing of fractures.

Types of Bone Healing

Bone healing is a well-orchestrated complex process that results in the reconstitution of bone continuity without the formation of scar tissue. It prerequisites the coordinated interplay of multiple cell types with local and systemic cytokines, chemokines, and growth factors. This local milieu is influenced and often regulated by the mechanical forces exerted locally. Bone healing can be divided into primary and secondary types of healing.

Primary

Primary bone healing occurs when there is a small fracture gap and absolutely no movement at the fracture site. The discovery of this type of healing occurred over a century ago with the introduction of stable internal fixation [1]. It was initially called "healing by primary intention" and subsequently "soudure autogène," but following histopathologic studies, the terms "direct" and "primary" bone healing were established [2]. Primary bone healing is the same process as the normal bone remodeling. Bone production and apposition to fill the fracture gap occur by the osteoblasts, in the same way that the Howship lacunae are filled after the action of "cutting cones." It occurs in cases where anatomic reduction and rigid internal fixation are achieved or in incomplete stable cracks of the bone. Fragment end resorption does not occur and no callus is formed. This form of bone healing is less frequent. The majority of fractures heal through secondary bone healing.

I. Pountos, M.B., M.D., E.E.C.
Academic Department of Trauma and Orthopaedics, School of Medicine, University of Leeds, Leeds, UK

P.V. Giannoudis, M.D., F.R.C.S. (✉)
Academic Department of Trauma and Orthopaedics, School of Medicine, University of Leeds, Leeds, UK

NIHR, Leeds, UK

Musculoskeletal Biomedical Research Center, Chapel Allerton Hospital, Leeds, UK
e-mail: pgiannoudi@aol.com

P.V. Giannoudis (ed.), *Fracture Reduction and Fixation Techniques*,
https://doi.org/10.1007/978-3-319-68628-8_1

Secondary Bone Healing

Secondary bone healing is the type of healing that occurs in the absence of rigid fixation. It represents an organized pattern of interlinked events that aim to activate a number of different cell types to prepare the fracture site for its consolidation, to restore the vascularity, to produce a stable mechanical environment, and once successful to conclude with the ossification of the area. It has been previously proposed that this type of healing occurs in three phases: the inflammatory, reparative, and remodeling phases. These generalized phases include a number of events, which are often overlapping. A more comprehensive description is that of the six stages of bone healing. Based on this descriptive system, healing starts at the time of the injury with the formation of fracture hematoma, followed by the inflammatory stage, which concludes with the formation of granulation tissue. Then, the formation of the soft callus occurs that eventually calcifies and remodels (Figs. 1.1 and 1.2).

Fracture Hematoma

The formation of fracture hematoma represents a distinct stage of the bone healing process. It is the first and possibly the most important determinant of the healing outcome. Several animal studies have shown that removing the fracture hematoma leads to an arrest of the healing process. Equally, when fracture hematoma is injected in ectopic sites, osteogenesis follows.

During fracture hematoma formation, a number of changes of the local microenvironment occur. The disruption of blood supply leads to a significant drop of the oxygen availability. The low local oxygen saturation changes the genetic expression of osteoprogenitor cells, promoting their proliferation, formation of extracellular matrix, and differentiation toward chondrocytes [3, 4]. This environment also induces the release of several inflammatory molecules, collagen, as well as angiogenic and osteogenic growth factors. In addition to the hypoxia, the CO_2 exudation from the dead and dying cells, the production of lactic acid, and the conversion of blood sugars make the local microenvironment acidic. This acidic environment favors osteoclast resorptive activity, and the levels of calcium increase by tenfold compared to peripheral circulating levels. Phosphorous, alkaline phosphatase, lactic acid, and beta and gamma globulins are also elevated in fracture hematoma [5].

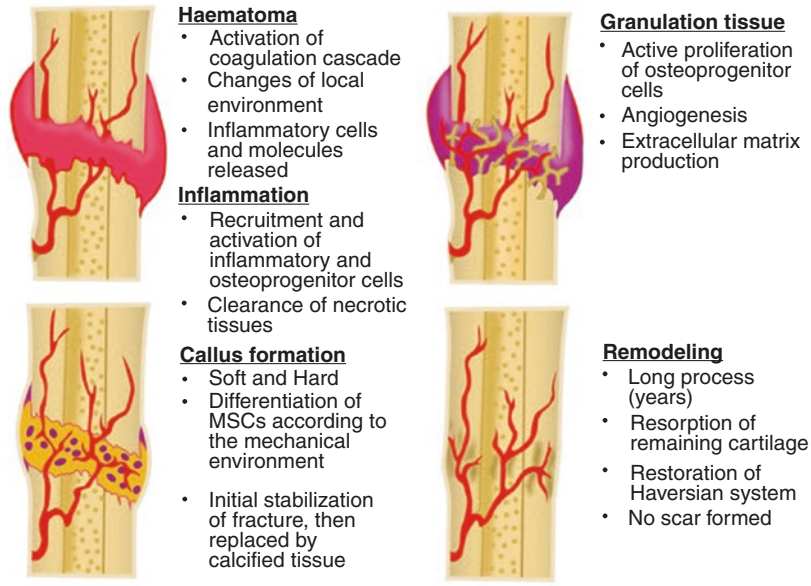


Fig. 1.1 The stages of secondary bone healing

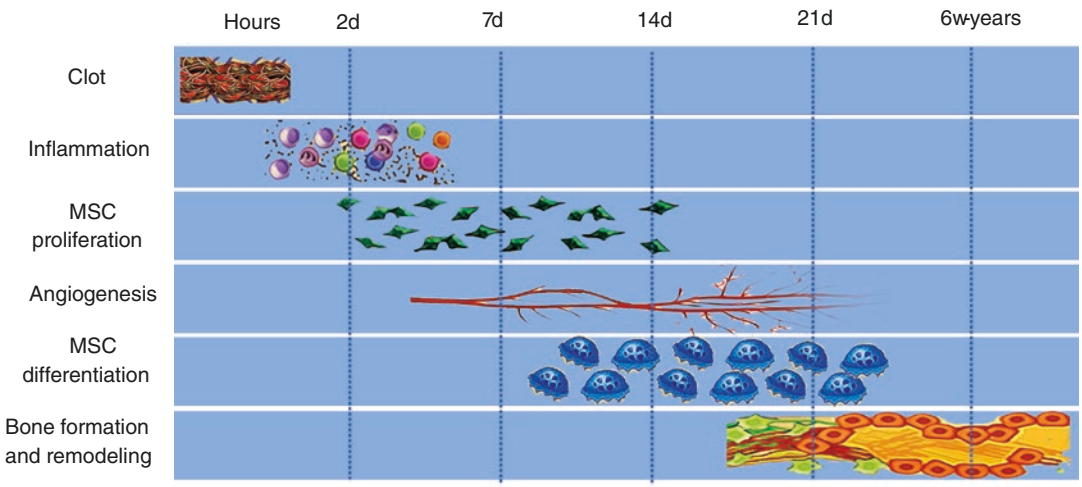


Fig. 1.2 Evolution of fracture healing over time

Inflammatory Stage

An adequate inflammatory phase is a prerequisite for successful bone healing [6, 7]. The inflammatory stage is activated after the hematoma formation and serves mainly two purposes. Firstly, it prepares the site for the upcoming healing process and secondly elicits pain that forces the individual to immobilize the affected limb. A large number of cells invade the fracture site attracted by the numerous inflammatory molecules. Polymorphonuclear leukocytes, lymphocytes, blood monocytes, and macrophages are present and release cytokines. They exert chemotactic effect, recruiting further inflammatory and mesenchymal cells, and stimulate angiogenesis, enhancing extracellular matrix synthesis. RUNX1 (runt-related transcription factor 1) expression predominates which is important for the proliferation of the hematopoietic stem cells and osteoprogenitor cells [8]. TNF-α plays an important role in the inflammatory stage, as it is significantly upregulated. Absence of TNF-α delays fracture healing, while excessive amounts destroy the bone [9, 10]. A number of cytokines are present, but their exact role is still largely obscure. Interleukin-17 (IL-17) has a dual effect enhancing osteogenic output but also bone resorption by the osteoclasts [11]. The levels of many inflammatory (IL-6, IL-8, IL-12) and anti-inflammatory (IL-10) molecules are significantly increased. Within the first week after the fracture, the fracture site develops an osteogenic identity.

Granulation Tissue

Once the inflammatory stage expires, the area of the fracture site is organized forming the granulation tissue. The granulation tissue is a loose aggregate of cells (mainly mesenchymal, endothelial, and immune cells) scattered inside an extracellular matrix. Mesenchymal stem cells from the periosteum and adjacent tissues are seen in the granulation tissue [12]. The fibrin deposits are removed by macrophages and through the actions of fibrinolytic enzymes. There is a significant mitogenic activity at the area, which is supported by the formation of new small blood vessels.

