ΕΠΙΣΤΗΜΟΝΙΚΗ ΕΚΔΗΛΩΣΗ
ΒΙΒΛΙΟΓΡΑΦΙΚΗ ΕΝΗΜΕΡΩΣΗ
Μεταβολικά Νοσήματα των Οστών
ΠΟΡΤΑΡΙΑ ΠΗΛΙΟΥ
18-20 ΜΑΡΤΙΟΥ 2022

Πώρωση καταγμάτων
Νεότερα δεδομένα

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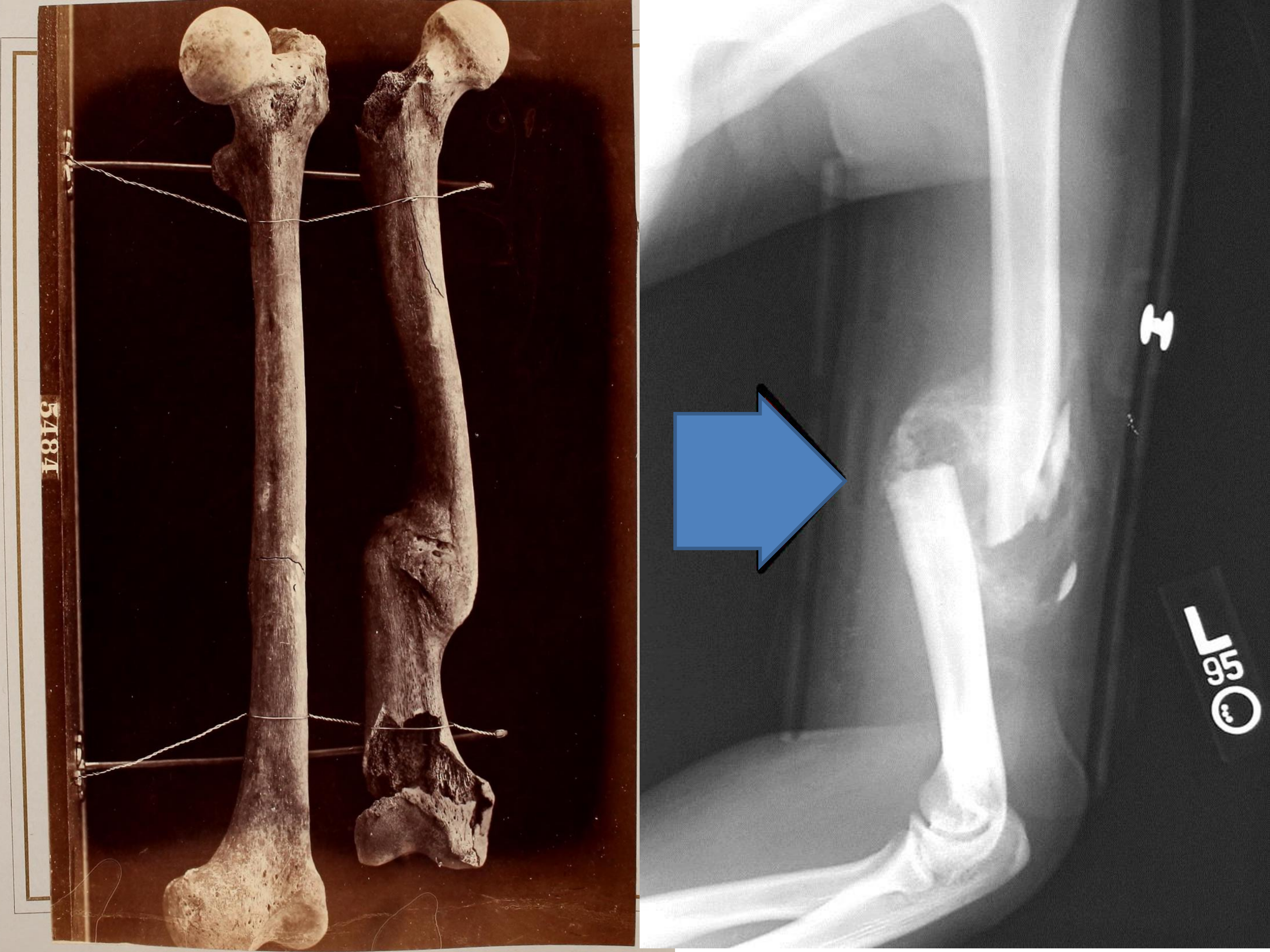
Επιμελητής Α΄ Ορθοπαιδικής Κλινικής 424 ΓΣΝΕ

Επιστημονικός Συνεργάτης Γ΄Πανεπιστημιακής Ορθοπαιδικής ΑΠΘ

Ερευνητική Ομάδα C.O.RE/ΚΕΔΕΚ/ΑΠΘ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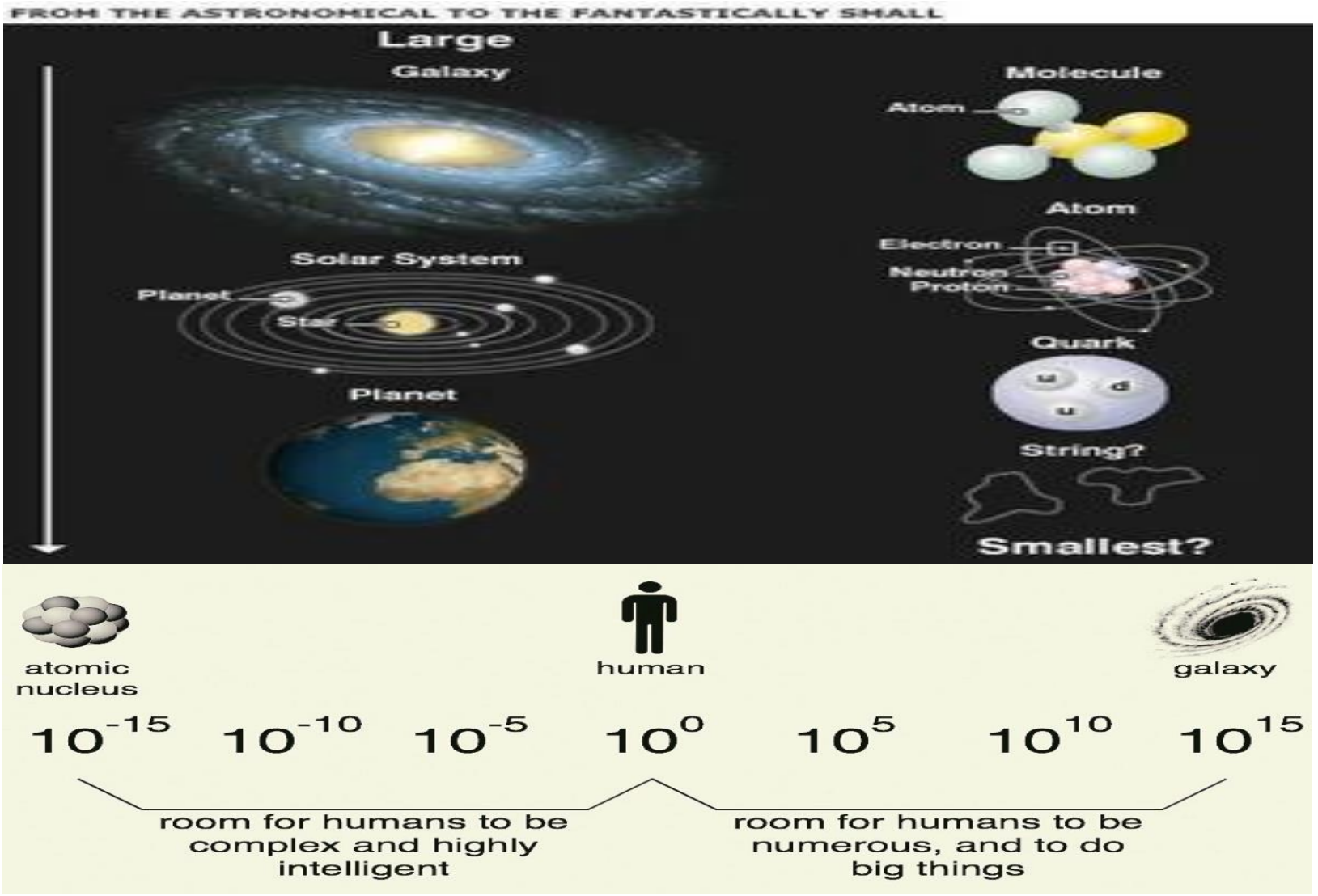
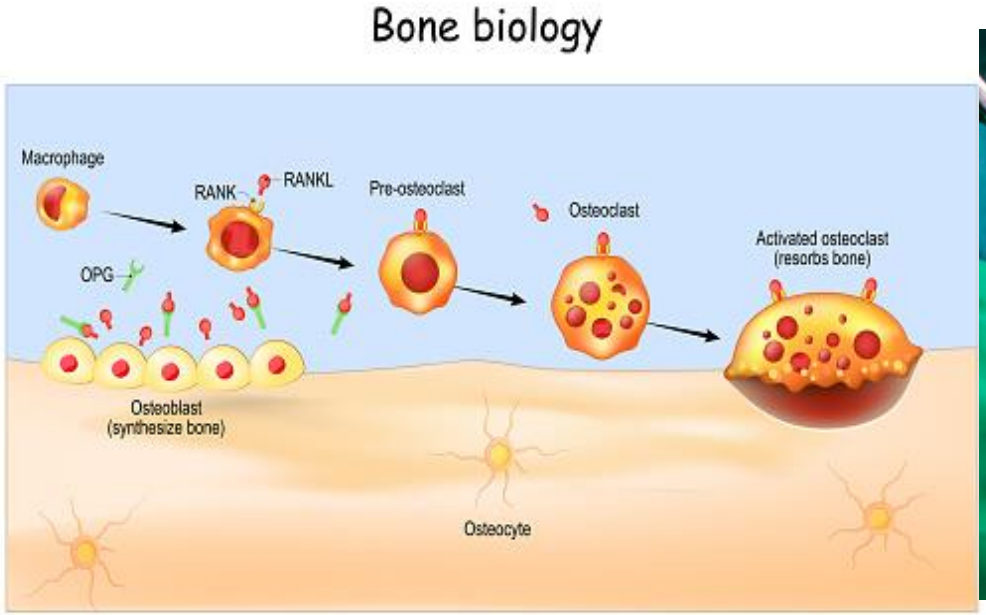
Fracture



Bone Healing

Fracture

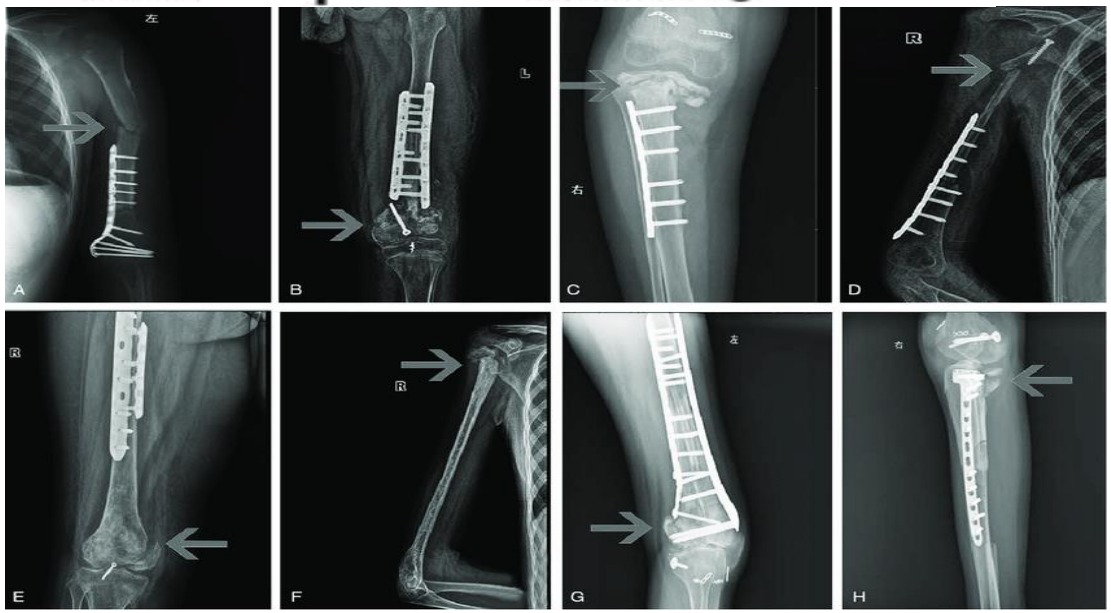


Bone Healing

Fracture


Day of Injury
2 Weeks
6 Weeks
3 Months
6 Months
1 Year
2 Years
Inflammation Phase
Soft Callus
Hard Callus
Bone Remodeling


"Look after the land and the land will look after you, destroy the land and it will destroy you."
ABORIGINAL PROVERB


A
B
C
D
E
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H

- ✓ Biology
- ✓ Biomechanic
- ✓ Biomaterial
- ✓ Fixation

Bone Healing

- Basic biomechanics
- Microanatomy
- Direct(primary)bone healing
- Indirect(secondary) bone healing
- Relative & Absolute Stability
- Complications of fractures healing
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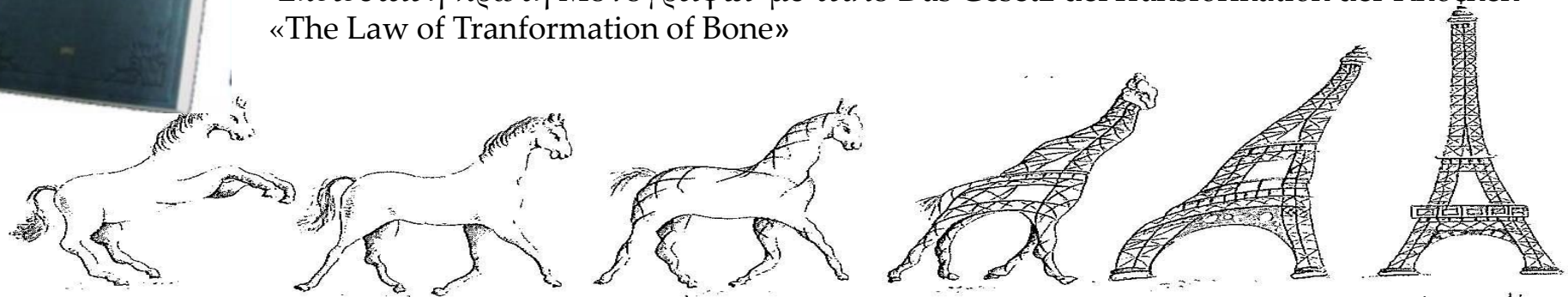
Basic biomechanics

Julius Wolff
1836-1902

- Wolff's law of 1892 describes the physiological response of normal bone to its mechanical environment during growth and remodeling
- a prolonged increase in strain will result in increased bone formation, while prolonged reduction in strain results in bone loss
- "Bone remodels according to the lines of stress placed on it"

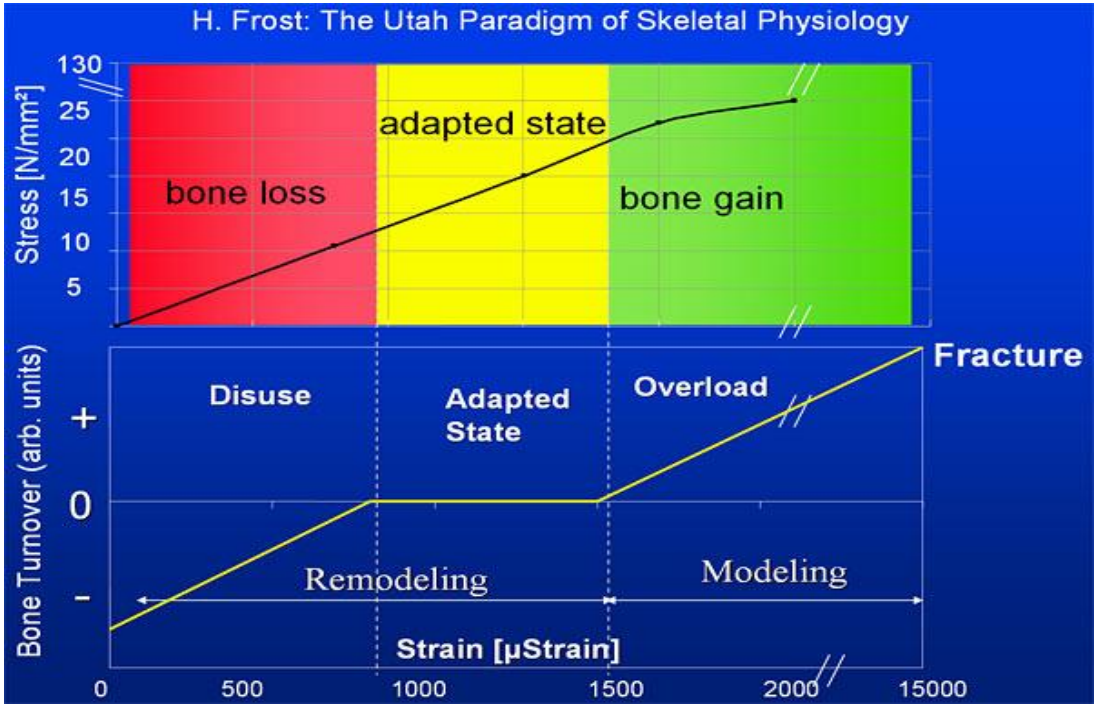
1892

Εκδίδεται η πρώτη Μονογραφία με τίτλο Das Gesetz derTransformation der Knochen
«The Law of Tranformation of Bone»



