We Can Make Giants – Distraction Osteogenesis Techniques from Bench to Bed

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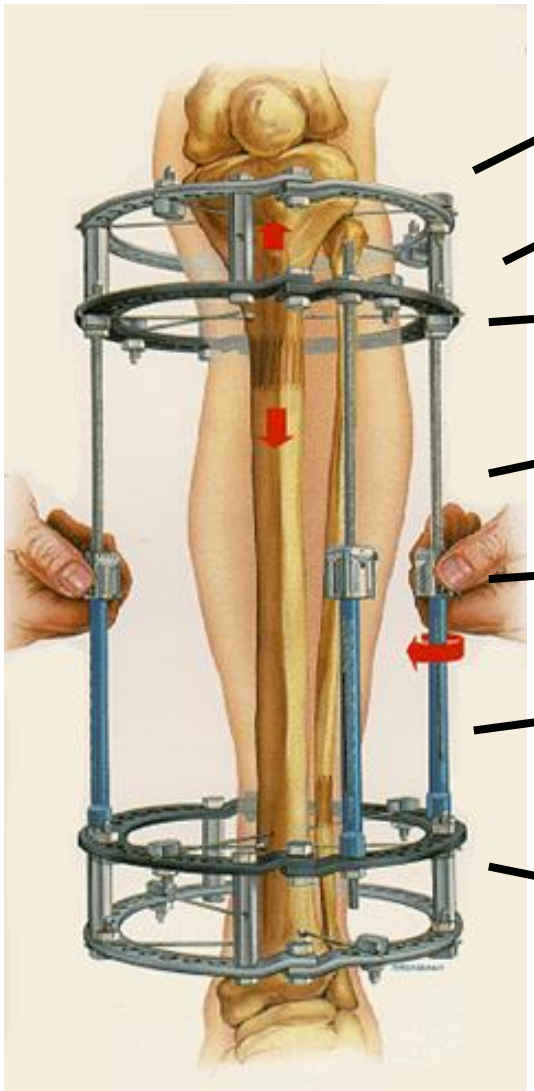
Skeletal tissues are formed spontaneously during DO. DO is a most cost-effective form of functional tissue engineering and is now being termed as distraction histogenesis (DH).



skin

muscle

ligament

vessels

tendon

nerve

bone

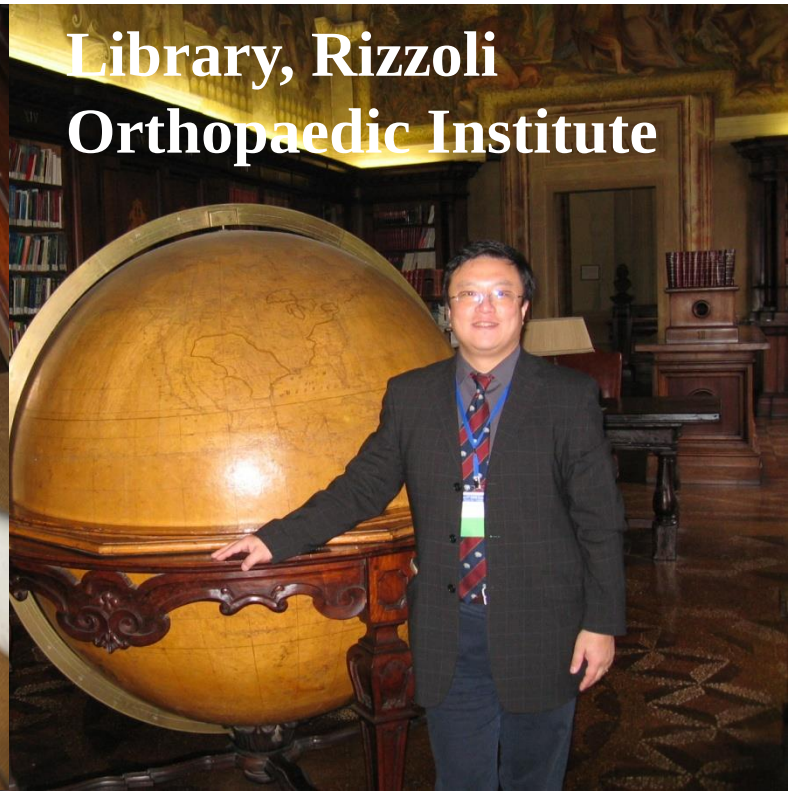
~~3-D constructs~~

~~cells~~

~~scaffold~~

~~growth factor~~

Distraction osteogenesis- History



Director, Rizzoli Orthopaedic Institute, Bologna, Italy (1899-1912)

Codivilla A. (1905) On the means of lengthening in the lower limbs, the muscles and tissues which are shortened through deformity. Am. J. Orthop. Surg., 2:353-369.