Soft Callus

Soft callus is closely related to the formation of cartilage through endochondral ossification. Endochondral ossification can be seen as an attempt of the body to improve the stability at the fracture site, allowing the ossification process to commence. The soft callus extends throughout the fracture gap connecting the ends of the bone. This process is similar to the bone growth observed in the growth plate. Chondrocytes start

preparing cartilage and extracellular matrix. The cellular density is significantly higher to that of healthy articular cartilage but its organization is different [13]. In addition to chondrocytes, fibroblasts start laying down stroma that helps and supports vascular ingrowth. It has been previously shown that smoking adversely affects this particular aspect of bone healing, i.e., vascular ingrowth [14, 15].

Hard Callus

Hard callus is synonymous to the formation of woven bone. Depending on the stability of the fracture site, woven bone can be formed immediately after the formation of granulation tissue through intramembranous ossification (stable fracture), or it can follow the endochondral ossification. During the intramembranous ossification, osteoprogenitor cells differentiate directly to osteoblasts, without the formation of cartilage as an intermediate step. In less stable fractures, the cartilage previously formed by chondrocytes is replaced by the bone. Irrespectively of the route followed, osteoblasts release vesicles that contain calcium phosphate complexes into the matrix [16]. They also release enzymes that degrade the proteoglycan-rich matrix and hydrolyze phosphate esters to provide phosphate ions for precipitation with calcium [17]. The transition from cartilage formation to bone formation is not yet fully elucidated. The simplest theory is based on the property of cells of mesenchymal origin to swap fates and become a different cell types. It was previously shown that fully differentiated osteoblasts with detectable alkaline phosphatase activity and elaboration of calcified extracellular matrix can redifferentiate to other cell types like adipocytes and vice versa. This phenomenon is termed genetic reprogramming or transdifferentiation. Another hypothesis suggests that chondrocytes became engulfed in the newly formed matrix, stop producing cartilage, and eventually die [18]. Chondrocyte cell death seems to occur at the border of the soft callus, just within the newly produced matrix [18].

Remodeling

The remodeling stage is the final stage of secondary bone healing that can last for many years. It represents a gradual modification of the architecture that ultimately reestablishes the typical osteon structure and the haversian system of the bone [19]. This is done under the same mechanical stresses involved in the normal remodeling of the bone [20]. The end result resembles the prefracture state of the bone.

Factors Affecting Bone Healing

The last century was characterized by a revolution in our understanding of bone biology and fracture management. Among the pioneers are the members of the Arbeitsgemeinschaft für Osteosynthesefragen (AO) group who identified some of the key principles governing fracture management, such as (1) accurate anatomical reduction, (2) rigid internal fixation, (3) sound atraumatic surgical technique, and (4) respect for the soft tissue envelope. A number of factors have been found to interrupt the normal flow of the bone healing process. These factors can be broadly divided in fracture or injury dependent and patient dependent (Table 1.1).

Table 1.1 Factors affecting bone healing

Local factors	Systemic factors
• Location • Type of the fracture • Fracture gap • Bone loss—comminution • Degree of local trauma (injury and iatrogenic) • Blood supply • Method of fixation • Level of fracture stability • Presence of infection, foreign material, debris, dead tissue	• Age • Metabolic state and nutrition • Vitamins and mineral deficiencies • Smoking, alcohol • Systemic diseases – Diabetes – Vascular disease – Cancer—radiotherapy • Drug • Corticosteroids • NSAIDs • Antibiotics • Anticoagulants • Antineoplastic

Patient Dependent

Age and Gender

Patient's gender does not increase the risk of delayed healing or non-union. Males, however, have an increased risk of complications with healing due to the higher incidence of high-energy fractures.

Children heal faster than adults and a non-union is a rare occurrence [21, 22]. Children have a higher regeneration potential and thick periosteum and form large subperiosteal hematoma [21]. These factors contribute to the rapid formation of callus (seen in children) [21, 22]. In adults, animal and experimental models have shown that bone healing potential declines with age [23]. Some clinical studies have shown that age is a negative predictor for healing in specific fracture types like fractures of the clavicle and hip [24, 25]. However, whether this increased risk is related to the age per se or is related to the increased number of comorbidities seen in elderly is yet to be further elucidated [26].

Comorbidities

Malnutrition and metabolic deficiencies represent major risk factors for unsuccessful bone healing. In addition to the general health state, the patient's body should be able to cope with the increased metabolic requirements [27]. Deficiencies in calcium, phosphorus, vitamins C and D, albumin, and proteins were all shown to affect bone healing and functional recovery following a fracture [28, 29]. These parameters should be checked and corrected in all high-risk patients.

Following a fracture, the local trauma and swelling impair the blood supply to the fracture site. In patients with peripheral vascular disease, blood supply is already compromised resulting in a critical supply to the bone and soft tissue envelope. The oxygen transport can be reduced as well as the cellular flow to the fracture site. Nutrient and systemically released molecule availability can be compromised. Literature has shown that in such situations, i.e., compromised peripheral blood supply, inhibition of the bone healing process can occur [30]. A circulatory assessment should always be performed in patients that have sustained a fracture especially those with vascular disease.

Increased healing times and higher risk of non-union have been demonstrated in patients with diabetes. Growth factors like the VEGF and TGF-β were found to be reduced in diabetes, and insulin availability seems to be an important factor during bone healing [31]. The effective management of diabetes in these patients is critical to minimize the potential complications [32].

Hypothyroidism has been found to inhibit endochondral ossification and delay bone healing [33]. As undiagnosed hypothyroidism is quite prevalent in the general population (approximately 5%), screening in high-risk patients should be performed [34].

Anemia is associated with significant deficiencies in bone healing. This has been evident in both clinical and animal studies [35]. These findings have been attributed to the availability of oxygen at the fracture site and the impairment of cellular functions like the production of collagen [36].

Other comorbidities that have been associated with an impairment of bone healing include renal disease, rheumatoid arthritis (possibly related to the use of steroids), and obesity [37].

Drug Administration

The antineoplastic drugs have strong antiproliferative and cytotoxic properties. They inhibit angiogenesis and callus formation and result in higher non-union rates [38]. Similarly, antiangiogenesis agents have a detrimental effect on fracture healing, and the final outcome resembles atrophic non-union [39].

Corticosteroid administration leads to osteoblast apoptosis, osteocyte apoptosis, and inhibition of osteoblastogenesis. Patients on long-term steroids are likely to suffer of low bone mass and have a higher incidence of fractures [40]. During bone healing the length of corticosteroid administration and dose are two critical parameters. Prolonged administration and high doses seem to be detrimental for bone healing. Smaller doses can downregulate fracture healing as well; hence, the clinicians should decide on risks versus the benefits basis [41]. In addition to corticosteroids, disease-modifying drugs like methotrexate are widely used for the treatment of chronic diseases. The available evidence is limited and mainly related to methotrexate. Methotrexate seems to have a dose-dependant effect on experimental studies with low doses being relatively safe [42]. The clinical case series presenting bone healing complications are related to higher doses similar to the ones used in cancer treatment [43]. There is limited evidence in regard to the remaining disease-modifying drugs [42].

Nonsteroidal anti-inflammatory drugs (NSAIDs) are effective medications for the management of acute musculoskeletal pain. They block the cyclooxygenase activity and inhibit the synthesis of prostaglandins, which are potent mediators of pain and inflammation [20]. Their analgesic effect in patients with fractures has been graded equal to that of stronger opiates [20]. The numerous experimental studies available are inconclusive and present diverse and contradicting results [20]. With regard to the clinical studies, there is sufficient evidence to suggest that NSAIDs can inhibit bone healing and the formation of heterotopic bone [44, 45]. Non-union risk was shown to double or even triple among various studies [46]. In balance of evidence, it seems judicious to avoid exposure to NSAIDs in patients with fractures.

Antibiotics play an important role in trauma care and fracture management. They are most frequently administered systemically but also applied locally, usually loaded onto the bone cement. Current literature is rather insufficient to allow a clear statement on whether they inhibit bone healing. Fluoroquinolones at therapeutic doses were found to interfere with the early stages of bone healing in small animal models [47]. Other drugs like tobramycin, rifampicin, and gentamicin were also found to downregulate the functions of osteoblasts [48]. Combinations of antibiotics could be detrimental in osteoprogenitor proliferation and differentiation, although the same antibiotics in isolation do not exhibit significant effects. Often underestimated are the kinetics of antibiotics loaded on cement which can reach concentrations 1000-fold higher that the systemically applied ones. Such high doses were shown to have detrimental effects on bone cells biology.