Basic biomechanics

1960
Harold Frost 's consept of the "mechanostat"



The elastic deformation of bone is measured in *µStrain*
1000µStrain = 0.1% change of length of the bone

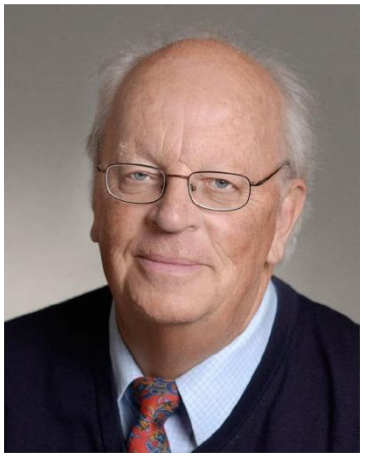
Frost H.M.: The Utah Paradigm of Skeletal Physiology Vol. 1, ISMNI, 1960
Frost H.M.: The Utah Paradigm of Skeletal Physiology Vol. 2, ISMNI, 1960

Basic biomechanics

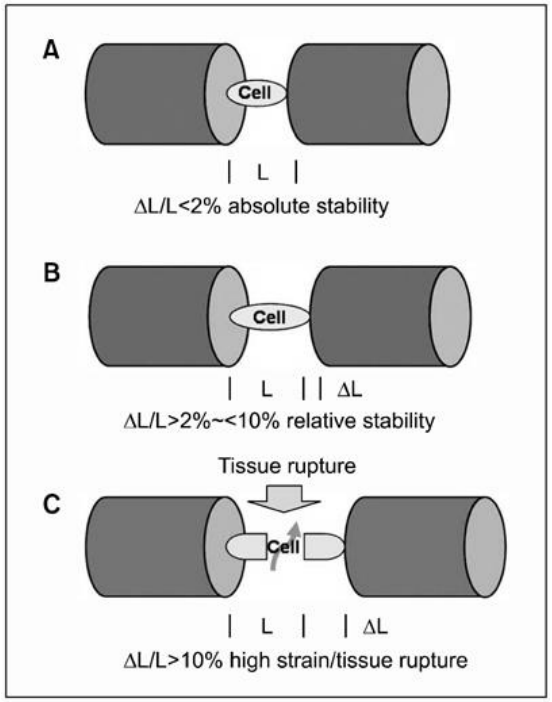
- ✓ Perren's strain theory of 1978 deals with the physiological response of broken bone to this environment

- ✓ All living biological material is subject to strain, and some tissues respond to it.The strain tolerance of a tissue is the maximum strain at which a tissue will continue to exhibit normal physiological function. Beyond this level, tissues stop functioning normally, or fail.

Perren stated that the strain tolerance of lamellar bone is 2%.



Professor Dr med Stephan Perren



Basic biomechanics

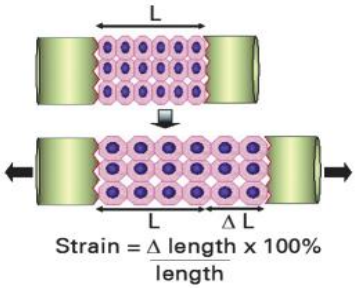


Fig. 1a

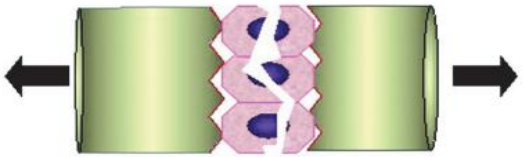
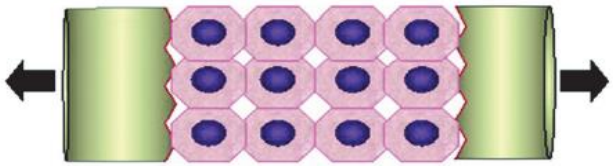


Fig. 1b



AO Foundation

***Fig/Animation** 3.3.2–4 Perren's strain theory. A simple fracture (small gap) fixed with a bridging plate (relative stability) is exposed to movement (high strain). Fracture healing is delayed or will not occur at all. The plate will eventually fail.*

***Fig/Animation** 3.3.2–5 Perren's strain theory. In a complex fracture (large gap) fixed with a bridging plate (relative stability) the strain will be low despite movement, and fracture healing will occur with callus formation (indirect bone healing).*

Basic biomechanics

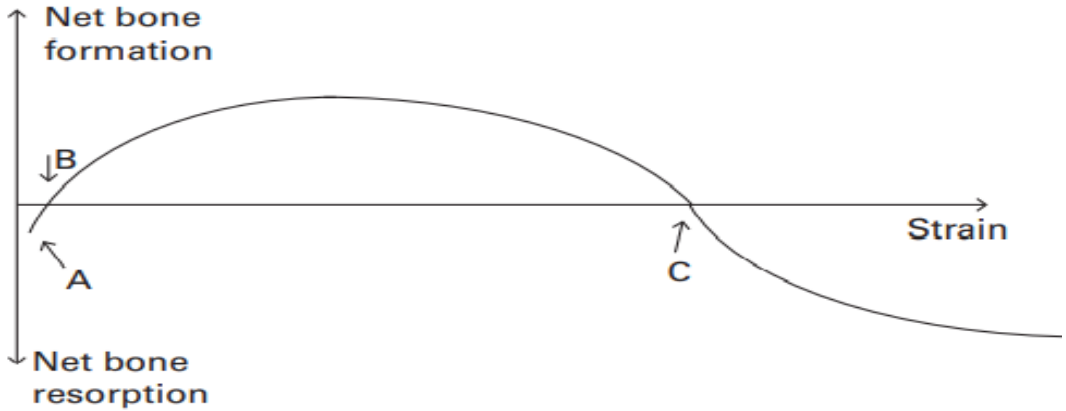


Fig. 2

Graph showing bone homeostasis, healing and nonunion theory.

> Bone Joint J. 2016 Jul;98-B(7):884-91. doi: 10.1302/0301-620X.98B7.36061.

A unified theory of bone healing and nonunion: BHN theory

D S Elliott [1], K J H Newman [1], D P Forward [2], D M Hahn [2], B Ollivere [2], K Kojima [3], R Handley [4], N D Rossiter [5], J J Wixted [6], R M Smith [7], C G Moran [2]

Affiliations — collapse

Affiliations

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2 Nottingham University Hospitals NHS Trust, Nottingham NG7 2UH, UK.
3 University of Sao Paulo, Rua Dr. Ovidio Pires de Campos, 333, Sao Paulo, Brazil.
4 John Radcliffe Hospital, Oxford, OX3 9DU, UK.
5 Basingstoke and Northamptonshire Hospital, RG24 9NA, UK.
6 Beth Israel Hospital, Boston, Massachusetts, USA.
7 Massachusetts General Hospital, Boston, Massachusetts, USA.

Bone Healing

- Basic biomechanics
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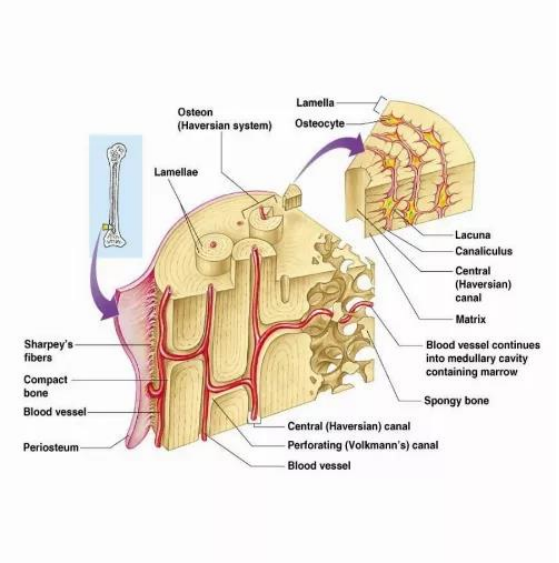
Microanatomy

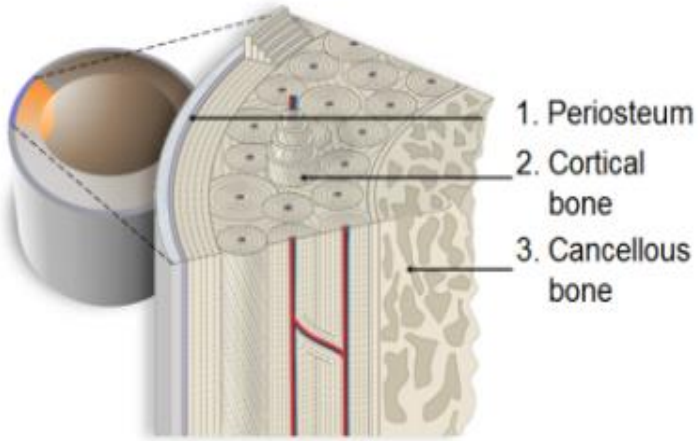
- ✓ Diaphyseal bone is organized to create the best balance between weight and structural strength



- ✓ The nonarticular surface of the bone is covered by a tough membrane—the periosteum

- ✓ The anatomy of the bone be considered

1. The periosteum
2. The cortical bone
3. The cancellous bone



Microanatomy

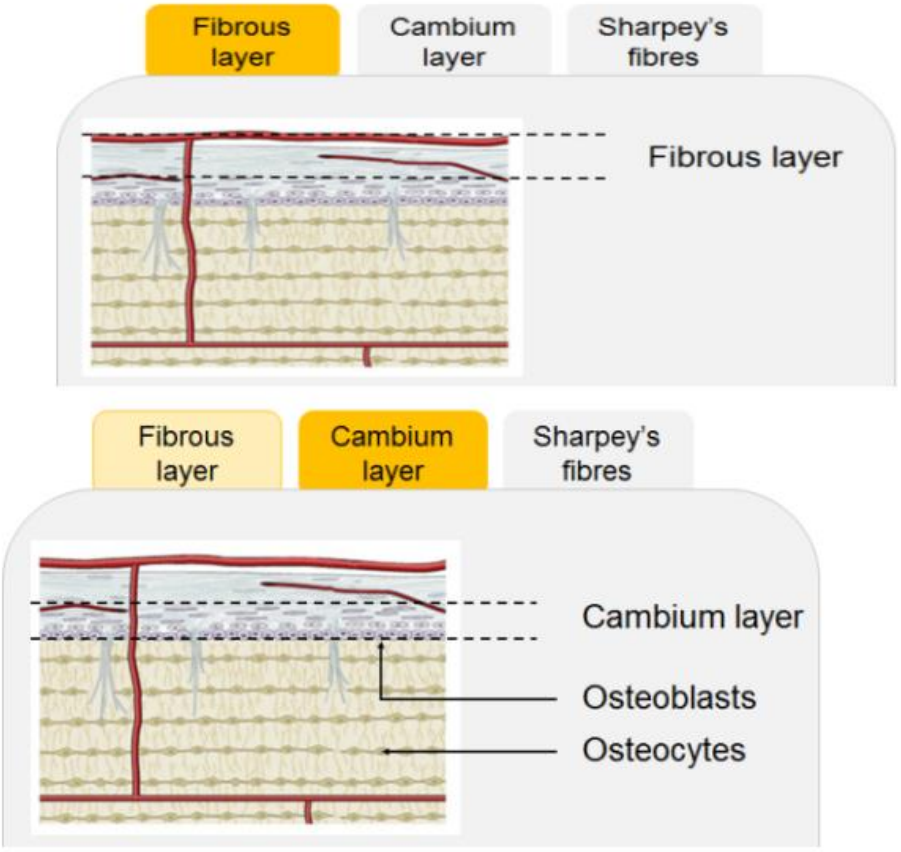
Periosteum

The periosteum envelopes the surfaces of diaphyseal bones,except where they are covered by articular cartilage and where tendons attach

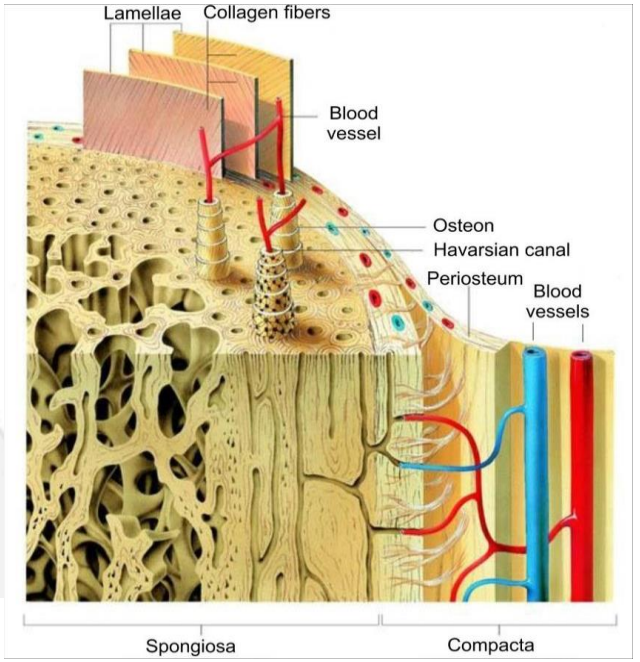
✓ The periosteum comprises two layers:

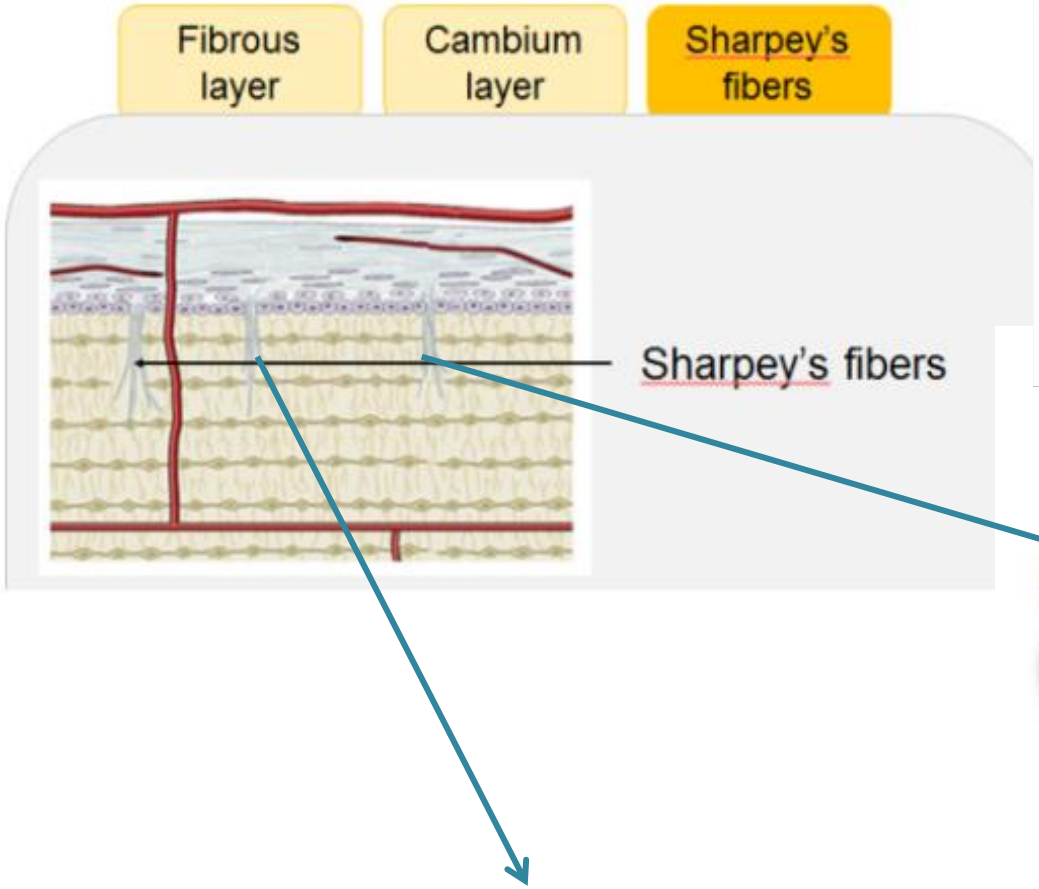
1. The fibrous layer

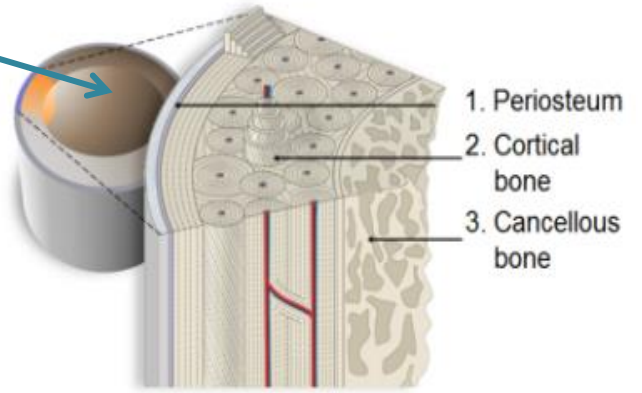
2. The cambium layer



Microanatomy





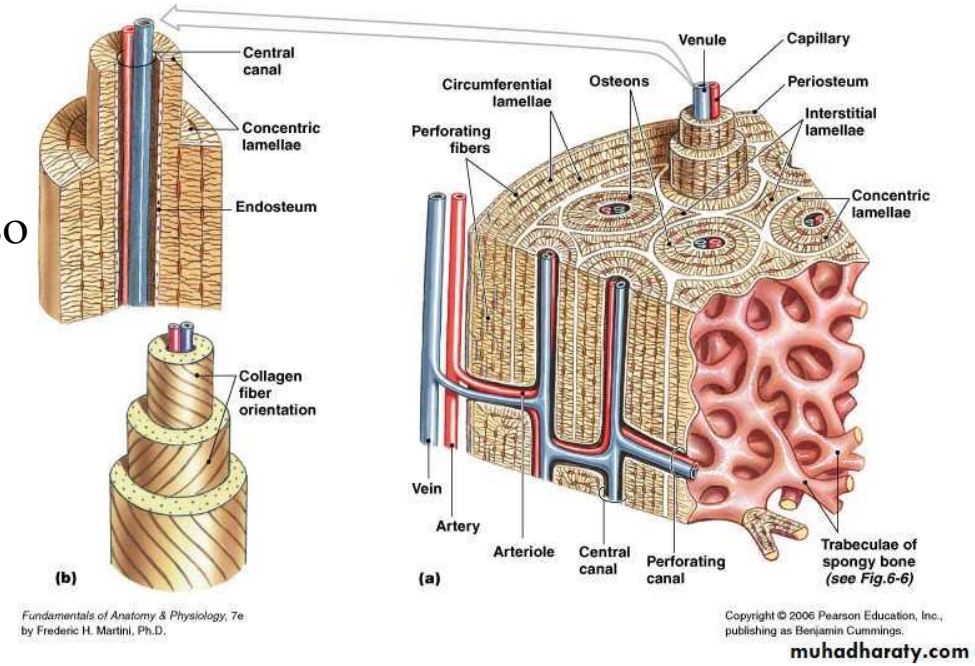


- ✓ The periosteum is tightly bound to the bone by the Sharpey‘s fibers

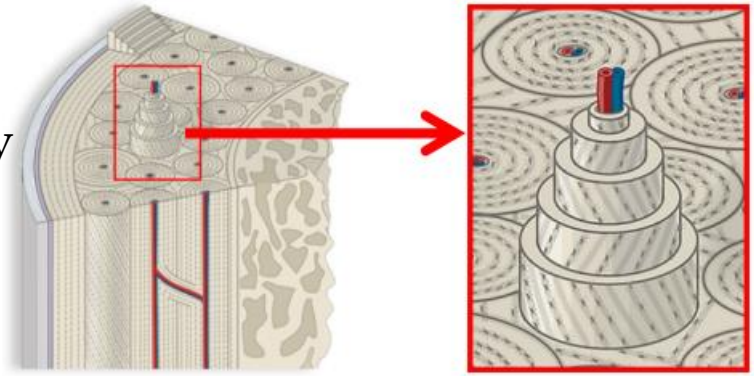
Microanatomy

Cortical bone—Osteon

- An osteon is a basic construction unit also called haversian system
- Each osteon has a centralcanal, containing blood vessels and a small amount of connective tissue with interconnecting channels surrounded by concentric layers or lammellae of bone



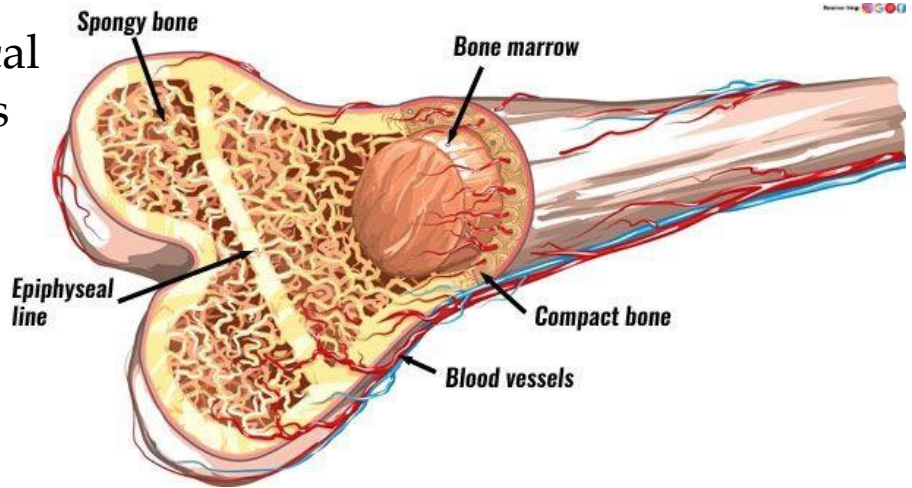
- Osteons (haversian systems) run longitudinally in the cortex



Microanatomy

Cancellous bone

- Cancellous (or trabecular/spongy) bone:20% of its volume is bone mass, less dense, more elastic, and of higher porosity
- It is the interior scaffolding of long bone ends and most short bones and helps maintain shape while resisting compressive forces
- Cancellous bone heals faster than cortical bone because of its vascularization leads
- Cancellous bone is remodeled by endosteum



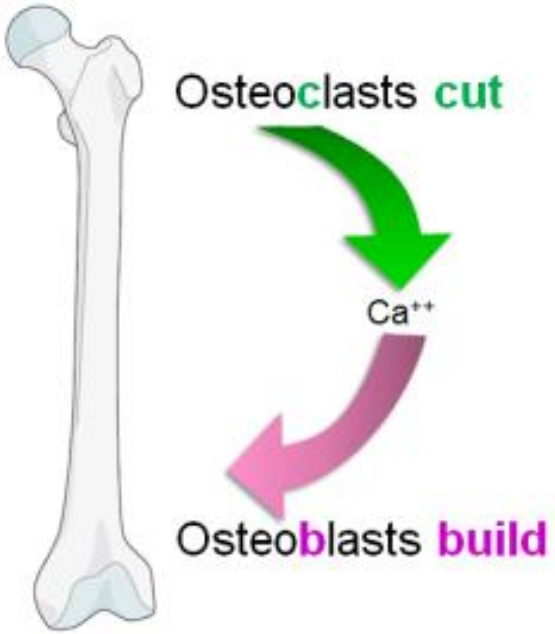
Microanatomy (Microenvironment)

Bone remodeling

All bone is in a state of constant turnover

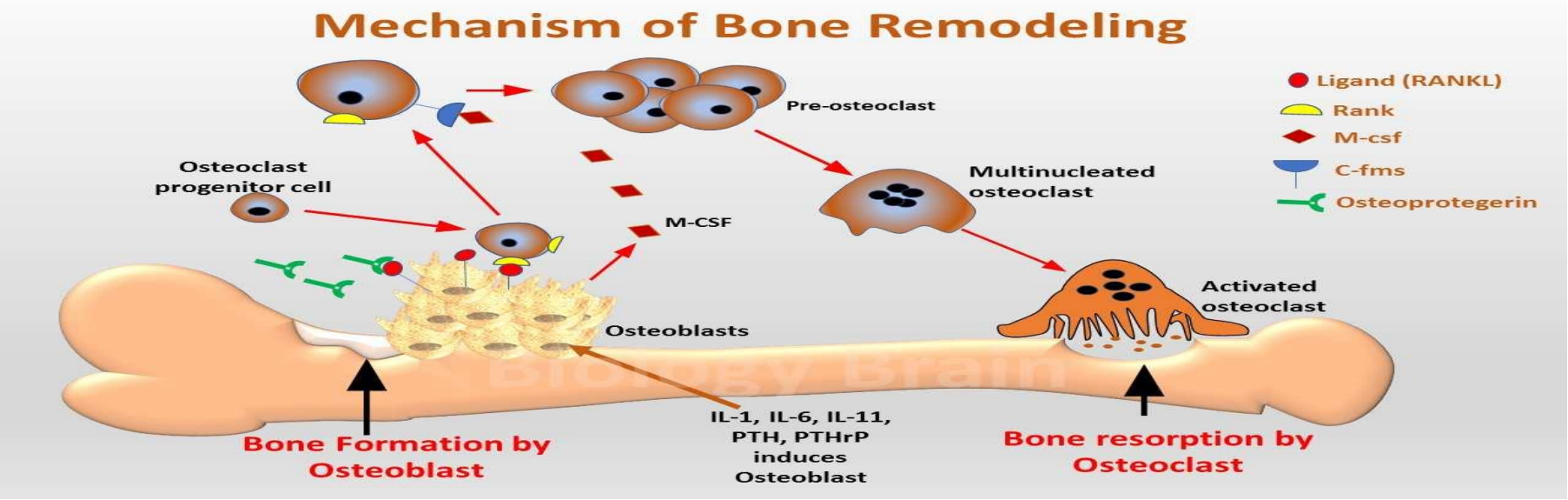
Bone is constantly being removed and replaced

This is an essential component of the body's metabolism



The removal of the bone liberates calcium into the blood stream

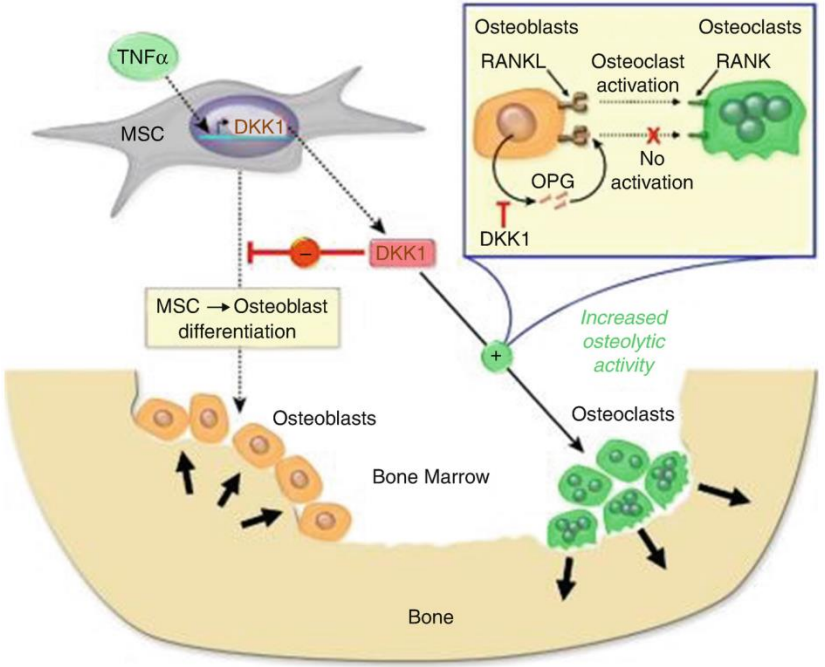
Microanatomy (Microenvironment)



- ✓ Osteoblasts are derived from mesenchymal precursors and have receptors for the parathyroid hormone, prostaglandins, vitamin D, and certain cytokines
- ✓ They synthesize bone matrix and regulate its mineralization by capturing calcium ions from the blood stream
- ✓ Osteoblasts mature into osteocytes, which are the cells of mature bone tissue

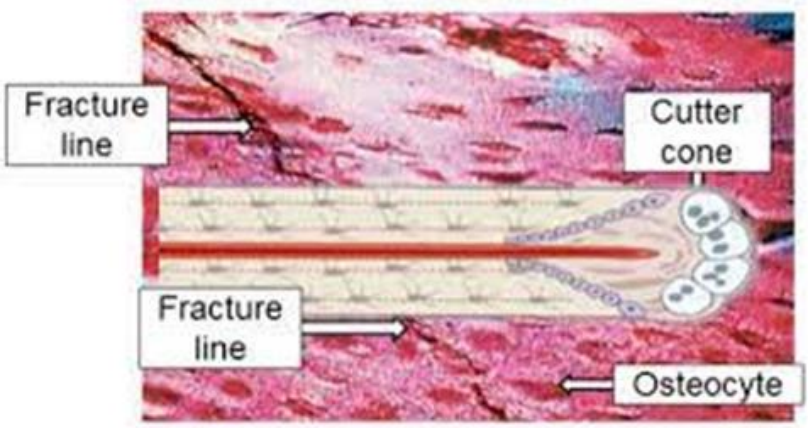
Microanatomy (Microenvironment)

- The coordinated actions of the osteoclasts and osteoblasts take place as cutter cones "drill" through old bone and lay down concentric lamellae of new bone to form new osteons



- Whether a cutter cone is taking part in the continuous process of bone turnover, or in bone healing, it functions similarly

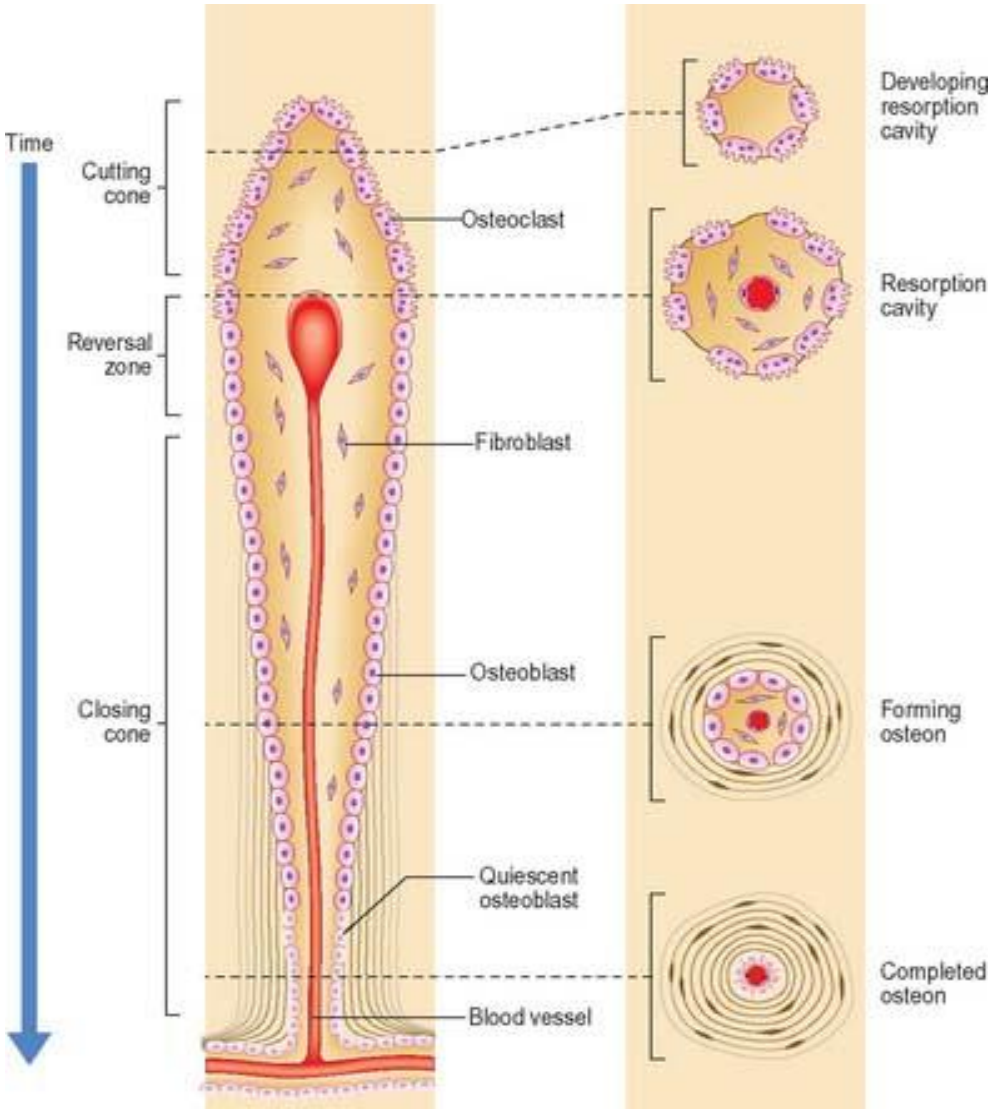
- Indeed,direct bone healing is accelerated bone remodeling



Microanatomy

Cutter cones

- Cells involved in remodelling bone – creates the osteons
- Osteoclasts at the tip
- Osteoblasts behind
- Lamellar bone laid down



Bone Healing

- Basic biomechanics
- Microanatomy
- Direct(primary)bone healing
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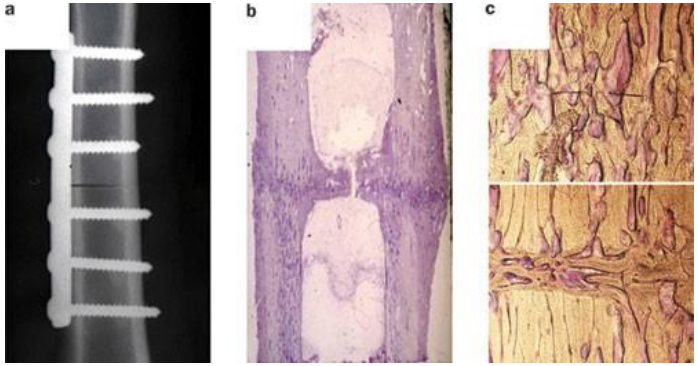
- New data