Distraction osteogenesis- History

Prof. G.A. Ilizarov
1921-1992

Ilizarov, G.A. -- Tension-Stress Principles
Clin Orthop, 238 & 239, 1989

Mechanical stimulation can promote and maintain skeletal tissues' regenerating potentials.

Birth place of Ilizarov Techniques

The Russian Ilizarov Centre, Kurgan, Russia

Dr. Ilizarov and me September, 1991,Beijing

РСФСР
МИНИСТЕРСТВО ЗДРАВООХРАНЕНИЯ
Всесоюзный Курганский научный центр
«Восстановительная травматология и ортопедия»

г. Курган, обл, ул. Марии Ульяновой, 6 Телефоны: генеральный директор 3-17-32, бухг. 3-29-87

№ 2387 «__» November, 26 1991 г.

Li Gang
Emergency 1st Department of Surgery
The General Hospital of PLA
Wu-Ke-Song Road
Beijing
P.R.China

Dear Dr. Li Gang,

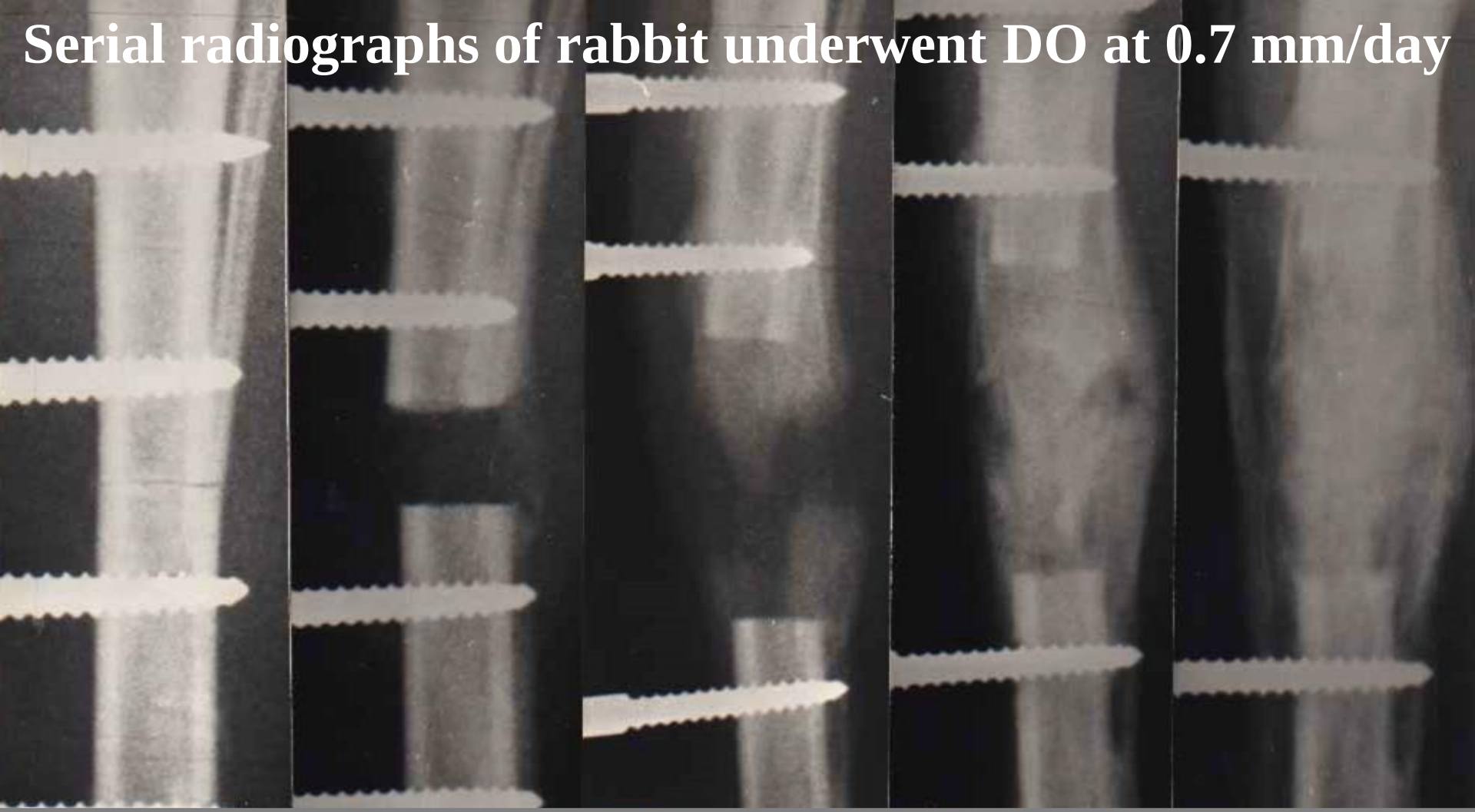
I would like to express my gratitude for your attention to me and also for the photo you sent to me.
Please find enclosed two of my publications and Course programmes. As you know we run 10-day Courses on various problems developed at our Centre.
Please inform us which of the Course you'd like to attend and as soon as the group for the topic is formed you will be advised additionally.