Anticoagulants are prescribed in the majority of hospitalized and non-weight-bearing patients to prevent deep venous thrombosis. Studies that evaluate their direct effect on human osteoprogenitor cells, quite uniformly, suggest that they reduce the proliferation and differentiation potential of osteoprogenitor cells and several osteogenic markers like BMP-2 and IGFs [49]. With regard to the in vivo experimental studies, contradictory results exist; some studies suggest that anticoagulants can impair bone healing, while others contradict these results [50]. At present there are no clinical studies to address this in humans [53].

Smoking and Alcohol

Smoking has several adverse effects on the human skeleton. It decreases the proliferative capacity of osteoblasts, reduces the overall bone mineral density, increases the rate of hip fractures, and decreases its healing capacity [51]. Currently several hypotheses exist for the mode of action of tobacco smoking on the skeleton; reduced blood supply, increase of oxygen intermediates, interference with arteriole receptors, and inhibition of vitamins are all potential pathways [52]. The vast majority of orthopedic literature highlights the importance of ceasing smoking with clinical studies uniformly showing that smoking delays bone healing, significantly increases the risk of non-union and, and at least doubles the risk of infection in patients undergoing surgery [53].

Chronic alcohol consumption induces osteopenia and increases the risk of falls. Alcohol is found to downregulate bone formation through a dose-dependant adverse effect on the functions of osteoblasts. It is of great interest that Saville have shown that the bone density measured in the left iliac crest of alcoholics below 45 years of age was similar to that of nonalcoholic men and women older than 70 years [54]. In addition, alcohol inhibits the proliferation and differentiation of MSCs as well as the production of ossified bone matrix [55]. Clinical studies have shown that alcoholism is associated with osteomalacia, impaired fracture healing, and aseptic necrosis (primarily necrosis of the femoral head) [55].

In addition to smoking and alcohol consumption, the use of recreational drugs also impairs bone mineral density and bone healing capacity. The available literature is limited, but the available studies clearly highlight an adverse effect [56].

Genetic Predisposition

A significant number of patients with an atrophic non-union do not have any of the aforementioned risk factors. These patients are most often young, active, fit and well, and without any conditions that are known to interfere with bone healing. The theory of "genetic predisposition" to equation of fracture non-union has been supported by a number of authors. Animal studies have shown that a downregulated expression of various bone morphogenetic proteins, bone morphogenetic protein inhibitors, fibroblast growth factor signaling pathway, and insulin-derived growth factor can result in non-union [57]. In humans, an association between the CCG haplotype of PDGF-A, specific variants of the TLR4 (mutated 1/W) and TGF-β (mutated homozygote T and heterozygote C/T), and the occurrence of non-unions has been shown [58]. In addition Dimitriou et al. showed that two specific polymorphisms of two inhibitors of the BMP pathway, the noggin (the G/G genotype of the rs1372857 SNP) and Smad6 (the T/T genotype of the rs2053423 SNP), were associated with a greater risk of fracture non-union [59].

Fracture Dependent

In addition to the patient-dependent factors, local factors related to the injury are important. Among them, the fracture personality, location, extent of soft tissue damage, and fixation method are critical elements for the bone healing process.

Fracture Personality and Location

The orientation of the fracture line and the underlying bone are two factors that can influence the bone healing process. The orientation of the fracture line influences the surface areas of bony contact and can influence the healing. The differences in the repair process between undisplaced and displaced fractures are well documented. They involve retardation of the rate as well as an increase in the amount of cartilage formed and a decrease in the amount of primary bone formation between the fracture ends [60]. The location of the fracture can be also an important factor. Different healing rates are reported between different bones. For instance, reported non-union rates ranged from up to 18% in tibial diaphysis but 1.7% in the femoral shaft after reamed nailing [61].

The fracture gap can directly influence the healing process. A gap of 2 mm or higher can adversely affect the bone healing process [62]. Claes et al. compared three different gap sizes: small, medium, and large [62]. Comparing the small to the medium fracture gaps, a large callus was noted with lower fracture stiffness in the group with medium fracture gap. The group with the large gap produced little callus and had low stiffness. In addition to the amount of callus formation, the fracture gap influences the revascularization of the fracture site [63]. Other factors that can influence the fracture healing process include the amount of bone loss, the fracture comminution, and the presence of debris or necrotic tissue or other foreign materials [64]. Finally, the presence of infection has devastating outcomes on the overall healing process.

Soft Tissue Envelope

The degree of local trauma is crucial for fracture healing. An intact soft tissue envelope will prevent the escape of fracture hematoma, provide osteoprogenitor cells, and contribute to the angiogenesis of the fracture site. It will also act as a barrier against pathogen invasion. The amount of trauma and the condition of the soft tissue envelope are related to the amount of callus that is formed. Moderate soft tissue trauma delays new bone formation but only in the early phase of fracture healing [65]. The latter occurs because the surrounding soft tissues are the primary sites to support the bone healing by acting as an important vascular source to deliver oxygen, nutrients, and osteoprogenitor cells to the fracture area. Vascular damage accompanying skeletal injury increases the rate of non-union by fourfold [66]. It requires muscle flap coverage that increases the local bone blood flow and the rate of osteotomy union compared to skin repair, thus supporting the vascular role of muscle in bone regeneration [67]. In addition to the blood flow, the surrounding soft tissue contributes in terms of osteogenic growth factors, cytokines, and chemokines [67]. Reverte et al. demonstrated that tibial fractures with associated soft tissue injury significantly impaired fracture healing [68]. They showed that the rate of delayed union or non-union in tibial fractures with associated compartment syndrome was 55%, in comparison to 17.8% in patients with tibial fracture without associated compartment syndrome [68].

Iatrogenic damage to the bones' soft tissue envelope is a parameter often overlooked. The surgical approach used, the manipulation to reduce the fracture, and the preparation for the application of the implant are all factors that can lead to a vascular compromise of the fracture site. Another factor often underestimate is the excessive stripping of the periosteum during plating and the pressure of the plates on the on the periosteal surfaces. A sound surgical technique and the use of low contact implants help to reduce the area of contact. Today's LC-DCP plates use a trapezoidal cross section, which varies along the length of the plate, to reduce the impact on the periosteum.

Fixation Method and Mechanical Stability

The mechanical stability is closely related to the fracture itself and the method used for fixation. It has been previously shown that small interfragmentary movement is beneficial to fracture healing but small interfragmentary movement is critical. Claes et al. have shown that the fate and output of osteogenic cells are related to the mechanical environment [69]. In particular, intramembranous ossification found to occur with small strain and small hydrostatic pressures, while endochondral ossification occurred with higher hydrostatic pressures. Large strains were found to lead to connective tissue formation. The proliferation and transforming growth factor beta production of osteoblasts were increased for strains up to 5% but decreased for larger strains. In addition to the in vitro models, it has been shown that excessive macroscopic movement can arrest the fracture healing process or result in the refracture of the hard callus [70]. On the other hand, the absence of any strains can result in the remodeling mechanisms to prevail over the modeling drifts, and the net result would be removal of callus with delayed or failed bone healing [70].

The fracture fixation can significantly change the biology of bone healing. Fractures treated with the AO principles of absolute stability heal through primary bone healing without the formation of callus. On the other hand, if the same fracture is fixed through the relative stability principle, the fracture will heal with indirect bone healing with callus formation (Fig. 1.3). In addition to the mode of healing, the type of fracture fixation used can alter the outcome. It has been shown, for example, that humeral shaft fractures treated with an intramedullary device carry worse outcome in comparison to those treated with plating [71]. Another example is the different union rates between reamed and unreamed femoral nail with regard to the delayed union and non-union rate [72]. Even minor adaptations of the principles can alter the outcome. In a study by Krettek et al., for instance, 99 open tibial shaft fractures were treated with external fixation, which was complemented with a lag screw [73].

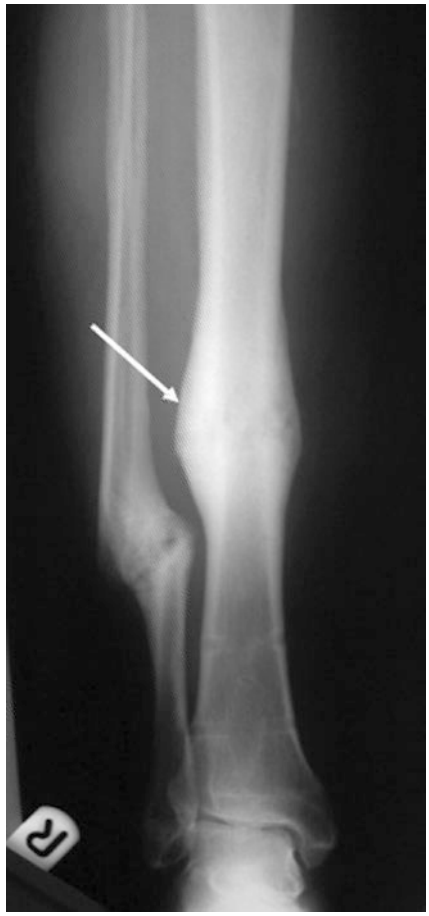


Fig. 1.3 Anteroposterior right tibia radiograph 14 months after originally the fracture was fixed with an intramedullary nail which was removed at 12 months following fracture union. The arrow demonstrates that union occurred with indirect/secondary bone healing (callus formation)

The result was a significant reduction in fracture consolidation. In a similar study, good union rates were documented with external fixation alone [74].