Direct(primary) bone healing

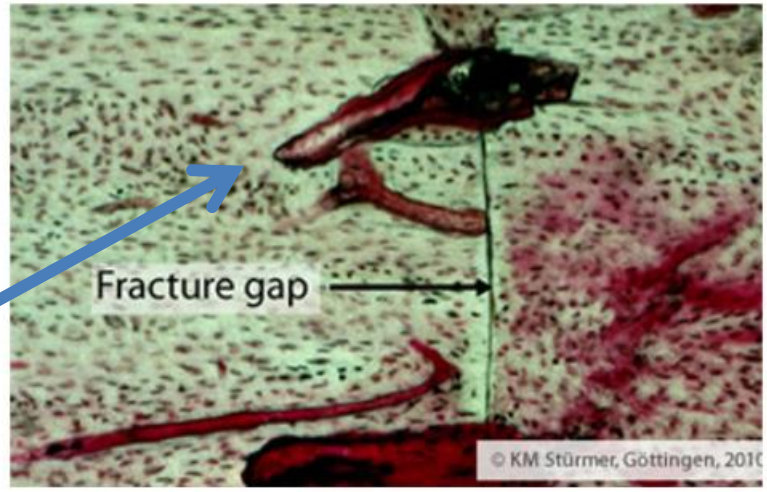
Direct fracture healing occurs:

- Under conditions of absolute fracture stability
- By direct osteonal remodeling
- Without callus formation



Primary healing occurs even if there is a minimal gap

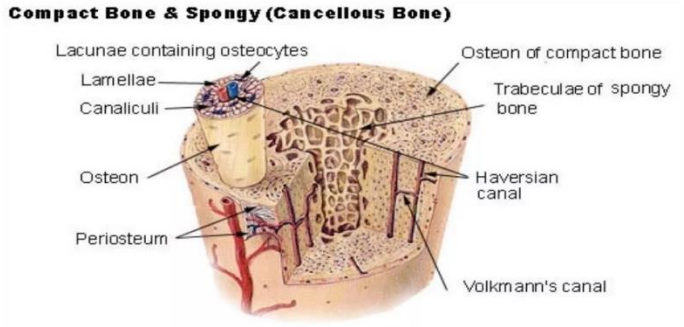
This is called gap healing

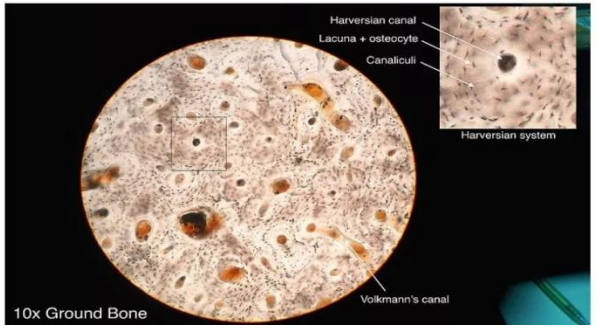


The bone is continually remodeled by cutter cones

Cutter cone → Osteon → Haversian system

✓ An osteon is a basic construction unit also called haversian system





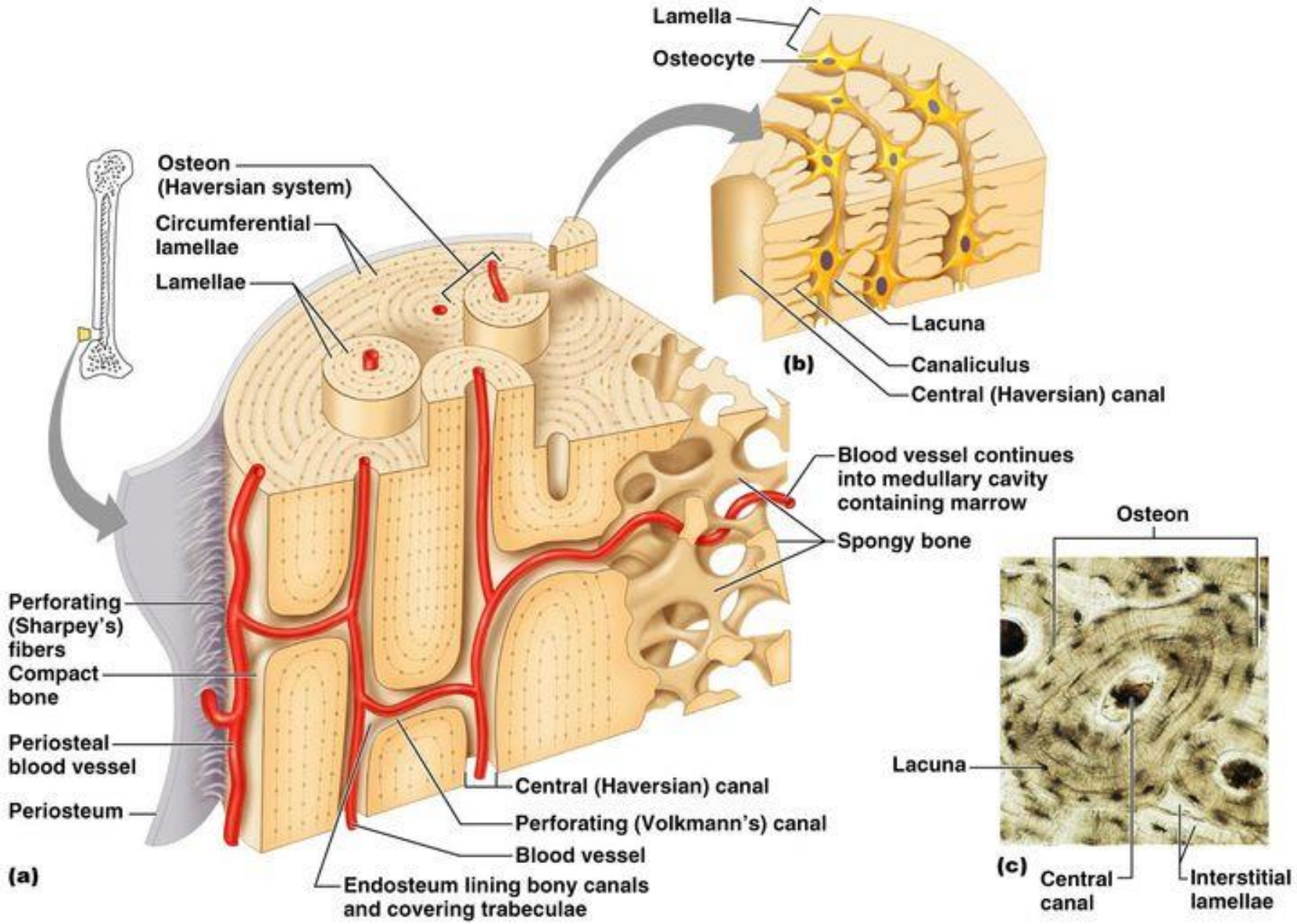
✓ There are no osteons in cancellous bone

✓ Osteoclasts are present where new bone is being resorbed

✓ Osteoblasts participate in the ossification process, present when new bone is formed

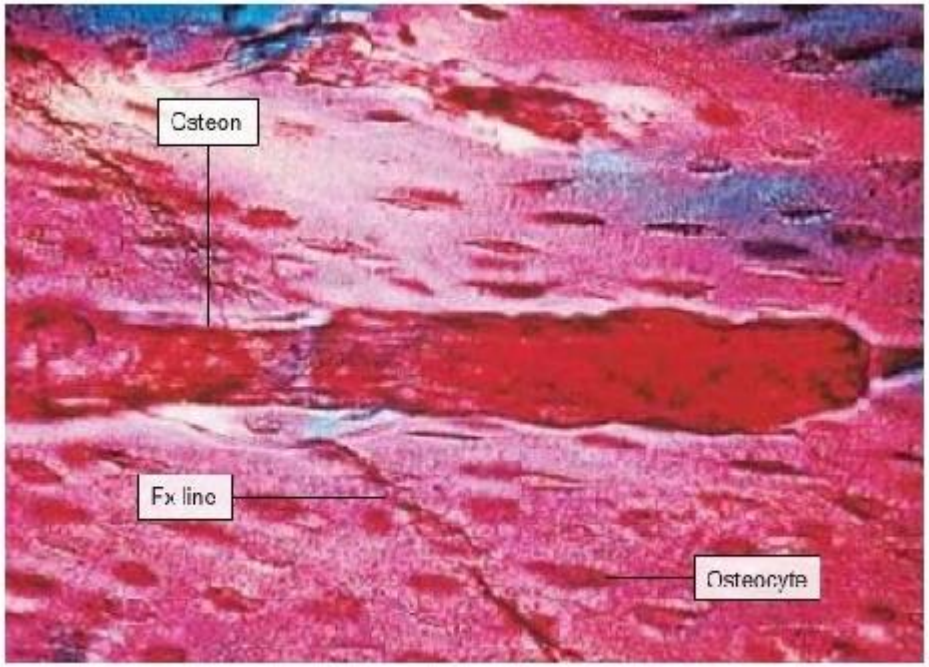
✓ Osteocytes are trapped within the bone lacunae, is active in the constant remodeling of bone

Lacunae communicate with each other and the canal of the osteons through canaliculae



Direct(primary) bone healing

Due to the activity of cutter cones, tunnels are cut through the compact bone, resulting in the creation of new haversian osteons in their wake



Direct(primary) bone healing

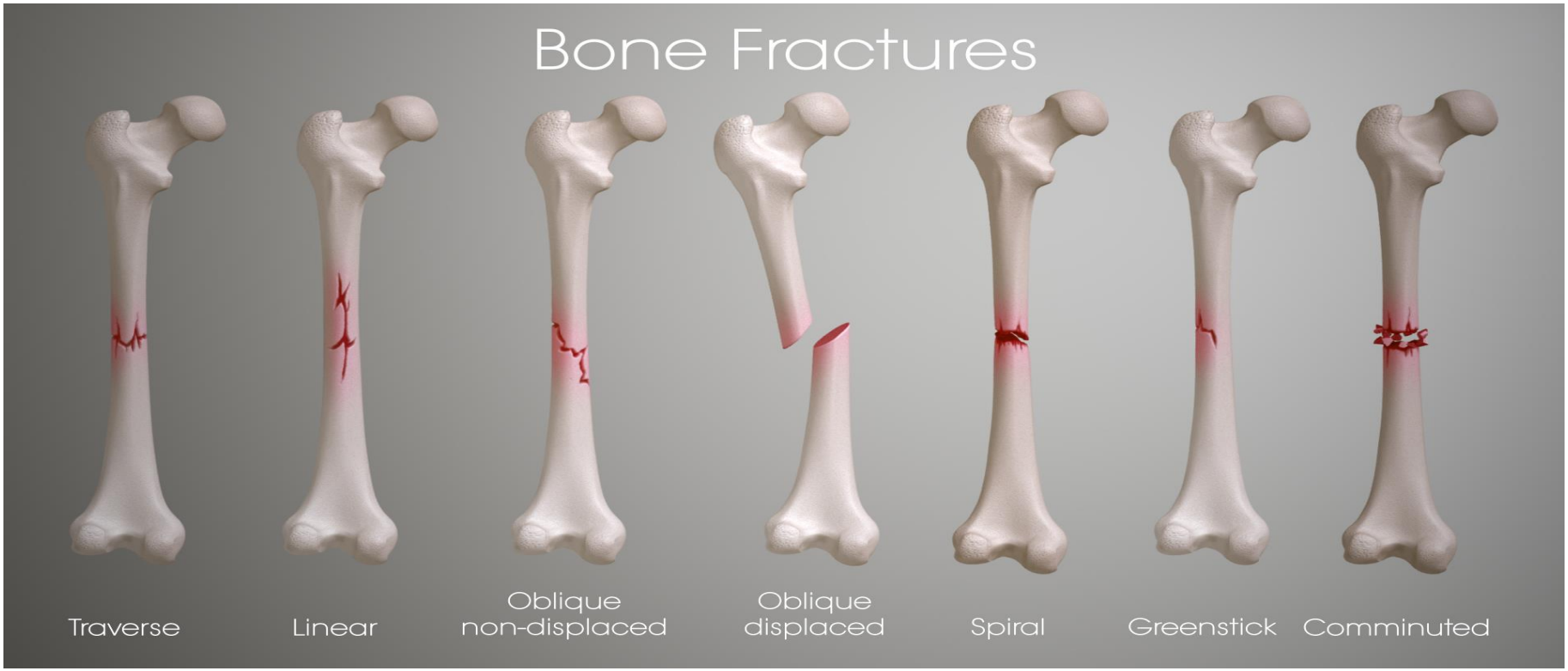
Direct fracture healing occurs:

- Under conditions of absolute fracture stability
- By direct osteonal remodeling
- Without callus formation

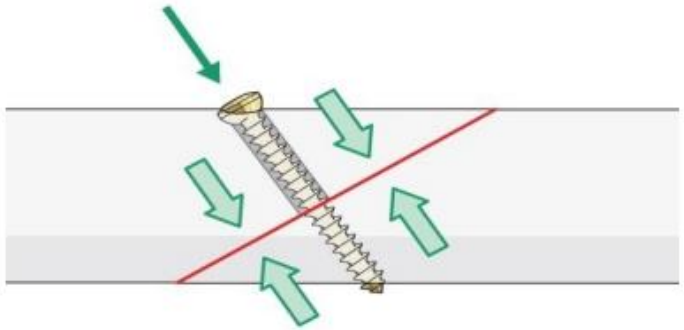
Direct(primary) bone healing

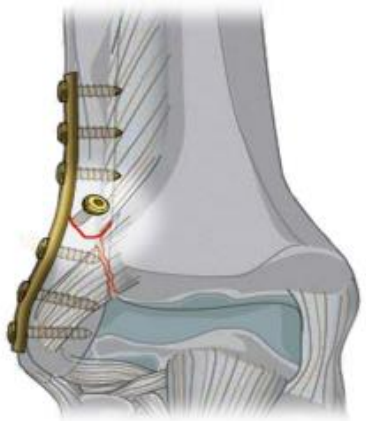
Absolute stability

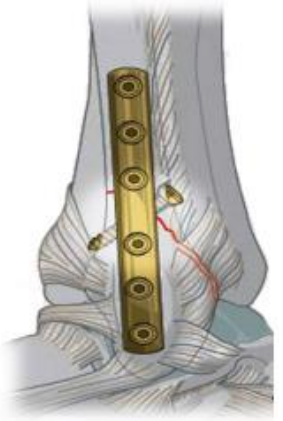
- ✓ Can only be obtained with surgery
- ✓ The operative treatment depends on the location and the fracture



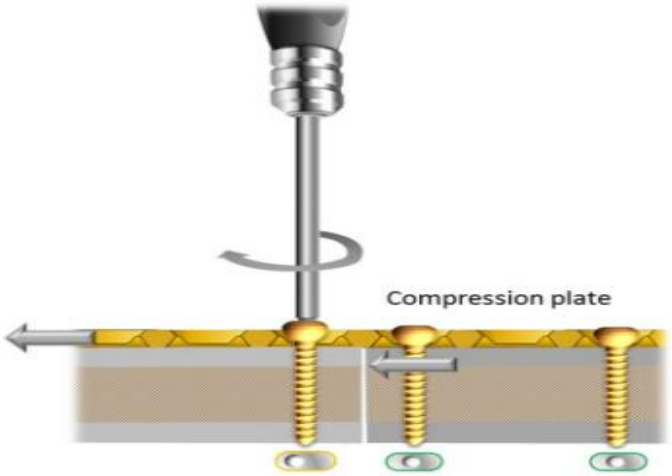
- Lag screw

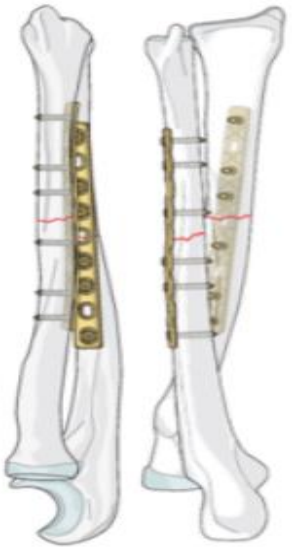






- Compression plate





Bone Healing

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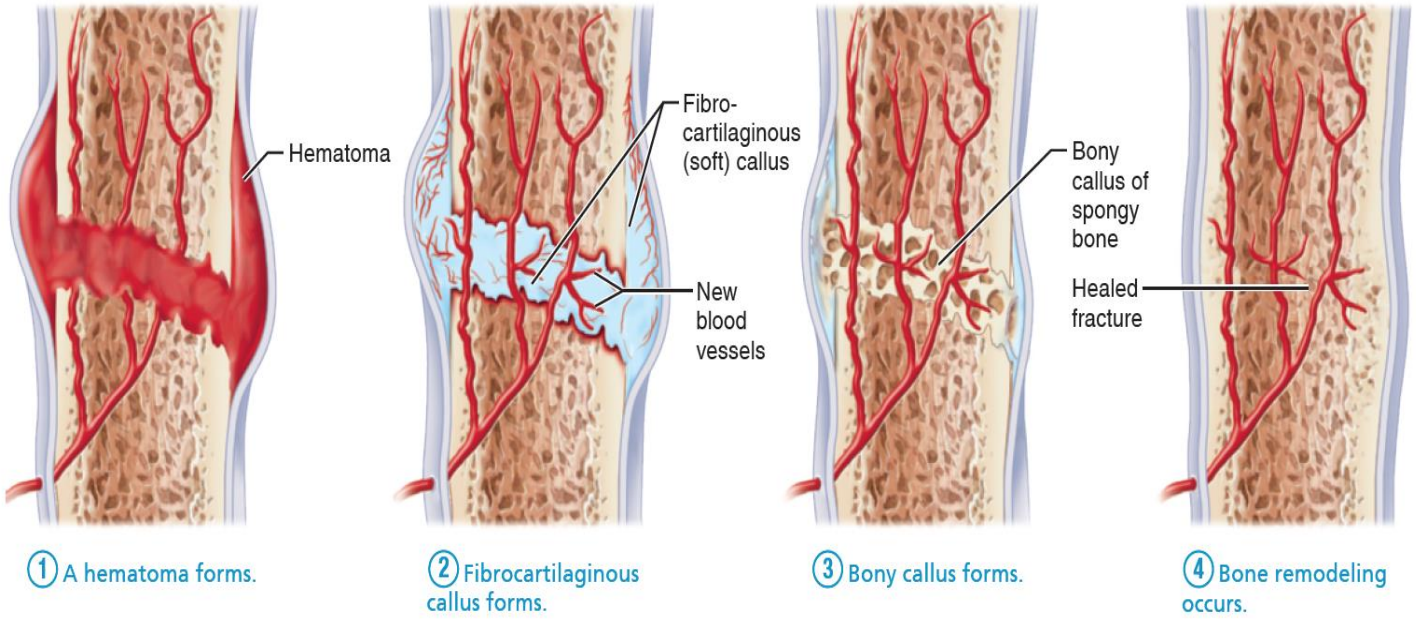
Indirect(secondary) bone healing

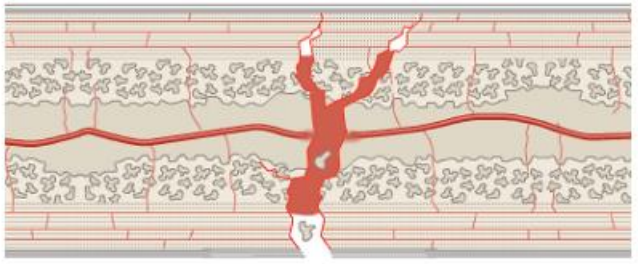
The phases of indirect bone healing are

- Inflammation
- Soft callus formation
- Hard callus formation
- Remodeling



Indirect(secondary) bone healing

1. *Inflammation (1–7 days postfracture)*



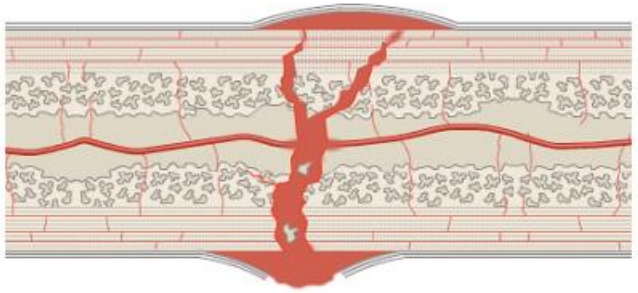
The fracture results in:

- Soft-tissue damage
- Disruption of blood vessels in bone
- Separation of small bony fragments

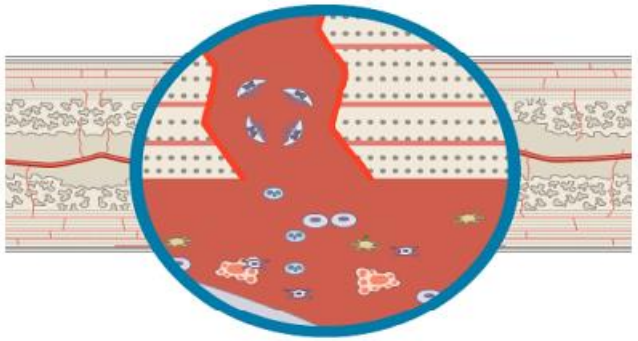
Indirect(secondary) bone healing

1.Inflammation (1–7 days postfracture)

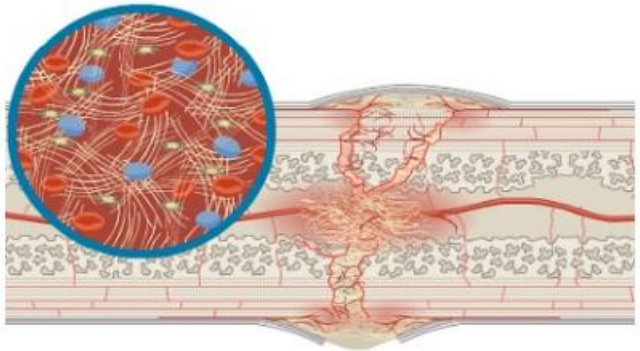
Hematoma forms and the periosteum ruptures partly



Cells migrate into the fracture hematoma



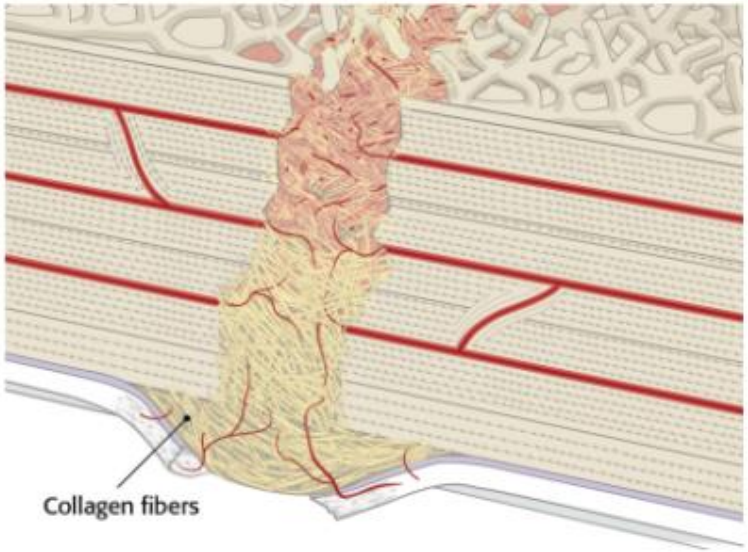
Coagulation starts
Fibrin fibers are formed and stabilize the hematoma (hematoma callus)



Indirect(secondary) bone healing

2. Soft callus formation (2–3 weeks post fracture)

Once injury occurs, the natural process of bone healing begins with the creation of soft callus



A cascade of cellular differentiation occurs

Indirect(secondary) bone healing

2. Soft callus formation (2–3 weeks postfracture)

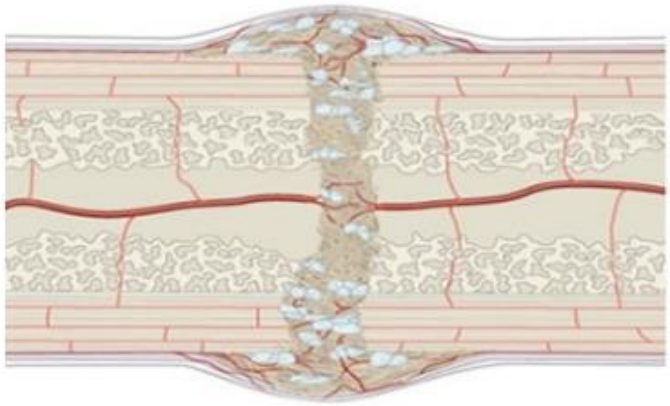
Phase 1: New blood vessels invade the organizing hematoma
Decrease of pain and swelling

Phase 2:
Fibroblasts, derived from periosteum, invade and colonize the hematoma

Phase 3:
Fibroblasts produce collagen fibers (granulation tissue)

Phase 4:
Collagen fibers are loosely linked to the bone fragments

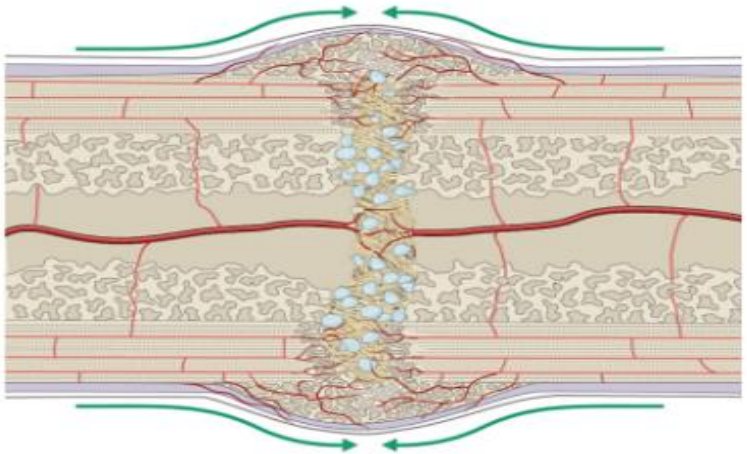
Phase 5:
The cells of the granulation tissue gradually differentiate to form fibrous tissue and subsequently fibrocartilage (replacing hematoma).



Indirect(secondary) bone healing

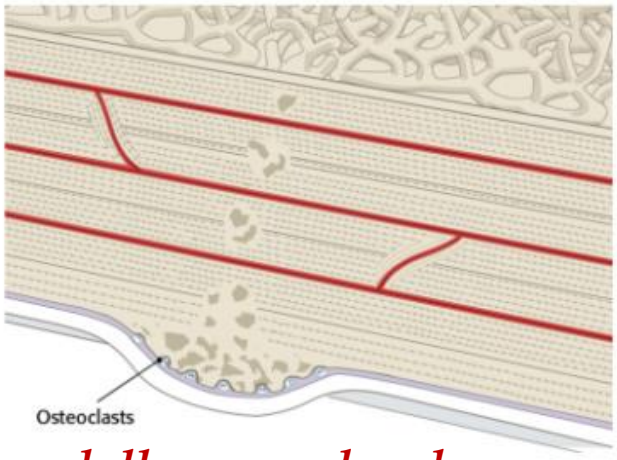
3. Hard callus formation (3–12 weeks postfracture)

Endochondral ossification converts the soft callus to woven bone starting at the periphery and moving towards the center, further stiffening the healing tissue. This continues until there is no more interfragmentary movement.

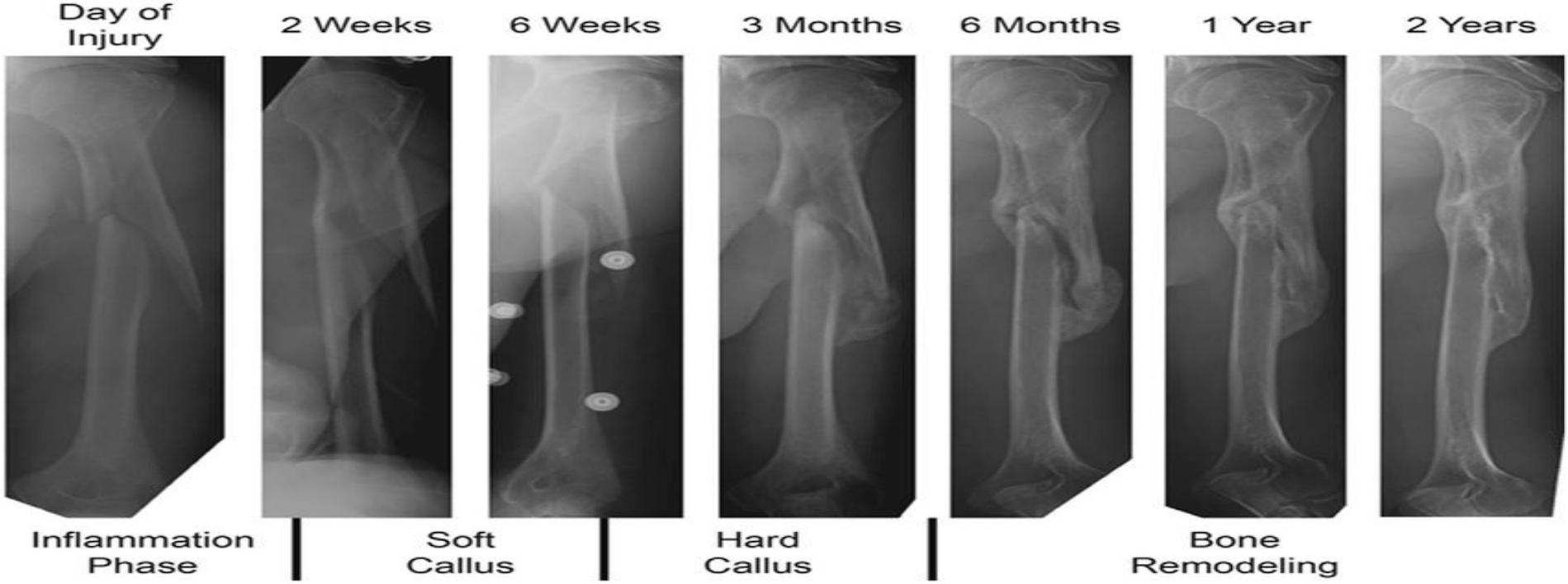


4. Remodeling (Process taking months to years)

The remodeling stage:
conversion of woven bone into lamellar bone through surface erosion and osteonal remodeling once interfragmentary movement ceases.



Fracture healing becomes complete with remodeling of the medullary canal and removal of parts of the external callus



Course of healing:

- ✓ Initially hematoma (blood coagulation) is formed between the fragment ends—negligible mechanical properties

- ✓ During the first few days hematoma changes to granulation tissue, which is a little stiffer

- ✓ As the tissue differentiates into more and more stiff forms, so the interfragmentary motion lessens, until it disappears when the hard bony callus bridges the fracture.

Bone Healing

- Basic biomechanics
- Microanatomy
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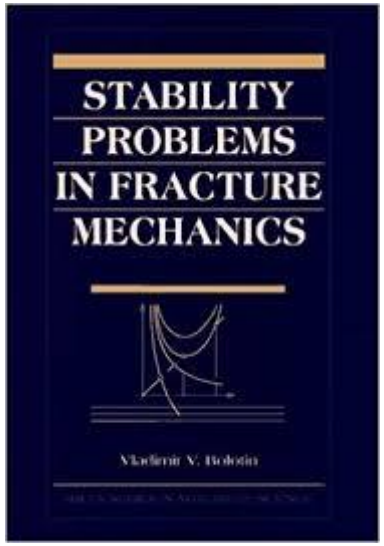
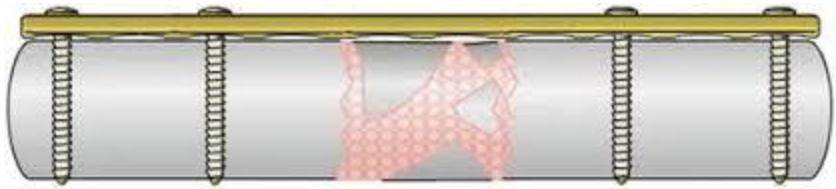
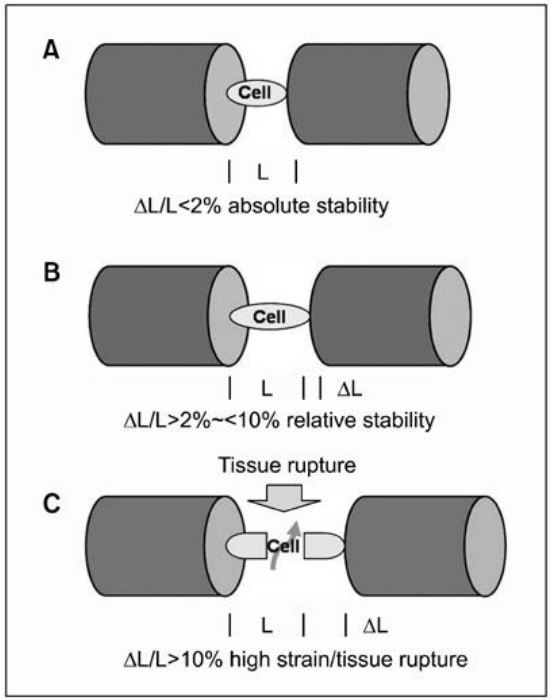
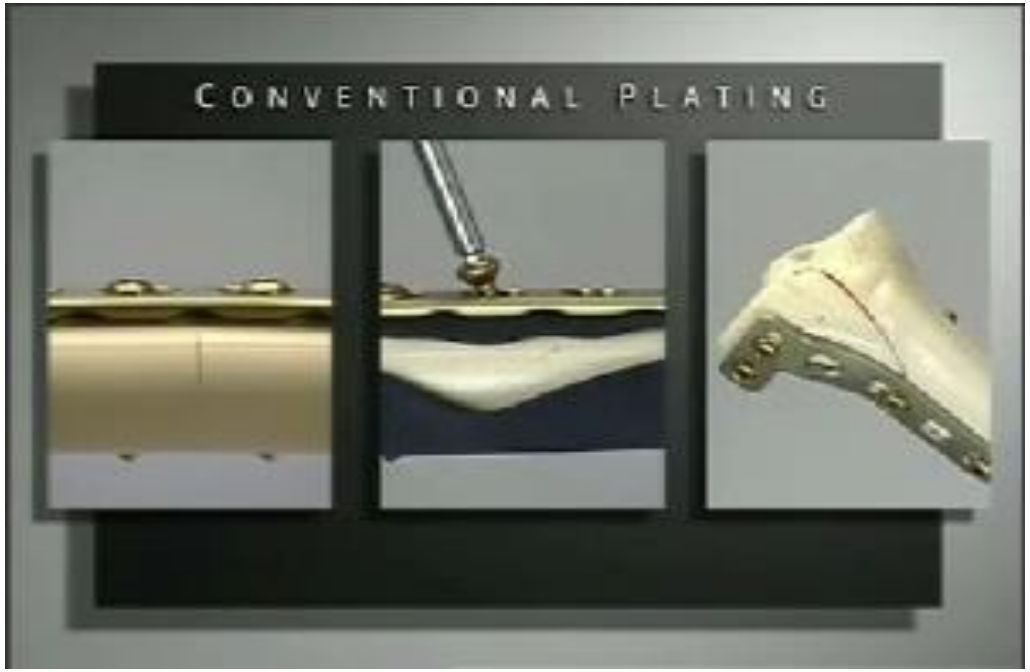
- Relative & Absolute Stability
- Complications of fractures healing
- New data

Relative & Absolute Stability









Relative & Absolute Stability

Figure 1. The AO Foundation/Orthopaedic Trauma Association (AO/OTA) type 43-A1 fracture treated with a bridging plate pre and postoperatively (a, b) and at 3-month follow-up (c).