Approaches to Enhance Bone Healing

A number of different approaches have been described to enhance the bone repair response (Table 1.2). Moreover, the conceptual framework of the diamond concept has been described to assist the clinicians to appreciate the most important components of fracture healing that must be present for a successful outcome (Fig. 1.4) [75].

Bone Grafting

Autologous bone grafting from the iliac crest contains all the required elements for bone healing [76]. It has osteoinductive, osteoconductive, and osteogenic properties. It can be harvested with a simple technique; it has low cost and no risk of disease transmission or immunorejection. On the other hand, autologous bone grafting is associated with significant donor site morbidity, often with persistent pain at the harvest site. It can be of limited volume, and the isolated graft, unless tricortical, does not offer any structural support [77].

Table 1.2 Potential applications for the upregulation of bone healing

Application of osteogenic materials	Systemic enhancement
Autologous bone Autologous bone marrow Reamer-irrigation aspiration graft Combined grafts (Diamond concept)	Parathyroid hormone Biphosphonates Anti-sclerostin antibodies Anti-Dickkopf-related protein 1 antibodies
Local growth factor applications	**Biophysical Stimulation**
Bone morphogenetic proteins (BMPs) Fibroblast growth factors (FGF) Vascular Endothelial growth factor (VEGF) Platelet-derived growth factors (PDGF) Molecules involved in Wnt pathway	Electromagnetic field stimulation Low-intensity pulsed ultrasound stimulation Etracorporeal shock wave therapy

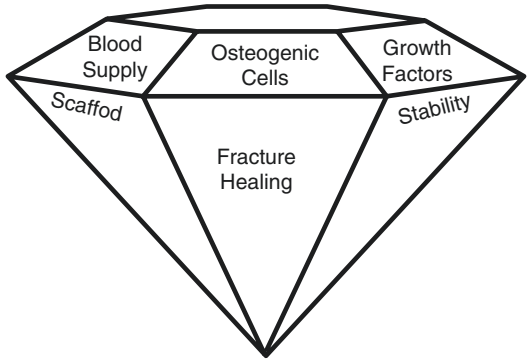


Fig. 1.4 Diamond concept of fracture healing demonstrating the key players that must be present for a successful bone repair response

In addition to the autologous grafting from the iliac crest, grafts obtained with the use of the reamer-irrigator-aspirator (RIA) system (Synthes®, Inc. West Chester, Philadelphia) have gained popularity over the years. A larger volume of graft material can be harvested, capable to fill large bone defects. Unfortunately, RIA grafts contain no or little osteoprogenitor cells (most contained in the waste water) [78] and are associated with a number of complications. Significant intraoperative blood loss with need for transfusion as well as thinning of the cortex and iatrogenic fractures can occur [74]. A large number of bone graft materials are currently commercially available; none, however, is found to outperform the autologous bone grafts.

Application of Cells

Bone marrow aspirates contain MSCs, which are renowned of their osteogenic and angiogenic properties. These cells have the capacity of self-regenerating and are able to produce some of the key molecules involved in bone healing (BMPs, VEGF, etc.). Several authors have shown that a simple bone marrow injection in the fracture or non-union site can result in healing in approximately 90% of cases [79]. Hernigou et al. found that there was a significant correlation between the numbers of MSCs with the clinical outcome. Techniques to concentrate the bone marrow aspirates exist; however, difficulties regarding the high volume of the injectable formulation and the technical issues resulting in inconsistencies in the number of MSCs and the volume of the bone marrow require further research.

Application of Growth Factors

Bone morphogenetic proteins (BMPs) are molecules involved in many functions of the body including development, repair, and regeneration. BMP-2 and BMP-7 have become commercially available for clinical applications including open tibial fractures and lumbar spine fusion or under a humanitarian device exception [80]. However, their off-label application has been diverse. BMP-2 and BMP-7 are potent osteoinductive molecules; both upregulate the osteogenic differentiation and osteogenic output. Clinical results of studies investigating the bone healing have been favorable [80, 81].

Platelet-rich plasma (PRP) is an increased concentration of autologous platelets suspended in a small amount of plasma after centrifugation. The activation of platelets results in the release of several molecules involved in the clotting cascade but also growth factors stored in the platelet α-granules. Such molecules include the platelet-derived growth factor (PDGF), insulin-like growth factor (IGF), vascular endothelial growth factor (VEGF), platelet-derived angiogenic factor (PDAF), and transforming growth factor beta (TGF-β) [82]. This technique is relatively safe and of low cost. The experimental studies have been favorable; however, in a recent meta-analysis including 23 RCTs and 10 prospective studies, the authors questioned its overall effectiveness in fracture healing [83].

Platelet-derived growth factor is a potent promoter of osteogenic cell proliferation, differentiation, and osteogenic output. It also regulates chemotaxis and angiogenesis at the fracture site [84]. A prospective RCT including 434 patients undergoing hindfoot or ankle arthrodesis has shown that PDGF with beta-tricalcium (Augment® Bone Graft, Wright Medical) results in comparable fusion rates as autologous

grafting but with less side effects and less complaints of pain [85].

Systemic Biological Factors

Parathyroid hormone (PTH) is a naturally occurring hormone that is known to increase the bone density. Its effect seems to be directly related to the osteogenic cell lineages and through interaction with the Wnt pathway. Experimental and clinical results have been encouraging [86]. In elderly patients with pelvic fractures, PTH administration resulted in a faster time to union compared to controls [86, 87]. In a similar study, faster healing times were also noted in patients suffering of distal radial fractures [88].

Bisphosphonates are inhibitors of osteoclastic activity. Experimental studies have shown however that they could also enhance fracture healing [89]. Despite the fact that the clinical studies are very limited, some of the data presented seem promising [90].

Physical Stimulation

Several devices nowadays are marketed as bone stimulators. They are appealing as they are non-invasive and with minimal complications. These devices can be broadly divided into three categories: electrical stimulators, low-intensity pulsed ultrasonography, and extracorporeal shock wave therapy.

Electrical stimulators are devices capable of generating an electrical potential at the fracture site. It was previously found that during fracture compression an electronegative potential is created which can trigger bone formation [91]. On the contrary an electropositive potential leads to bone loss. Therefore, applying the appropriate electrical potential can result in bone formation at the fracture site. Experimental studies were in the majority in favor of this theory [91]. Clinical studies have been inconclusive. A recent meta-analysis has concluded that there was no significant impact of electromagnetic stimulation on delayed unions or ununited long bone fractures. However, some uncertainty exists due to the methodological limitations and the high between-study heterogeneity [91].

The low-intensity pulsed ultrasonography (LIPUS) principle is based on the production of its sound waves that generate micro-stresses at the fracture site. The cells present at the fracture site can be stimulated by these stresses and increase their osteogenic output. LIPUS was found to accelerate mineralization in vitro through the upregulation of the expression of osteocalcin, alkaline phosphatase, VEGF, and MMP-13 [92]. In vivo evidence also suggests that LIPUS can accelerate all stages of the fracture repair process (inflammation, soft callus formation, hard callus formation). However, in a recent meta-analysis of the available evidence, it was suggested that LIPUS does not improve outcomes and probably has no effect on radiographic bone healing [93].

Extracorporeal shock wave therapy produces a single high-amplitude sound wave that propagates through the fracture site. These shock waves stimulated cellular changes promoting the production of several osteogenic growth factors. Some evidence that extracorporeal shock wave therapy is effective for hypertrophic non-unions than atrophic non-unions exists, but most of the current knowledge is based on level 4 evidence, and further studies are needed to confirm whether any benefit exists [94, 95].

Conflict of Interest No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this chapter.