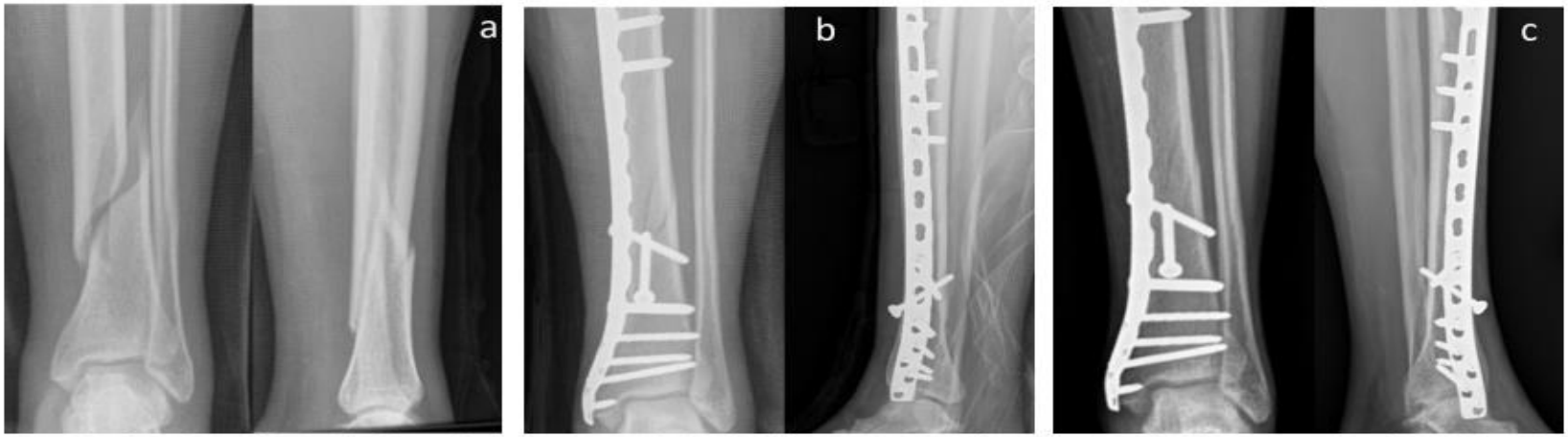
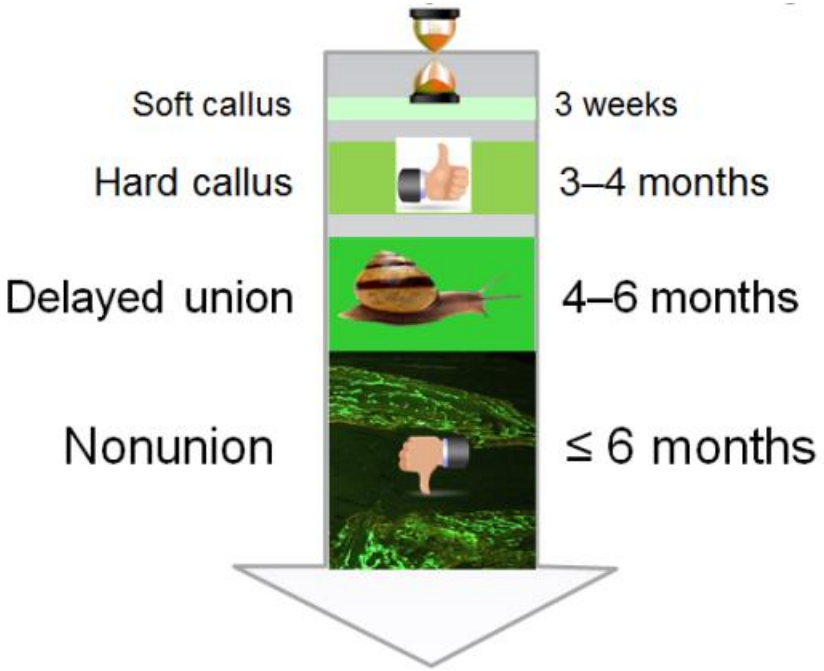


Figure 2. The AO Foundation/Orthopaedic Trauma Association (AO/OTA) type 43-A1 fracture treated with compression plate using a lag screw pre and postoperatively (a, b) and at 3-month follow-up (c).

Fracture



Bone Healing

Bone Healing

- Basic biomechanics
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- New data

Complications of fractures healing

The "personality" of the injury problem

This depends on the factors:

- ✓ Complexity of the fracture
- ✓ Extent of the soft-tissue injury
- ✓ Closed or open injury?
- ✓ Periosteal stripping?
- ✓ Status of the patient

Complications of fractures healing

Review > J Orthop Traumatol. 2019 Apr 11;20(1):21. doi: 10.1186/s10195-019-0528-0.

The 'diamond concept' for long bone non-union management

Paul Andrzejowski [1], Peter V Giannoudis [2]

Affiliations — collapse

Affiliations

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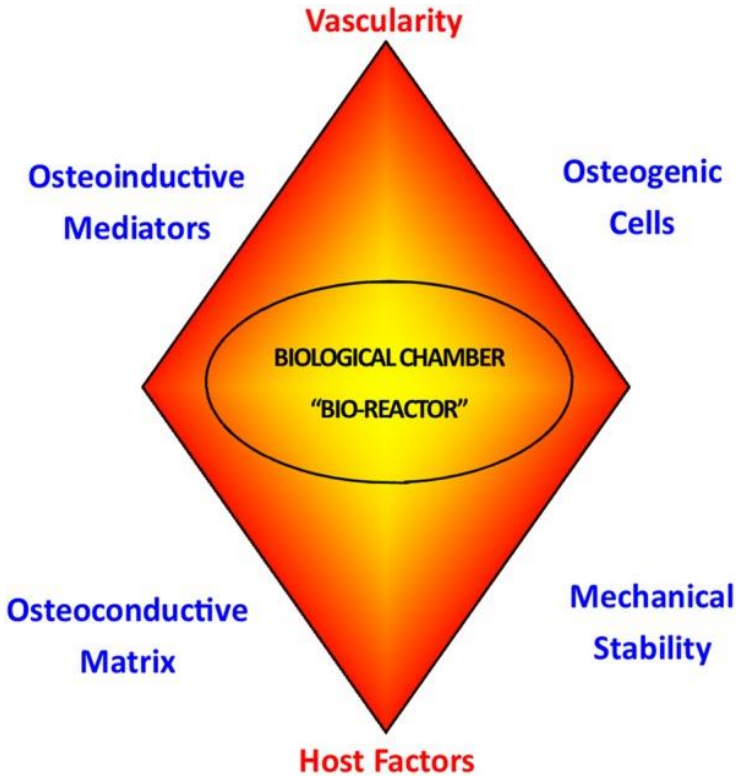
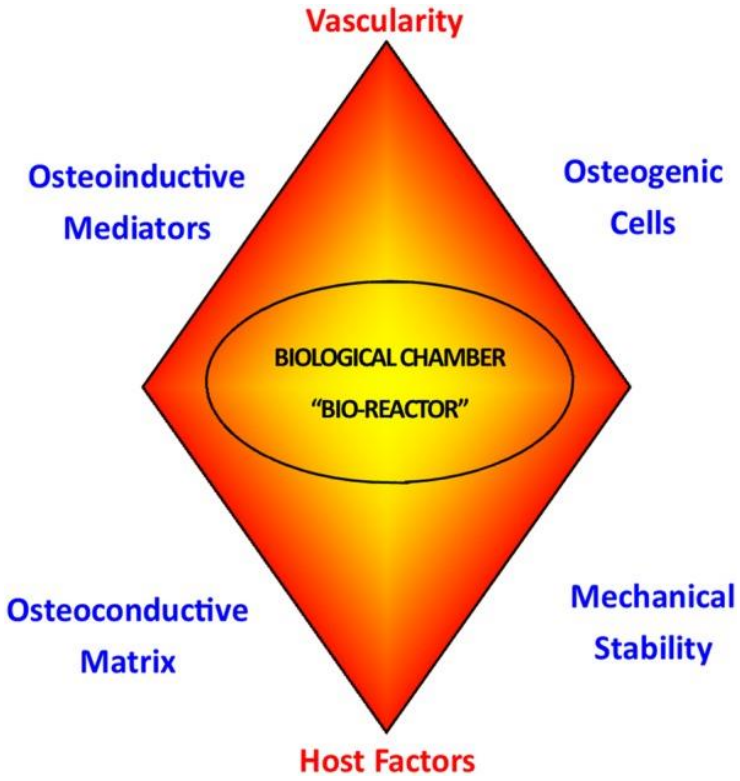
PMID: 30976944 PMCID: PMC6459453 DOI: 10.1186/s10195-019-0528-0

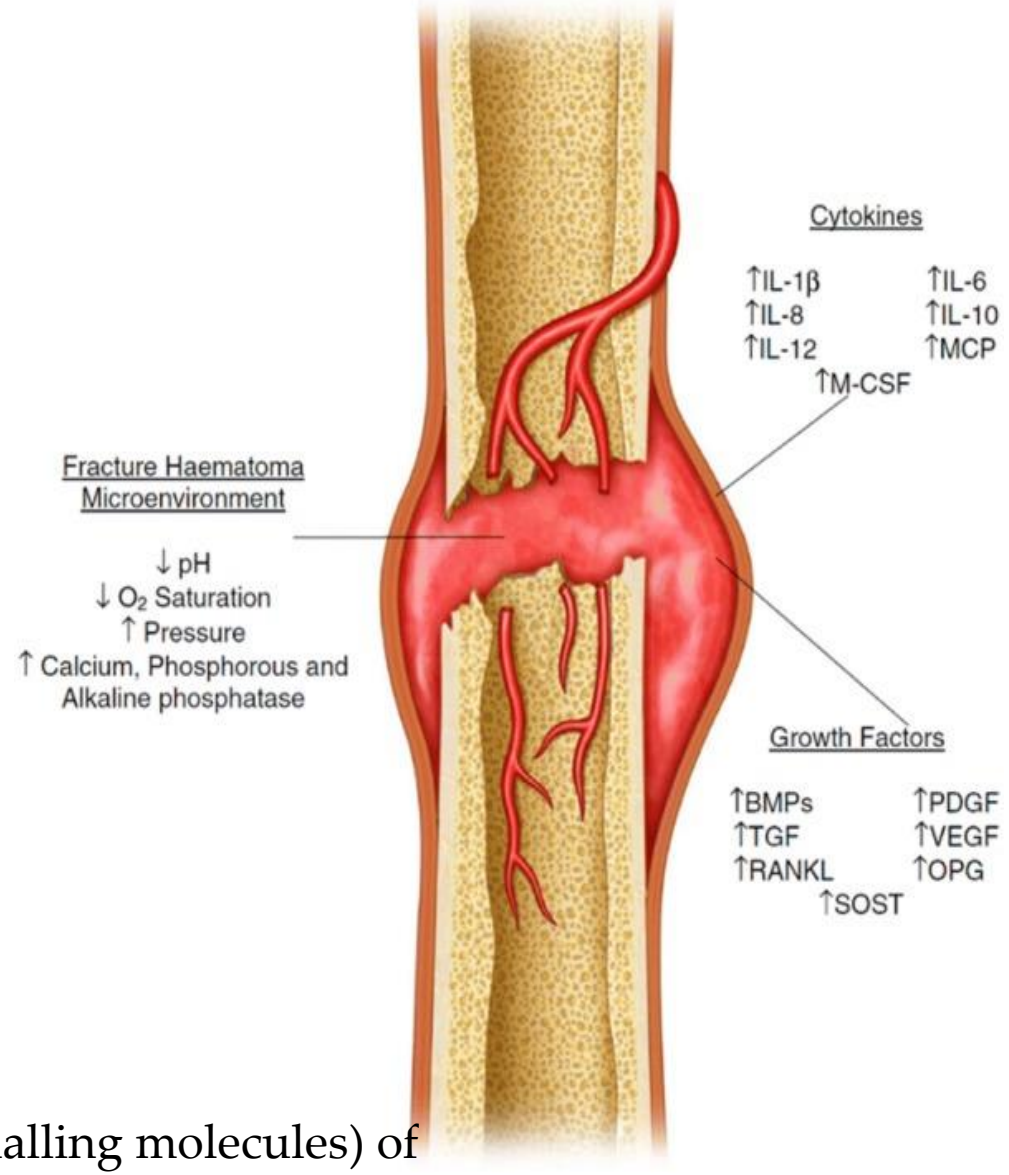


Complications of fractures healing

Table 1 Risk factors for non-union

Patient dependent		Patient independent
Modifiable	**Non-modifiable**	
Smoking	Age	Open reduction (poor quality of primary ORIF)[a]
Alcohol	Male gender	Open fracture (more bone loss and soft tissue injury)
Nutritional deficiency (including vitamin D)	Genetic predisposition[b]	Wedge and multi-fragmentary fracture pattern
High BMI	Diabetes (metabolic disease)	Initial displacement
	Peripheral vascular disease	Compartment syndrome[a]
	Osteoporosis	Affected bone: highest in tibia
	Chronic inflammatory disease	Fracture site in relation to vascularisation zone
	Renal insufficiency	Presence of fracture gap post-surgery[a]
	Insulin[a]	Poor mechanical stability by initial implant[a]
	Opiates[a]	Infection[a]
	NSAIDs[a]	
	Steroids[a]	
	Antibiotics[a]	
	Anticoagulants[a]	
	Chemotherapeutics[a]	