References

1. Lane WAL. The operative treatment of fractures. 2nd ed. London: The Medical Publishing Co. Ltd; 1914.
2. Danis R. Théorie et pratique de l'ostéosynthèse. Paris: Masson; 1949.
3. Kolar P, Gaber T, Perka C, Duda GN, Buttgereit F. Human early fracture hematoma is characterized by inflammation and hypoxia. Clin Orthop Relat Res. 2011;469(11):3118–26.
4. Burke D, Dishowitz M, Sweetwyne M, Miedel E, Hankenson KD, Kelly DJ. The role of oxygen as a

regulator of stem cell fate during fracture repair in TSP2-null mice. J Orthop Res. 2013;31(10):1585–96.
5. Wray JB. The biochemical characteristics of the fracture hematoma in man. Surg Gynecol Obstet. 1970;130(5):847–52.
6. Mountziaris PM, Mikos AG. Modulation of the inflammatory response for enhanced bone tissue regeneration. Tissue Eng Part B Rev. 2008;14(2):179–86.
7. Xing Z, Lu C, Hu D, Miclau T 3rd, Marcucio RS. Rejuvenation of the inflammatory system stimulates fracture repair in aged mice. J Orthop Res. 2010;28(8):1000–6.
8. Friedman AD. Cell cycle and developmental control of hematopoiesis by Runx1. J Cell Physiol. 2009;219(3):520–4.
9. Karnes JM, Daffner SD, Watkins CM. Multiple roles of tumor necrosis factor-alpha in fracture healing. Bone. 2015;78:87–93.
10. Mountziaris PM, Spicer PP, Kasper FK, Mikos AG. Harnessing and modulating inflammation in strategies for bone regeneration. Tissue Eng Part B Rev. 2011;17(6):393–402.
11. Nam D, Mau E, Wang Y, Wright D, Silkstone D, Whetstone H, Whyne C, Alman B. T-lymphocytes enable osteoblast maturation via IL-17F during the early phase of fracture repair. PLoS One. 2012;7(6):e40044.
12. Einhorn TA. The cell and molecular biology of fracture healing. Clin Orthop Relat Res. 1998;(355 Suppl):S7–21.
13. Bianco P, Cancedda FD, Riminucci M, Cancedda R. Bone formation via cartilage models: the "borderline" chondrocyte. Matrix Biol. 1998;17(3):185–92.
14. Daftari TK, Whitesides TE Jr, Heller JG, Goodrich AC, McCarey BE, Hutton WC. Nicotine on the revascularization of bone graft. An experimental study in rabbits. Spine (Phila Pa 1976). 1994;19(8):904–11.
15. Rubenstein I, Yong T, Rennard SI, Mayhan WG. Cigarette smoke extract attenuates endothelium-dependent arteriolar dilatation in vivo. Am J Phys. 1991;261(6 Pt 2):H1913–8.
16. Brighton CT, Hunt RM. Histochemical localization of calcium in the fracture callus with potassium pyroantimonate. Possible role of chondrocyte mitochondrial calcium in callus calcification. J Bone Joint Surg Am. 1986;68(5):703–15.
17. Einhorn TA, Hirschman A, Kaplan C, Nashed R, Devlin VJ, Warman J. Neutral protein-degrading enzymes in experimental fracture callus: a preliminary report. J Orthop Res. 1989;7(6):792–805.
18. Ford JL, Robinson DE, Scammell BE. The fate of soft callus chondrocytes during long bone fracture repair. J Orthop Res. 2003;21(1):54–61.
19. Claes L, Recknagel S, Ignatius A. Fracture healing under healthy and inflammatory conditions. Nat Rev Rheumatol. 2012;8(3):133–43. https://doi.org/10.1038/nrrheum.2012.1.
20. Pountos I, Georgouli T, Calori GM, Giannoudis PV. Do nonsteroidal anti-inflammatory drugs affect bone healing? A critical analysis. Sci World J. 2012;2012:606404.
21. Lindaman LM. Bone healing in children. Clin Podiatr Med Surg. 2001;18:97–108.
22. Wilkins KE. Principles of fracture remodeling in children. Injury. 2005;36(Suppl 1):A3–11.
23. Aho AJ. Electron microscopic and histologic studies on fracture repair in old and young rats. Acta Chir Scand Suppl. 1966;357:162–5.
24. Parker MJ. Prediction of fracture union after internal fixation of intracapsular femoral neck fractures. Injury. 1994;25(Suppl 2):B3–6.
25. Robinson CM, Court-Brown CM, McQueen MM, Wakefield AE. Estimating the risk of nonunion following nonoperative treatment of a clavicular fracture. J Bone Joint Surg Am. 2004;86-A(7):1359–65.
26. Zura R, Braid-Forbes MJ, Jeray K, Mehta S, Einhorn TA, Watson JT, Della Rocca GJ, Forbes K, Steen RG. Bone fracture nonunion rate decreases with increasing age: A prospective inception cohort study. Bone. 2017;95:26–32.
27. Hayda RA, Brighton CT, Esterhai JL Jr. Pathophysiology of delayed healing. Clin Orthop Relat Res. 1998;(355 Suppl):S31–40.
28. Einhorn TA, Gerstenfeld LC. Fracture healing: mechanisms and interventions. Nat Rev Rheumatol. 2015;11(1):45–54.
29. Einhorn TA, Bonnarens F, Burstein AH. The contributions of dietary protein and mineral to the healing of experimental fractures. A biomechanical study. J Bone Joint Surg Am. 1986;68(9):1389–95.
30. Brinker MR, Bailey DE Jr. Fracture healing in tibia fractures with an associated vascular injury. J Trauma. 1997;42(1):11–9.
31. Bibbo C, Lin SS, Beam HA, Behrens FF. Complications of ankle fractures in diabetic patients. Orthop Clin North Am. 2001;32(1):113–33.
32. Gorter EA, Krijnen P, Schipper IB. Vitamin D status and adult fracture healing. J Clin Orthop Trauma. 2017;8(1):34–7.
33. Kowalewski K, Yong S. Bone and urinary hydroxyproline in normal and hypothyroid rat with a long bone fracture. Acta Endocrinol. 1967;56(3):547–53.
34. Bilous RW, Tunbridge WM. The epidemiology of hypothyroidism-an update. Bailliere Clin Endocrinol Metab. 1988;2(3):531–40.
35. Dix B, Grant-McDonald L, Catanzariti A, Saltrick K. Preoperative Anemia in Hindfoot and Ankle Arthrodesis. Foot Ankle Spec. 2017;10(2):109–15.
36. Gruson KI, Aharonoff GB, Egol KA, Zuckerman JD, Koval KJ. The relationship between admission hemoglobin level and outcome after hip fracture. J Orthop Trauma. 2002;16(1):39–44.
37. Chakkalakal DA, Novak JR, Fritz ED, Mollner TJ, McVicker DL, Lybarger DL, McGuire MH, Donohue TM Jr. Chronic ethanol consumption results in deficient bone repair in rats. Alcohol Alcohol. 2002;37(1):13–20.

38. Hazan EJ, Hornicek FJ, Tomford W, Gebhardt MC, Mankin HJ. The effect of adjuvant chemotherapy on osteoarticular allografts. Clin Orthop Relat Res. 2001;385:176–81.
39. Hausman MR, Schaffler MB, Majeska RJ. Prevention of fracture healing in rats by an inhibitor of angiogenesis. Bone. 2001;29(6):560–4.
40. Aaron JE, Francis RM, Peacock M, Makins NB. Contrasting microanatomy of idiopathic and corticosteroid-induced osteoporosis. Clin Orthop Relat Res. 1989;243:294–305.
41. Pountos I, Georgouli T, Blokhuis TJ, Pape HC, Giannoudis PV. Pharmacological agents and impairment of fracture healing: what is the evidence? Injury. 2008;39(4):384–94.
42. Pountos I, Giannoudis PV. Effect of methotrexate on bone and wound healing. Expert Opin Drug Saf. 2017;16(5):535–45.
43. Gerster JC, Bossy R, Dudler J. Bone non-union after osteotomy in patients treated with methotrexate. J Rheumatol. 1999;26:2695–7.
44. Neal BC, Rodgers A, Clark T, Gray H, Reid IR, Dunn L, MacMahon SW. A systematic survey of 13 randomized trials of non-steroidal anti-inflammatory drugs for the prevention of heterotopic bone formation after major hip surgery. Acta Orthop Scand. 2000;71(2):122–8.
45. Miller GK. Editorial Commentary: The Efficacy of Nonsteroidal Anti-inflammatory Drugs for Prophylaxis of Heterotopic Ossification in Hip Arthroscopy-Do We Treat Patients or X-rays? Arthroscopy. 2016;32(3):526–7.
46. Jeffcoach DR, Sams VG, Lawson CM, Enderson BL, Smith ST, Kline H, Barlow PB, Wylie DR, Krumenacker LA, McMillen JC, Pyda J, Daley BJ, University of Tennessee Medical Center, Department of Surgery. Nonsteroidal anti-inflammatory drugs' impact on nonunion and infection rates in long-bone fractures. J Trauma Acute Care Surg. 2014;76(3):779–83.
47. Perry AC, Prpa B, Rouse MS, Piper KE, Hanssen AD, Steckelberg JM, Patel R. Levofloxacin and trovafloxacin inhibition of experimental fracture-healing. Clin Orthop Relat Res. 2003;414:95–100.
48. Miclau T, Edin ML, Lester GE, Lindsey RW, Dahners LE. Bone toxicity of locally applied aminoglycosides. J Orthop Trauma. 1995;9(5):401–6.
49. Pilge H, Fröbel J, Prodinger PM, Mrotzek SJ, Fischer JC, Zilkens C, Bittersohl B, Krauspe R. Enoxaparin and rivaroxaban have different effects on human mesenchymal stromal cells in the early stages of bone healing. Bone Joint Res. 2016;5(3):95–100.
50. Street JT, McGrath M, O'Regan K, Wakai A, McGuinness A, Redmond HP. Thromboprophylaxis using a low molecular weight heparin delays fracture repair. Clin Orthop Relat Res. 2000;(381):278–89.
51. Melhus H, Michaëlsson K, Holmberg L, Wolk A, Ljunghall S. Smoking, antioxidant vitamins, and the risk of hip fracture. J Bone Miner Res. 1999;14(1):129–35.
52. Porter SE, Hanley EN Jr. The musculoskeletal effects of smoking. J Am Acad Orthop Surg. 2001;9(1):9–17.
53. Castillo RC, Bosse MJ, MacKenzie EJ, Patterson BM, LEAP Study Group. Impact of smoking on fracture healing and risk of complications in limb-threatening open tibia fractures. J Orthop Trauma. 2005;19(3):151–7.
54. Saville PD. Changes in bone mass with age and alcoholism. J Bone Joint Surg Am. 1965;47:492–9.
55. Arlot ME, Bonjean M, Chavassieux PM, Meunier PJ. Bone histology in adults with aseptic necrosis. Histomorphometric evaluation of iliac biopsies in seventy-seven patients. J Bone Joint Surg Am. 1983;65:1319–27.
56. Nogueira-Filho Gda R, Cadide T, Rosa BT, Neiva TG, Tunes R, Peruzzo D, Nociti FH Jr, César-Neto JB. Cannabis sativa smoke inhalation decreases bone filling around titanium implants: a histomorphometric study in rats. Implant Dent. 2008;17(4):461–70.
57. Dimitriou R, Kanakaris N, Soucacos PN, Giannoudis PV. Genetic predisposition to non-union: evidence today. Injury. 2013;44(Suppl 1):S50–3.
58. Zeckey C, Hildebrand F, Glaubitz LM, Jürgens S, Ludwig T, Andruszkow H, Hüfner T, Krettek C, Stuhrmann M. Are polymorphisms of molecules involved in bone healing correlated to aseptic femoral and tibial shaft non-unions? J Orthop Res. 2011;29(11):1724–31. https://doi.org/10.1002/jor.21443.
59. Dimitriou R, Carr IM, West RM, Markham AF, Giannoudis PV. Genetic predisposition to fracture non-union: a case control study of a preliminary single nucleotide polymorphisms analysis of the BMP pathway. BMC Musculoskelet Disord. 2011;12:44.
60. Rhinelander FW, Baragry RA. Microangiography in bone healing: Undisplaced closed fractures. J Bone Joint Surg. 1962;44A:1273.
61. Fong K, Truong V, Foote CJ, Petrisor B, Williams D, Ristevski B, et al. Predictors of nonunion and reoperation in patients with fractures of the tibia: an observational study. BMC Musculoskelet Disord. 2013;14:103.
62. Claes L, Augat P, Suger G, Wilke HJ. Influence of size and stability of the osteotomy gap on the success of fracture healing. J Orthop Res. 1997 Jul;15(4):577–84.
63. Claes L, Eckert-Hübner K, Augat P. The fracture gap size influences the local vascularization and tissue differentiation in callus healing. Langenbeck's Arch Surg. 2003;388(5):316–22.
64. Riehl JT, Connolly K, Haidukewych G, Koval K. Fractures Due to Gunshot Wounds: Do Retained Bullet Fragments Affect Union? Iowa Orthop J. 2015;35:55–61.
65. Claes L, Maurer-Klein N, Henke T, Gerngross H, Melnyk M, Augat P. Moderate soft tissue trauma delays new bone formation only in the early phase of fracture healing. J Orthop Res. 2006;24(6):1178–85.

66. Lu C, Miclau T, Hu D, Marcucio RS. Ischemia leads to delayed union during fracture healing: a mouse model. J Orthop Res. 2007;25(1):51–61.
67. Reverte MM, Dimitriou R, Kanakaris NK, Giannoudis PV. What is the effect of compartment syndrome and fasciotomies on fracture healing in tibial fractures? Injury. 2011;42(12):1402–7.
68. Claes LE, Heigele CA, Neidlinger-Wilke C, Kaspar D, Seidl W, Margevicius KJ, Augat P. Effects of mechanical factors on the fracture healing process. Clin Orthop Relat Res. 1998;(355 Suppl): S132–47.
69. Mavčič B, Antolič V. Optimal mechanical environment of the healing bone fracture/osteotomy. Int Orthop. 2012;36(4):689–95.
70. Hu X, Xu S, Lu H, Chen B, Zhou X, He X, Dai J, Zhang Z, Gong S. Minimally invasive plate osteosynthesis vs conventional fixation techniques for surgically treated humeral shaft fractures: a meta-analysis. J Orthop Surg Res. 2016;11(1):59.
71. Duan X, Li T, Mohammed AQ, Xiang Z. Reamed intramedullary nailing versus unreamed intramedullary nailing for shaft fracture of femur: a systematic literature review. Arch Orthop Trauma Surg. 2011;131(10):1445–52.
72. Krettek C, Haas N, Tscherne H. The role of supplemental lag-screw fixation for open fractures of the tibial shaft treated with external fixation. J Bone Joint Surg Am. 1991;73(6):893–7.
73. Claes L, Grass R, Schmickal T, Kisse B, Eggers C, Gerngross H, Mutschler W, Arand M, Wintermeyer T, Wentzensen A. Monitoring and healing analysis of 100 tibial shaft fractures. Langenbeck's Arch Surg. 2002;387(3–4):146–52.
74. Pountos I, Panteli M, Georgouli T, Giannoudis PV. Neoplasia following use of BMPs: is there an increased risk? Expert Opin Drug Saf. 2014;13(11):1525–34.
75. Giannoudis PV, Einhorn TA, Marsh D. Fracture healing: the diamond concept. Injury. 2007;38(Suppl 4):S3–6.
76. Crist BD, Stoker AM, Stannard JP, Cook JL. Analysis of relevant proteins from bone graft harvested using the reamer irrigator and aspirator system (RIA) versus iliac crest (IC) bone graft and RIA waste water. Injury. 2016;47(8):1661–8.
77. Marchand LS, Rothberg DL, Kubiak EN, Higgins TF. Is This Autograft Worth It?: The Blood Loss and Transfusion Rates Associated With Reamer Irrigator Aspirator Bone Graft Harvest. J Orthop Trauma. 2017;31(4):205–9.
78. Pountos I, Georgouli T, Kontakis G, Giannoudis PV. Efficacy of minimally invasive techniques for enhancement of fracture healing: evidence today. Int Orthop. 2010;34(1):3–12.
79. Kanakaris NK, Calori GM, Verdonk R, Burssens P, De Biase P, Capanna R, Vangosa LB, Cherubino P, Baldo F, Ristiniemi J, Kontakis G, Giannoudis PV. Application of BMP-7 to tibial non-unions: a 3-year multicenter experience. Injury. 2008;39(Suppl 2):S83–90.
80. Anitua E, Andia I, Ardanza B, Nurden P, Nurden AT. Autologous platelets as a source of proteins for healing and tissue regeneration. Thromb Haemost. 2004;91(1):4–15.
81. Sheth U, Simunovic N, Klein G, Fu F, Einhorn TA, Schemitsch E, Ayeni OR, Bhandari M. Efficacy of autologous platelet-rich plasma use for orthopaedic indications: a meta-analysis. J Bone Joint Surg Am. 2012;94(4):298–307.
82. Pountos I, Georgouli T, Henshaw K, Bird H, Jones E, Giannoudis PV. The effect of bone morphogenetic protein-2, bone morphogenetic protein-7, parathyroid hormone, and platelet-derived growth factor on the proliferation and osteogenic differentiation of mesenchymal stem cells derived from osteoporotic bone. J Orthop Trauma. 2010;24(9):552–6.
83. DiGiovanni CW, Lin SS, Baumhauer JF, Daniels T, Younger A, Glazebrook M, Anderson J, Anderson R, Evangelista P, Lynch SE, North American Orthopedic Foot and Ankle Study Group. Recombinant human platelet-derived growth factor-BB and beta-tricalcium phosphate (rhPDGF-BB/β-TCP): an alternative to autogenous bone graft. J Bone Joint Surg Am. 2013;95(13):1184–92.
84. Tzioupis CC, Giannoudis PV. The Safety and Efficacy of Parathyroid Hormone (PTH) as a Biological Response Modifier for the Enhancement of Bone Regeneration. Curr Drug Saf. 2006;1(2):189–203.
85. Peichl P, Holzer LA, Maier R, Holzer G. Parathyroid hormone 1-84 accelerates fracture-healing in pubic bones of elderly osteoporotic women. J Bone Joint Surg Am. 2011;93(17):1583–7.
86. Aspenberg P, Johansson T. Teriparatide improves early callus formation in distal radial fractures. Acta Orthop. 2010;81(2):234–6.
87. Türker M, Aslan A, Çırpar M, Kochai A, Tulmaç ÖB, Balcı M. Histological and biomechanical effects of zoledronate on fracture healing in an osteoporotic rat tibia model. Eklem Hastalik Cerrahisi. 2016;27(1):9–15.
88. 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.
89. Kuzyk PR, Schemitsch EH. The science of electrical stimulation therapy for fracture healing. Indian J Orthop. 2009;43(2):127–31.
90. Korenstein R, Somjen D, Fischler H, Binderman I. Capacitative pulsed electric stimulation of bone cells. Induction of cyclic-AMP changes and DNA synthesis. Biochim Biophys Acta. 1984;803(4):302–7.
91. Mollon B, da Silva V, Busse JW, Einhorn TA, Bhandari M. Electrical stimulation for long-bone fracture-healing: a meta-analysis of randomized controlled trials. J Bone Joint Surg Am. 2008;90(11):2322–30.
92. Pounder NM, Harrison AJ. Low intensity pulsed ultrasound for fracture healing: a review of the clinical