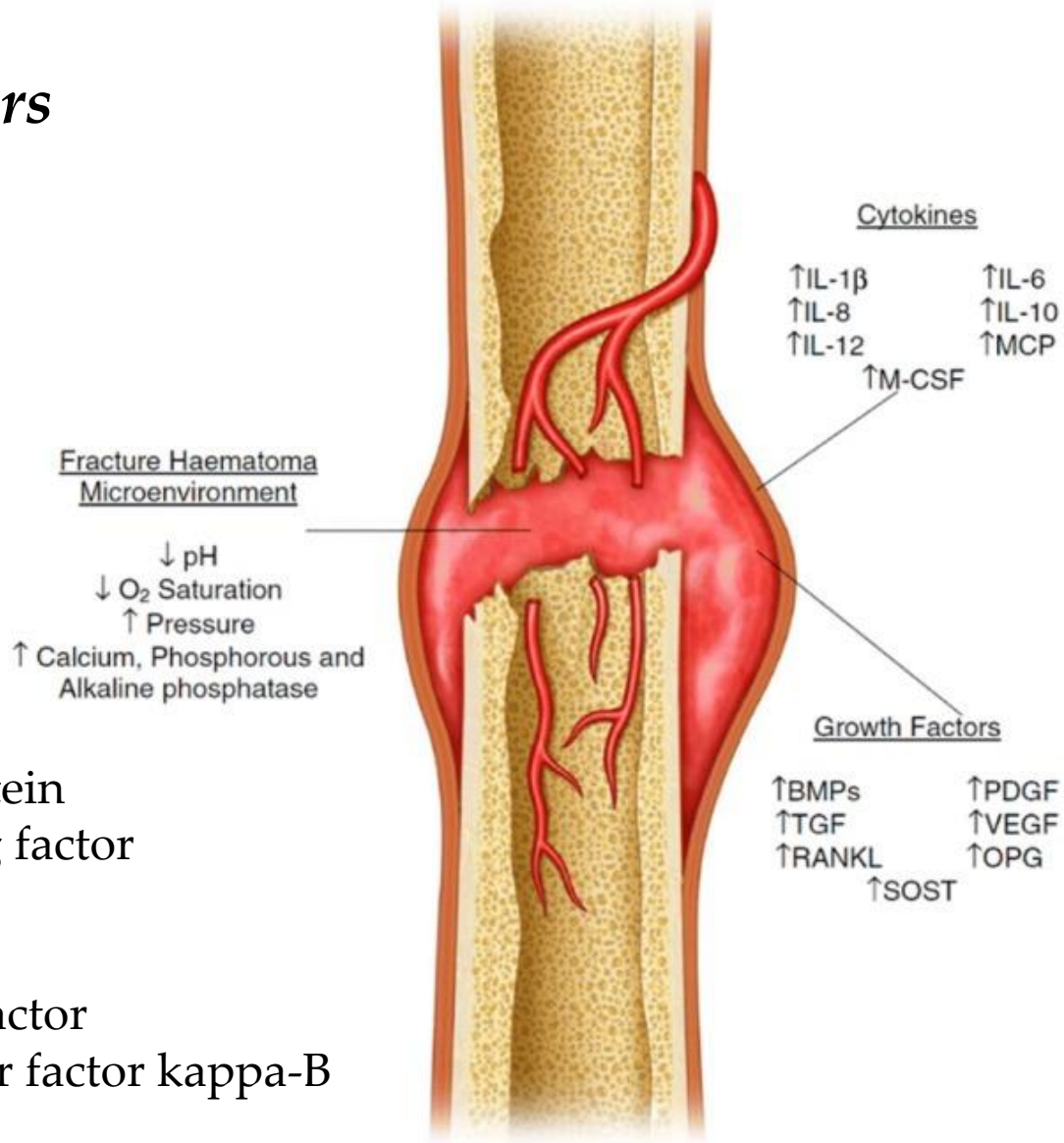


Osteoinductive mediators

- platelets and macrophages

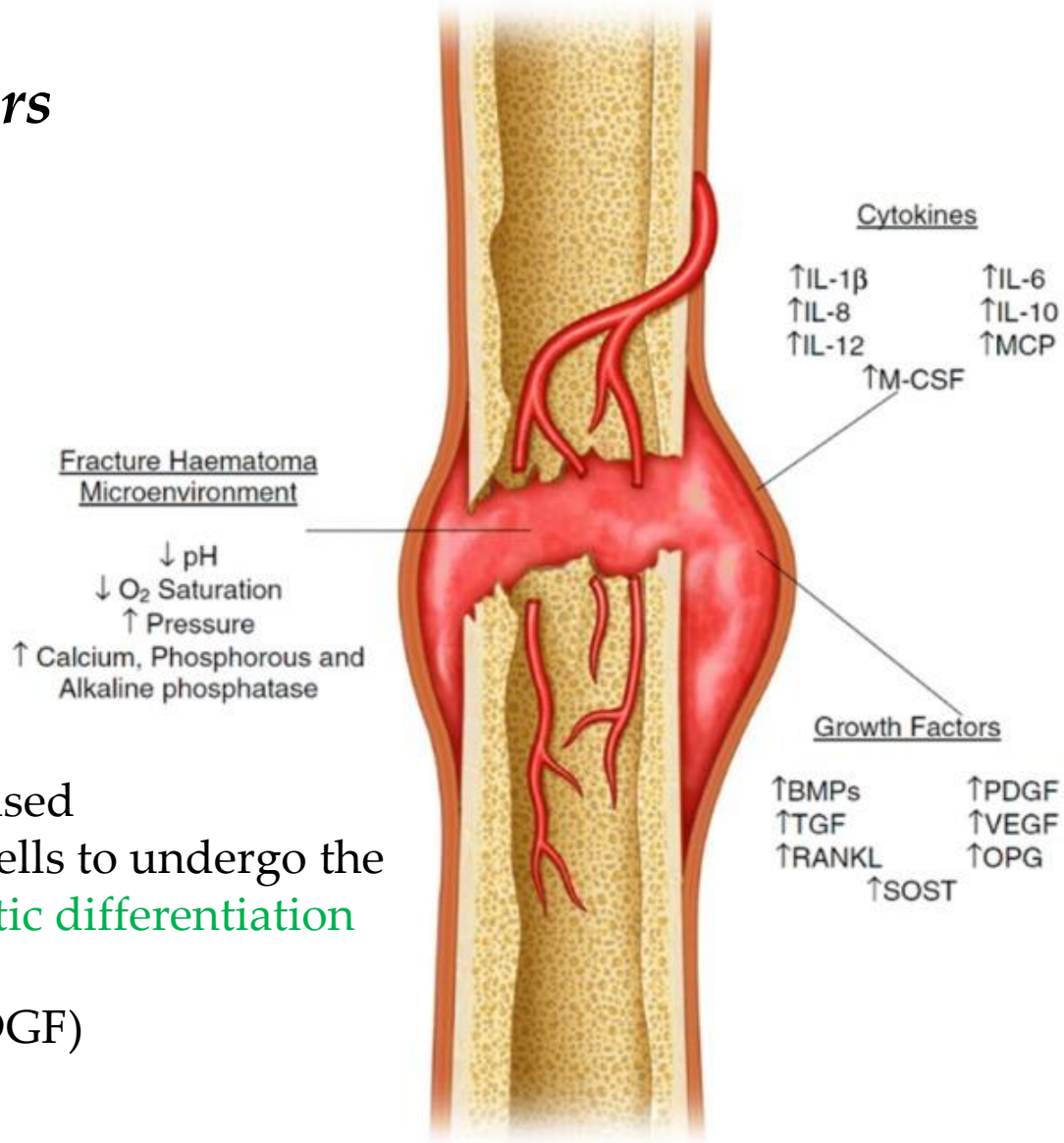
release a series of cytokines (cell signalling molecules) of different types, stimulating a cascade of events to initiate healing

Osteoinductive mediators



IL interleukin
MCP monocyte chemoattractive protein
M-CSF monocyte colony-stimulating factor
BMP bone morphogenic protein
PDGF platelet-derived growth factor
VEGF vascular endothelial growth factor
RANKL receptor activator of nuclear factor kappa-B ligand
OPG osteoprotegerin
SOST sclerostin

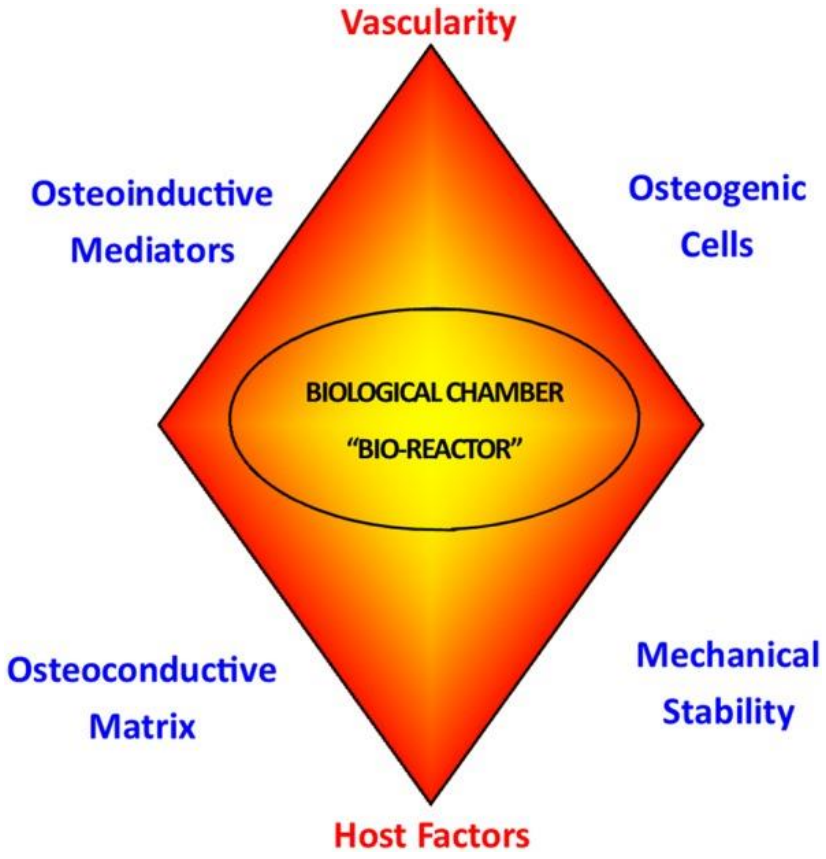
Osteoinductive mediators



The most important mediators released having a direct effect on progenitor cells to undergo the process of mitogenesis and osteoblastic differentiation include

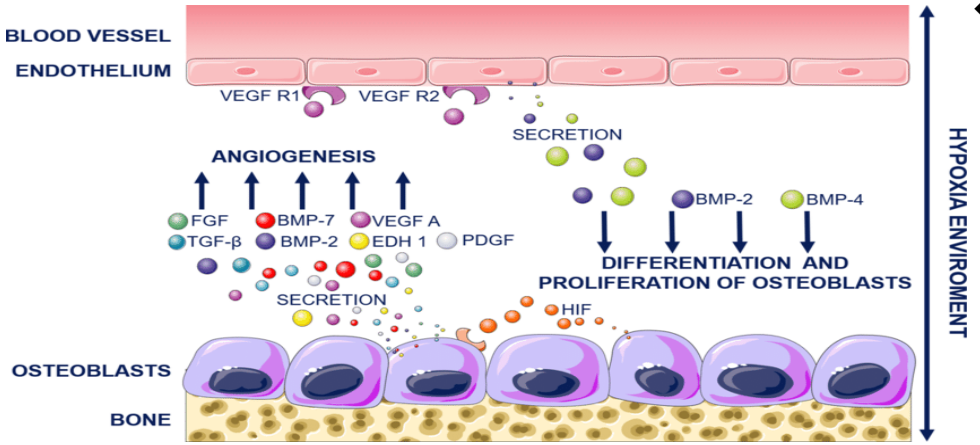
- platelet-derived growth factor (PDGF)
- fibroblast growth factor (FGF)
- insulin-like growth factor (IGF)

- transforming growth factor beta (TGFβ) proteins (bone morphogenic protein(BMP)-2, 4, 6 and 7



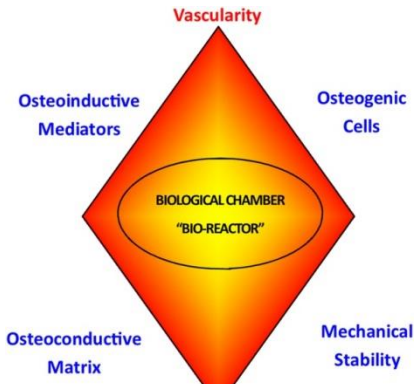
Osteogenic cells

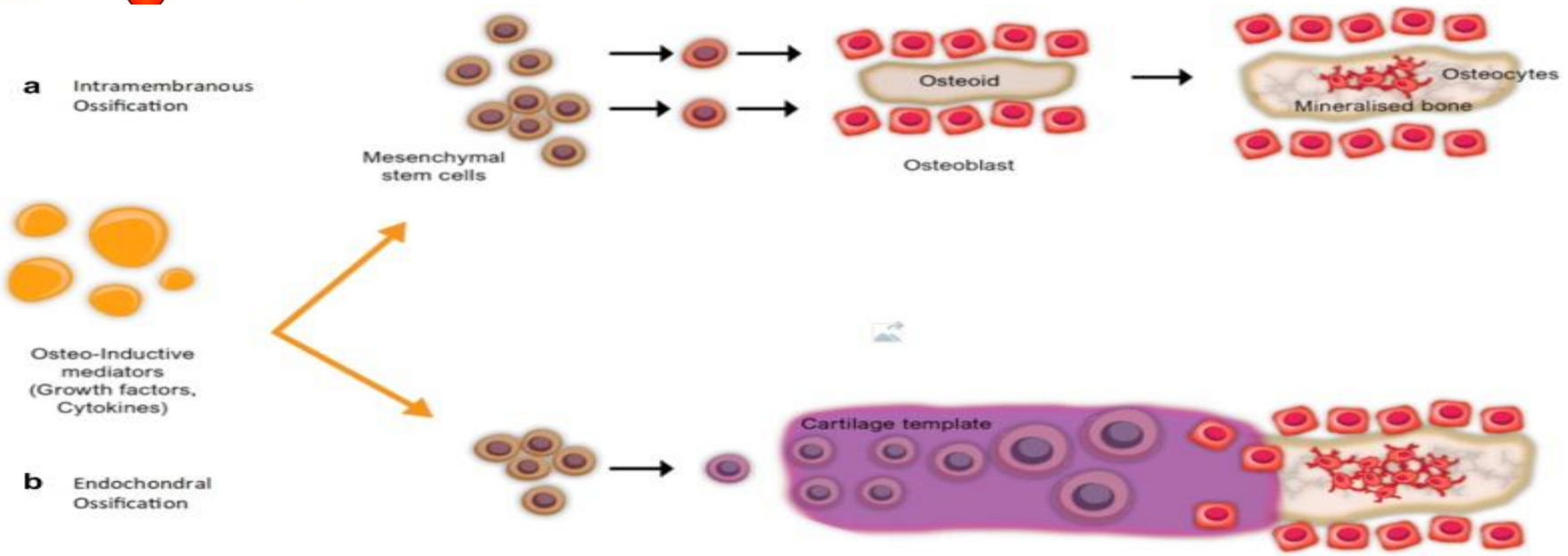
- Comprise both committed osteoprogenitor cells from the periosteum as well as undifferentiated multipotent stem cells (MSCs) from bone marrow and endothelial progenitor cells, are also activated according to the local fracture environment in the haematoma



- Higher oxygen tension at periosteal surfaces distal to the fracture site,as well as other factors, encourages preferential MSC differentiation into osteoblasts

Osteogenic cells





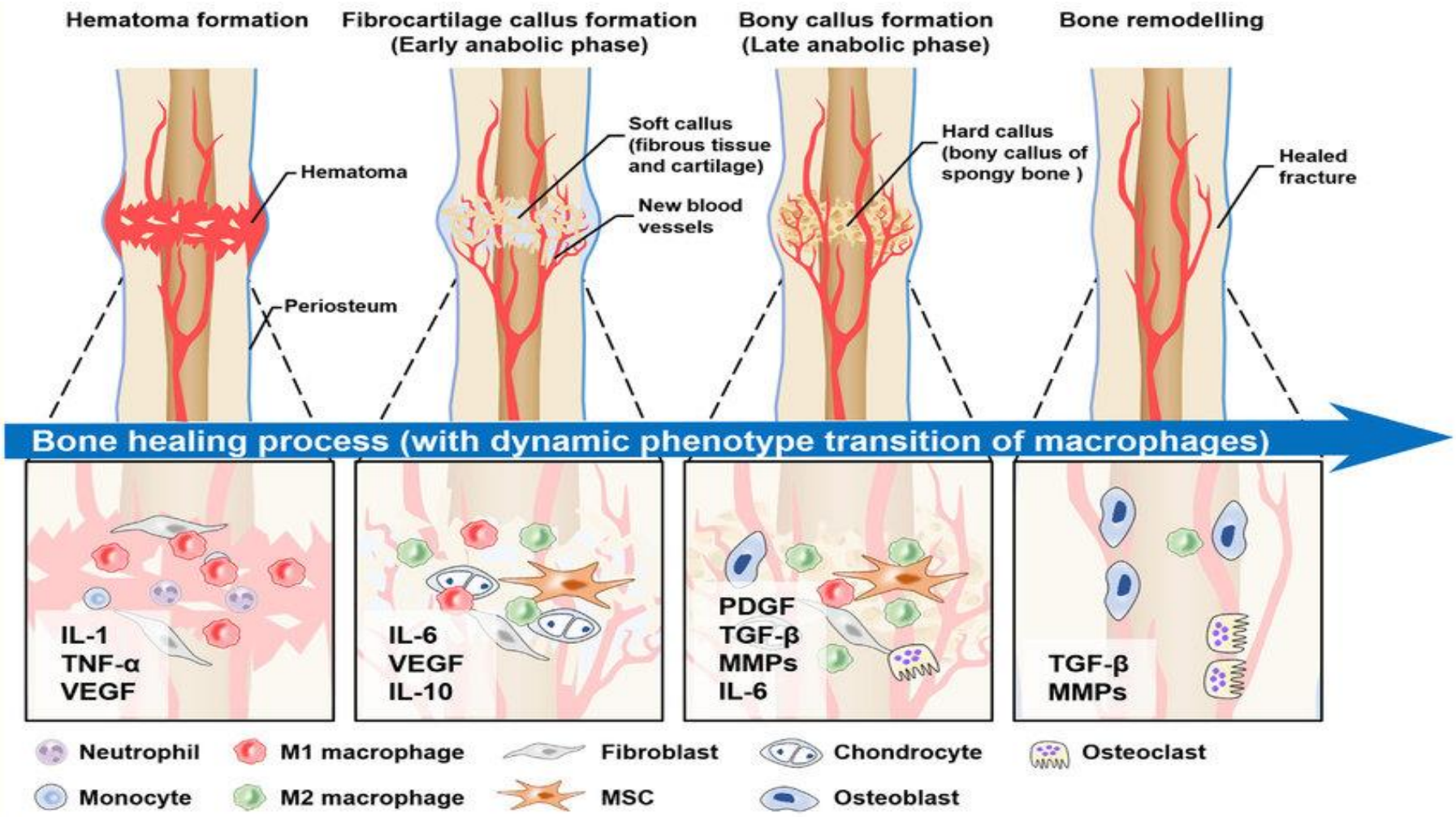
Diagrammatic representation of ossification:

a.Intramembranous ossification. Osteoinductive mediators induce osteogenic MSCs to differentiate into osteoblasts,which lay down osteoid(collagen-1 rich),this mineralises to form an ossification centre,whence mineralisation extends.There is terminal differentiation into osteocytes,becoming entombed in the bone matrix.

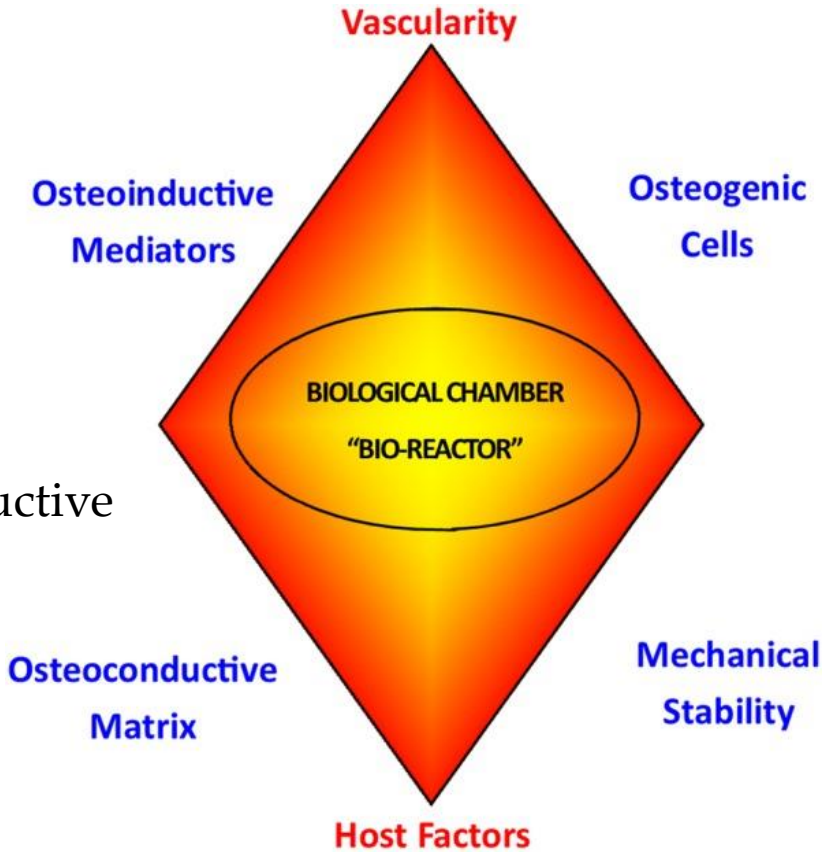
b.Endochondral ossification.Osteoinductive mediators induce osteogenic MSCs to differentiate into chondrocytes,a cartilage matrix is secreted which forms the template for endochondral bone formation.Chondrocytes then undergo hypertrophic differentiation and mineralise the surrounding matrix.They eventually undergo apoptosis—resulting in vascular invasion.Invading blood vessels convey osteoblasts which form bone on the cartilage template

Bone Healing

Static → Dynamic



Extracellular Osteoconductive Matrix(scaffold)



- Promoting migration and adhesion of osteoinductive and osteogenic cells to the fracture site, is essential for fracture healing

- Where there is good apposition of bone,necrotic bone at the fracture site serves this purpose

- If there is insuficient 'natural' scafold, then autograft, or allograft demineralised bone matrix (DBM), which also has inherent osteoinductive capability thanks to retained growth factors including BMP, can be used when treating non-union of bone defects

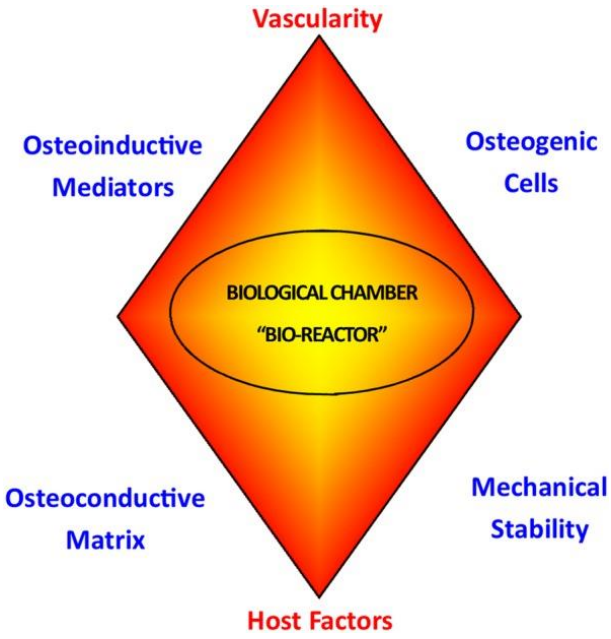
biomedicines

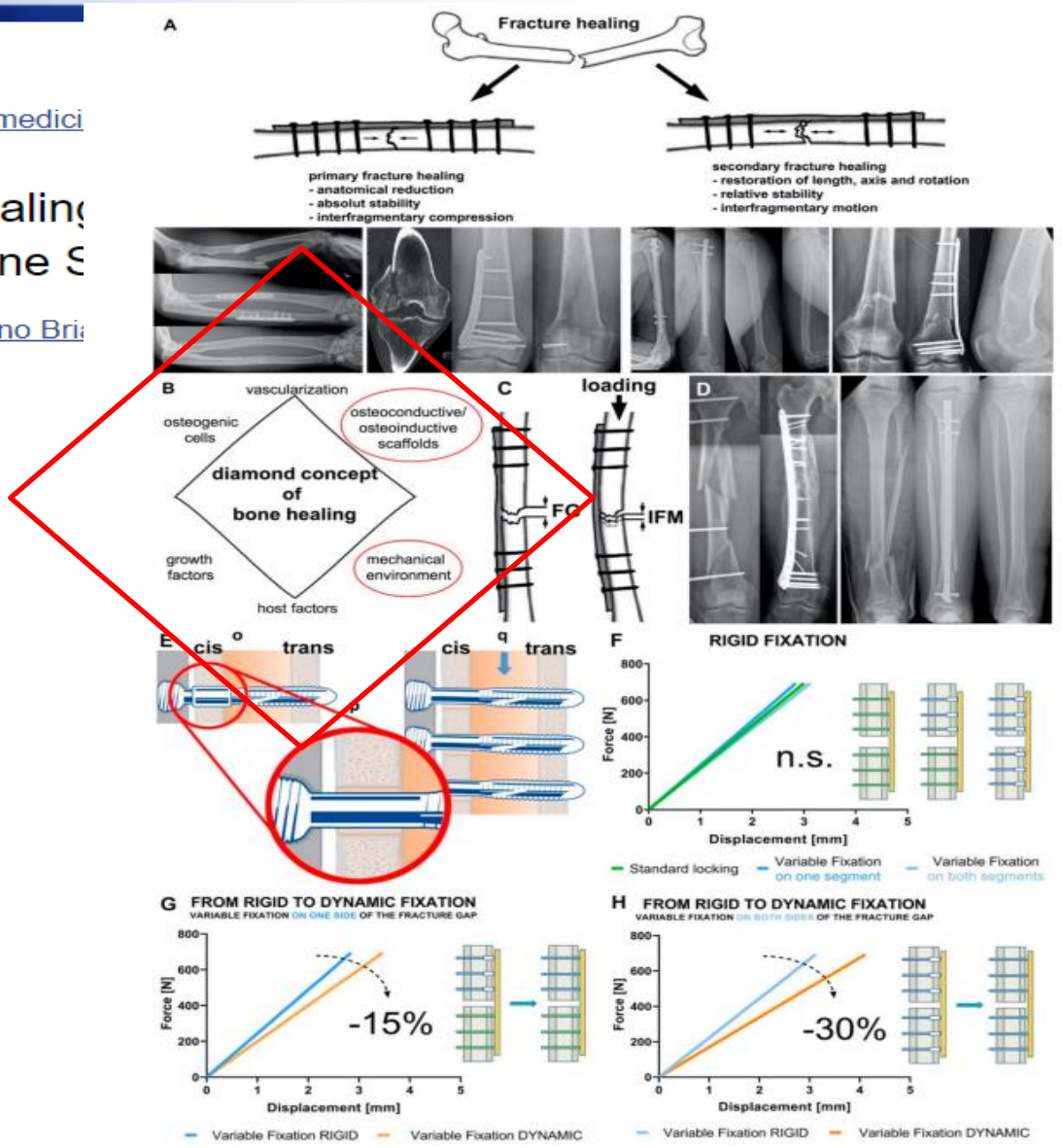
MDPI

Biomedicines. 2021 Jul; 9(7): 746.
Published online 2021 Jun 28. doi: 10.3390/biomedici

Strategies to Improve Bone Healing Nano-/Micro-Topography of Bone S

Dirk Wähnert,[1,2,†] Johannes Greiner,[2,3,†] Stefano Bria and Barbara Kaltschmidt[2,3,5,*†]





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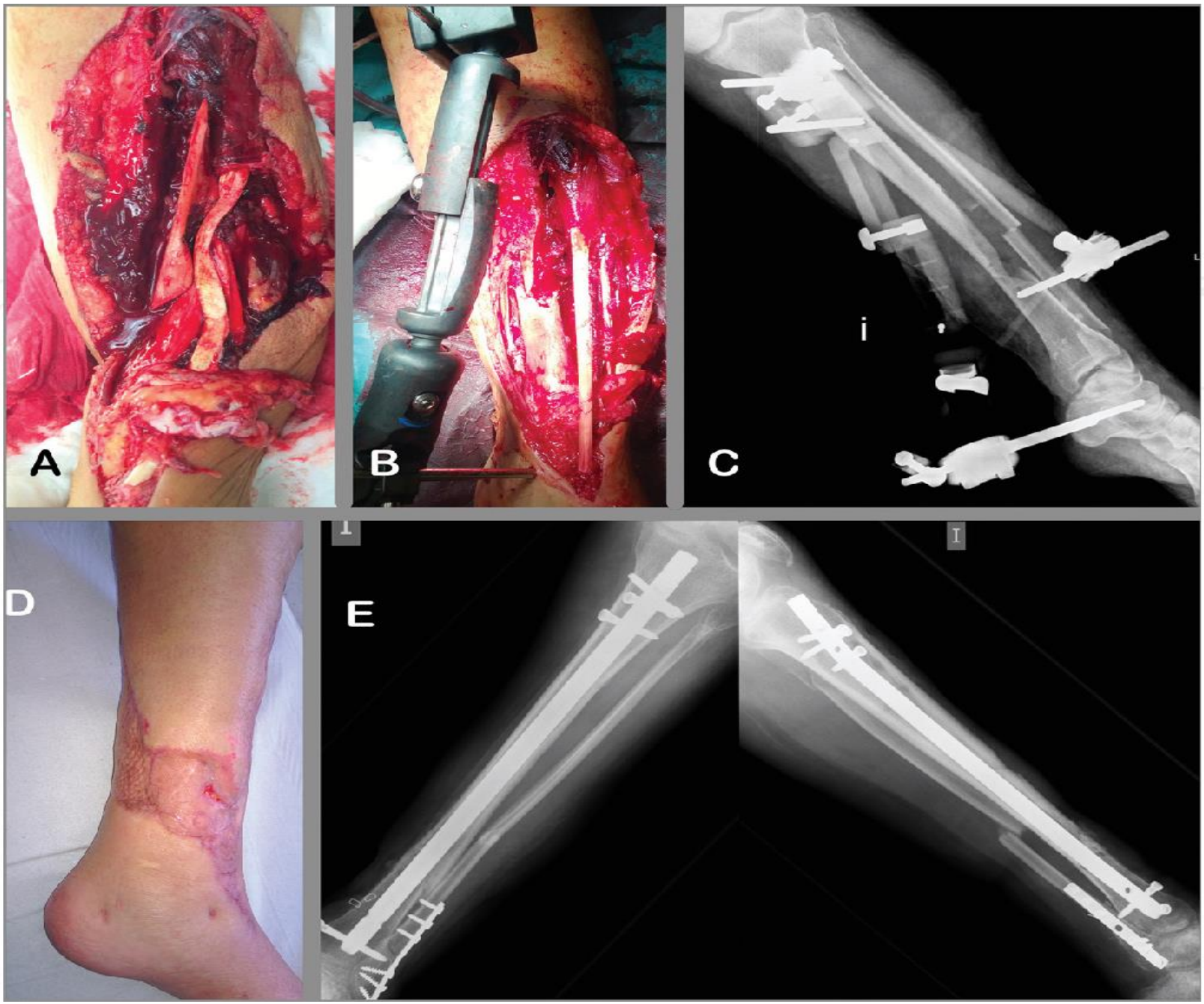
- ✓ Biology
- ✓ Biomechanic
- ✓ Biomaterial
- ✓ Fixation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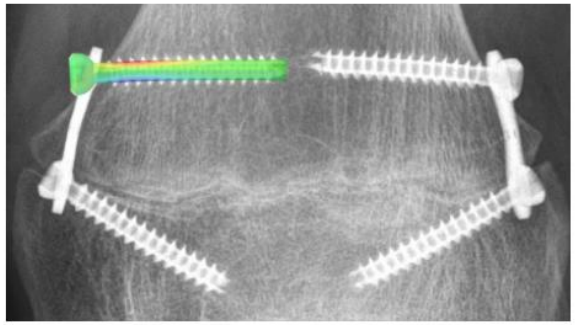
Research programs

Regenerative Orthopaedics

The Regenerative Orthopaedics program is a multidisciplinary group taking an holistic approach to regenerative medicine for the repair of traumatic injuries of the musculoskeletal system.

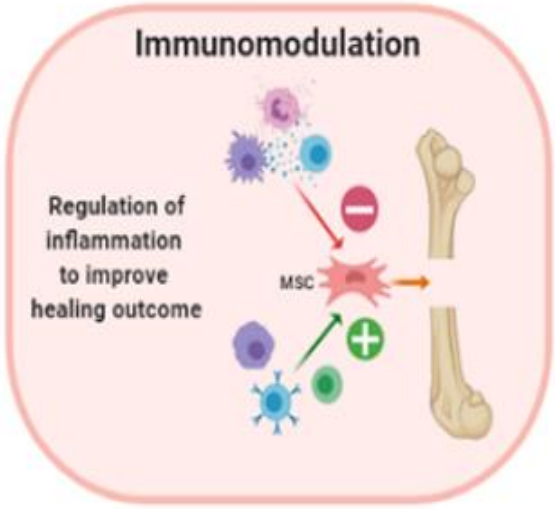


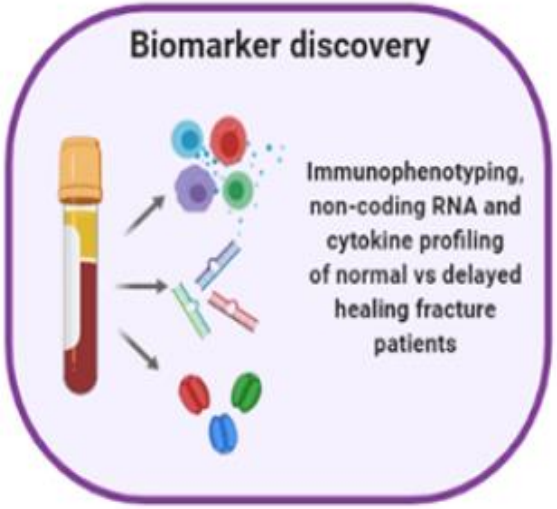
Biomedical Development

The Biomedical Development program offers extensive know-how, expertise, and experience in the fields of biomechanical testing and computational analyses to advance patient care.

Preclinical Services

Preclinical Services conduct all AO Research Institute Davos in vivo studies—often in close collaboration with other focus areas.

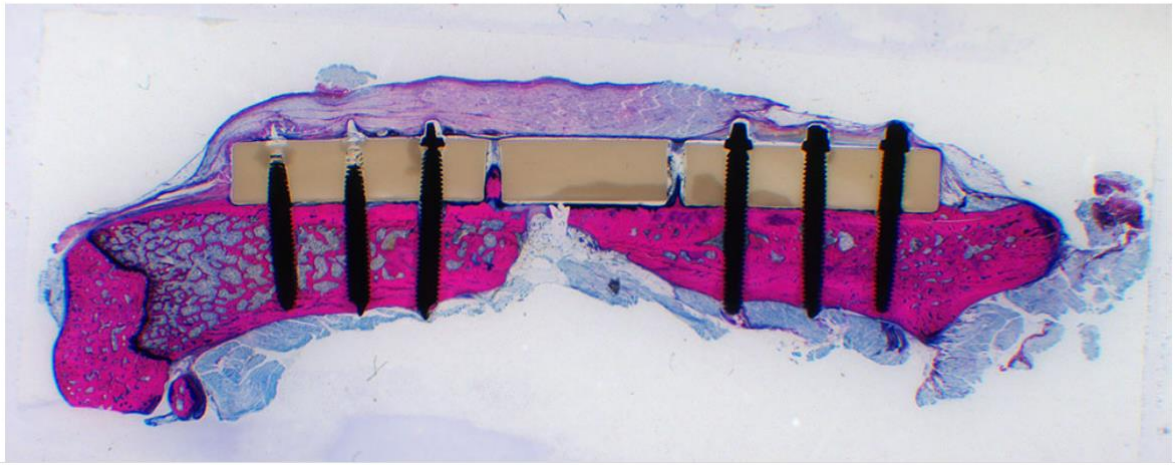




AO Research Institute Davos News

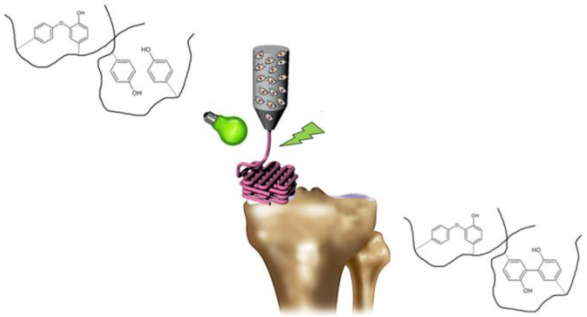
Bone Biology

Revascularizing and replacing damaged bone tissue



Biomedical Materials

Developing advanced biomaterials and biomanufacturing technologies for the next generation of repair and regenerative therapies in orthopaedics



ΕΠΙΣΤΗΜΟΝΙΚΗ ΕΚΔΗΛΩΣΗ
ΒΙΒΛΙΟΓΡΑΦΙΚΗ ΕΝΗΜΕΡΩΣΗ

Μεταβολικά Νοσήματα των Οστών

ΠΟΡΤΑΡΙΑ ΠΗΛΙΟΥ

18-20 ΜΑΡΤΙΟΥ 2022