evidence and the associated biological mechanism of action. Ultrasonics. 2008;48(4):330–8.
93. Schandelmaier S, Kaushal A, Lytvyn L, Heels-Ansdell D, Siemieniuk RA, Agoritsas T, Guyatt GH, Vandvik PO, Couban R, Mollon B, Busse JW. Low intensity pulsed ultrasound for bone healing: systematic review of randomized controlled trials. BMJ. 2017;356:j656.
94. Vulpiani MC, Vetrano M, Conforti F, Minutolo L, Trischitta D, Furia JP, Ferretti A. Effects of extracorporeal shock wave therapy on fracture nonunions. Am J Orthop (Belle Mead NJ). 2012;41(9):E122–7.
95. Zelle BA, Gollwitzer H, Zlowodzki M, Bühren V. Extracorporeal shock wave therapy: current evidence. J Orthop Trauma. 2010;24(Suppl 1):S66–70.

2 Instruments Used in Fracture Reduction

Ippokratis Pountos, K. Newman, and Peter V. Giannoudis

Fracture reduction can be achieved by either direct or indirect means [1, 2]. Direct reduction means that the forces and moments applied when attempting to realign the bony fragments act at the vicinity of the fracture site, while, in indirect reduction, the forces are applied distally to the fracture site [3]. Direct reduction is often performed by direct visualization of the fracture site through surgical exposure. Utilising minimally invasive approaches, fractures can also be reduced percutaneously.

Indirect reduction involves forces along the axis of the limb, which in turn can result in fracture realignment through the action of the surrounding soft tissues (ligamentotaxis) [4, 5]. Indirect reduction can involve manual traction with manipulation or can be combined with tools like traction tables, distractors or external fixators.

I. Pountos, M.B., M.D., E.E.C.
Academic Department of Trauma & Orthopaedics, School of Medicine, University of Leeds, Leeds, UK

K. Newman, F.R.C.S.
St Peter's Hospitals NHS Foundation Trust, Chertsey, Surrey, UK

P.V. Giannoudis, M.D., F.R.C.S. (✉)
Academic Department of Trauma & Orthopaedics, School of Medicine, University of Leeds, Leeds, UK
NIHR, Leeds, UK

Musculoskeletal Biomedical Research Center, Chapel Allerton Hospital, Leeds, UK
e-mail: pgiannoudi@aol.com

In reality, not infrequently, combination of both direct and indirect techniques is often performed. Irrespectively of the reduction technique used, our current armamentarium in fracture reduction aids is ever expanding. The most commonly used instruments are described below. In general terms the instruments can be divided into external devices and internal devices.

External Devices

In this category the most commonly used devices include fracture tables, bumps and bolsters, crutches, skeletal traction, PORD, F-tool, large distractor and external fixator devices, amongst others.

Fracture tables with the capacity for skeletal traction are widely used in fracture management [6]. Fracture tables are radiolucent and designed to achieve and maintain satisfactory reduction of the fracture. The two most commonly used fracture tables are the traction table (Fig. 2.1) and the OSI table (Figs. 2.2 and 2.3).

Most often no further manipulation of the fracture is required once the patient is positioned. Patient positioning on the fracture table is often critical. A thorough preoperative planning with anticipation of potential difficulties and easy access for fluoroscopic imaging is essential [6]. Nowadays, fracture tables are modular, can adjust patient's position with easiness and can take numerous attachments to assist

P.V. Giannoudis (ed.), *Fracture Reduction and Fixation Techniques*,
https://doi.org/10.1007/978-3-319-68628-8_2

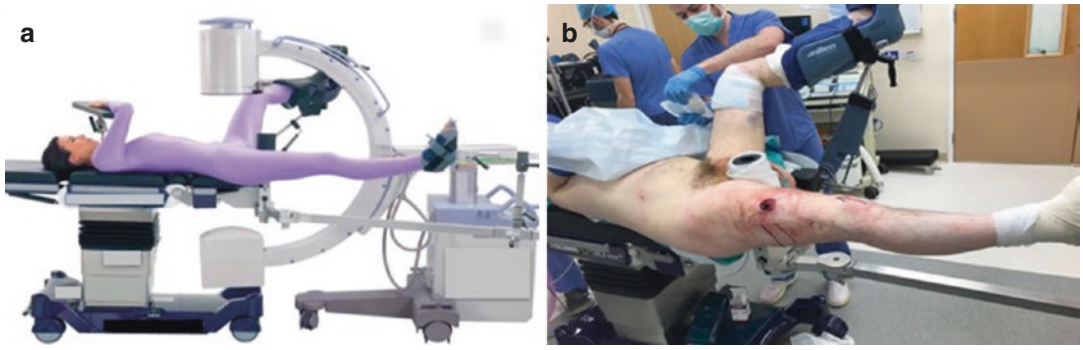


Fig. 2.1 (**a**) Schematic representation of traction applied to right lower leg using a fracture table. (**b**) Patient placed in the supine position on a fracture table with an open right femoral fracture. Traction has been applied on the right hand side to reduce the femoral fracture

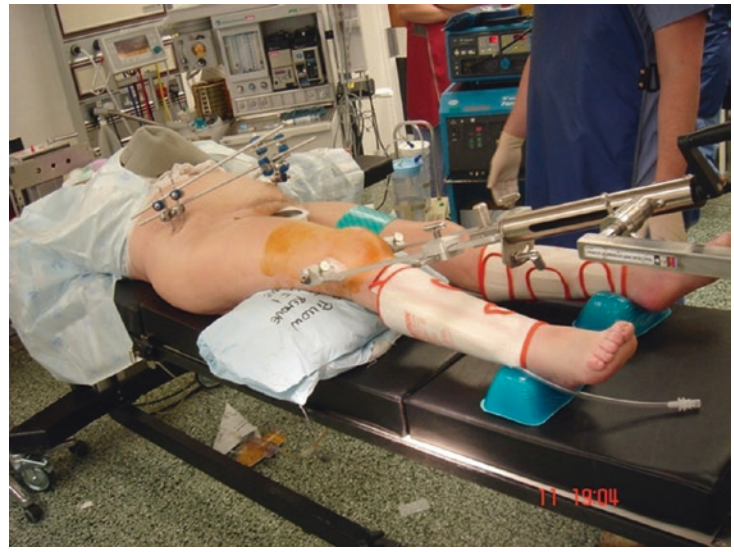


Fig. 2.2 A polytrauma patient with a pelvic external fixator (sustained vertical shear fracture) is placed supine on an OSI table where, with the appropriate attachment device, traction is applied through a right distal femoral pin to reduce the right hemipelvic disruption

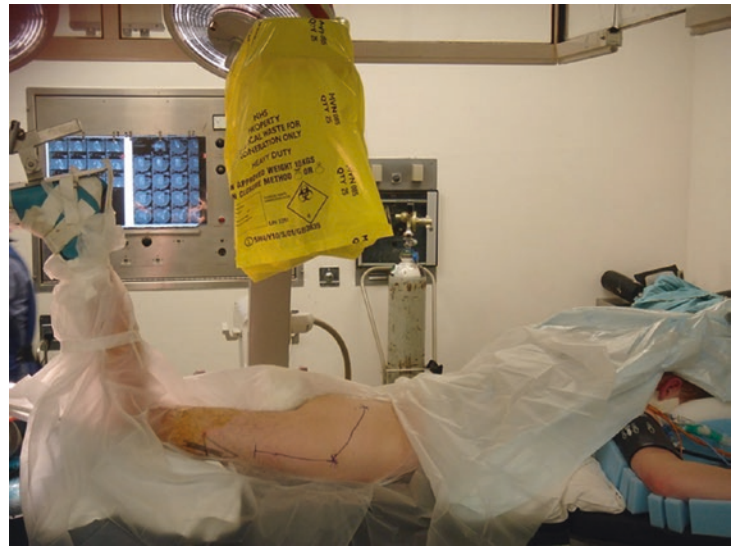


Fig. 2.3 Patient has been positioned prone on the OSI table with skeletal traction (distal femoral pin) applied on the right distal femur to reduce acetabulum fracture

fracture reduction (Fig. 2.4). Setting up the patient can be labour intensive, which increases operative time, and performing multiple surgeries in the same setting is often challenging [7, 8]. Noteworthy, complications from patient positioning can occur and must be minimized. Such complications can range from skin necrosis, nerve palsy and compartment syndrome to iatrogenic fractures [9].

Coexisting injuries and body habitus often preclude the use of the fracture table. In such circumstances the use of the standard radiolucent table is required. Manual traction or the use of skeletal traction (Fig. 2.5) devices can accomplish the same objective with no impact on the final outcome [10]. However, an additional assistant devoted to holding and maintaining traction is required.

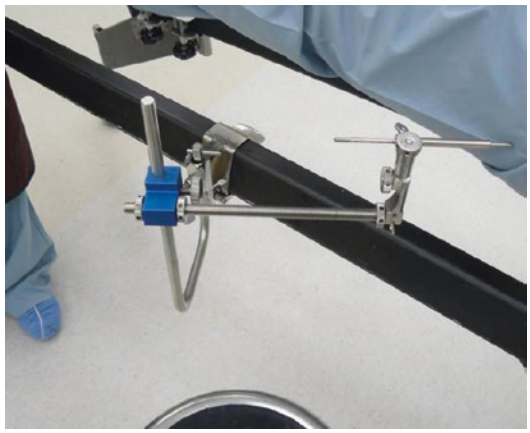


Fig. 2.4 Complementary reduction device attached on the OSI table to assist the reduction of pelvic/acetabulum fractures

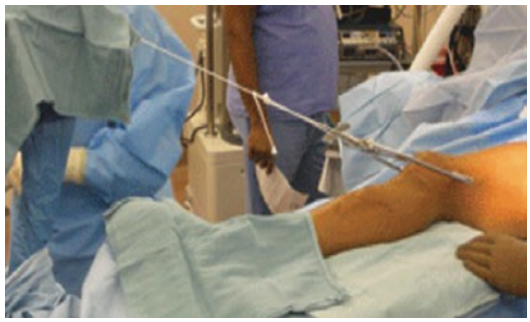


Fig. 2.5 Traction applied using a distal femoral pin intraoperatively

A number of adjuncts can be used during patient positioning on the operating table. Bumps and bolsters can change patient position, maintain the correct orientation of the limb or assist in muscle relaxation during fracture reduction (Figs. 2.6 and 2.7) [11]. Alternatively, special table attachments can be used, for example, the posterior reduction device, (PORD™), which can be used as a fulcrum to relax the gastrocnemius and soleus complexes in femoral or hip fracture fixation (Fig. 2.8) [11, 12].

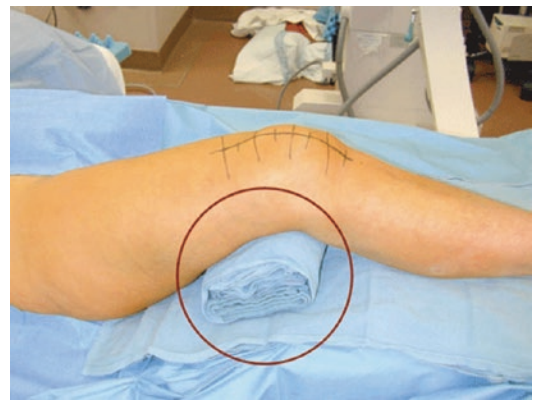


Fig. 2.6 Intraoperative picture showing a bump to control AP sag of knee

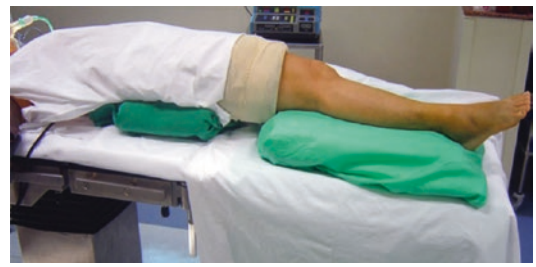


Fig. 2.7 Bolsters to control rotation of leg

Fig. 2.8 Posterior reduction device (PORD)

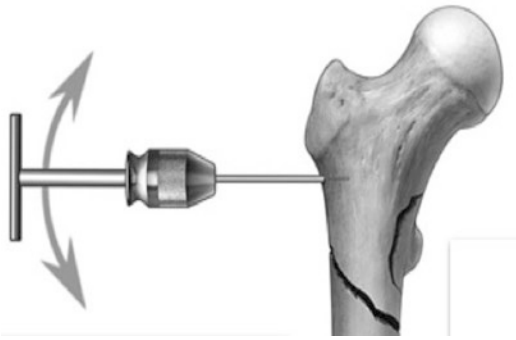


Fig. 2.9 Use of a Schanz screw attached to a T-handed chuck for fracture reduction in sagittal and coronal planes for insertion of nails

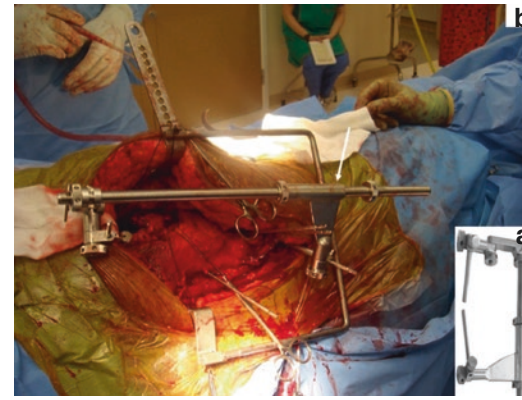


Fig. 2.10 (**a**) Femoral distractor. (**b**) Intraoperative picture of a patient in prone position demonstrating the application of a femoral distractor to reduce a combined acetabulum and proximal femoral fracture

Schanz screws can be inserted percutaneously and can be used as joysticks for manipulation and reduction of the most displaced fracture segment (Fig. 2.9). The T-handed chuck attached to a Schanz pin can be a powerful combination in manipulation and derotating large bony fragments. K-wires applied on the fracture fragments can be used also as joysticks to achieve fracture reduction [13]. Further interfragmentary K-wires can be used as a temporary fixation method to maintain intrafocal reduction. In large bone fragments or when manipulation of the whole limb is required, Schanz pins can be used. Kapandji technique involves the insertion of a K-wire through the fracture gap [14]. Similar to the reduction technique with the use of a Hohmann retractor, manipulation of the distal fragment can occur. Definite stabilization is achieved by passing the K-wire through the distal cortex.

The femoral distractor is composed of a threaded spindle carrying a fixed and a sliding end piece (Fig. 2.10). Schanz screws are fixed through the end pieces, and the distractor is positioned parallel to the axis of the bone. An excursion of about 27 cm is built into the device. More excursion is possible, but angular malposition of the end of the device may occur. Once the bony fragments are adequately reduced, the position is maintained by the secure tightening of the connections. The distractor allows correction of length, rotation and angulation. Also, unlike to the skeletal traction where distraction forces are applied to the whole limb, the femoral distractor applies forces directly to the bone. This makes the distractor readily adaptable in coping with the awkward positioning problems. It also eliminates the risk of nerve injuries, for example, peroneal nerve palsy or pudendal crush syndrome.

The external fixator is a versatile device. Its use can range from the local damage control in cases of compromised soft tissue envelope to the definite management of fractures or bone transport [15]. Not infrequently, the external fixator is a valuable adjunct in fracture reduction and stabilization. With the use of the external fixator, the indirect reduction of the bony fragments can be accomplished under image intensification. Once reduced the position can be maintained while the internal fixation plate is slipped under the soft tissues. In some situations in which the internal fixation does not provide adequate stability, the external fixator can be left in situ for a short period of time, to provide additional support (Fig. 2.11).

The F-tool is a simple device composed of a bar on which different rods can be installed [16]. It allows focused forces to be concentrated at the apex of the deformity. Once longitudinal traction is applied to the limb, the F-tool can be used to correct deformity and angulation along one plane (Fig. 2.12). The F-tool is not radiolucent and should only be used in simple fracture configurations.