Yours sincerely,

Prof. G.A.Ilizarov
AM USSR Academy of Sciences
General Director
All-Union Kurgan Scientific Centre for
Restorative Traumatology and Orthopaedics
Kurgan USSR


РОССИЙСКИЙ НАУЧНЫЙ ЦЕНТР
"ВОССТАНОВИТЕЛЬНАЯ ТРАВМАТОЛОГИЯ И ОРТОПЕДИ
ИМЕНИ АКАДЕМИКА Г.А. ИЛИЗАРОВА
ПРИВЕТСТВУЕМ УЧАСТНИКОВ КОНФЕ

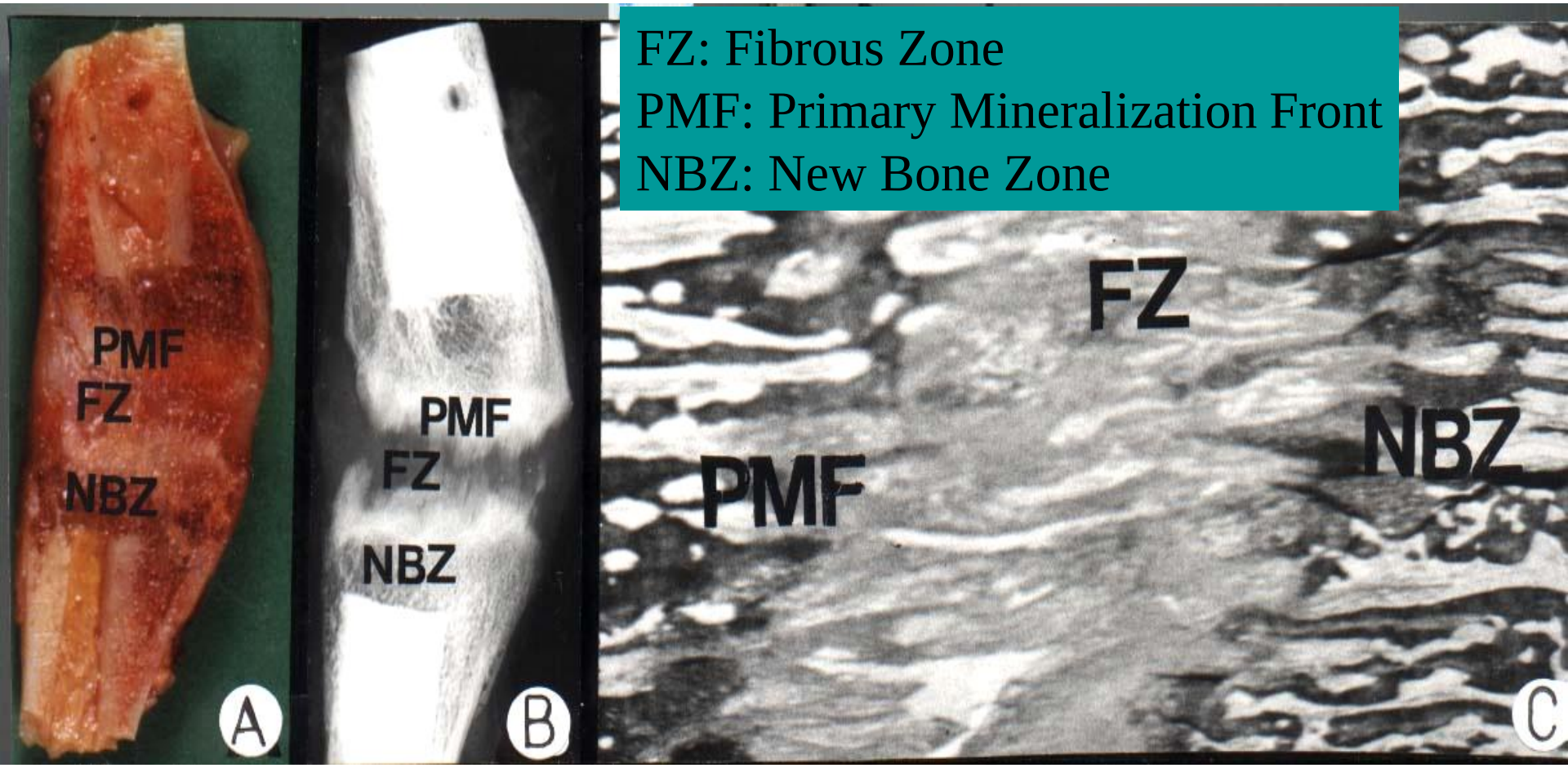
Serial radiographs of rabbit underwent DO at 0.7 mm/day



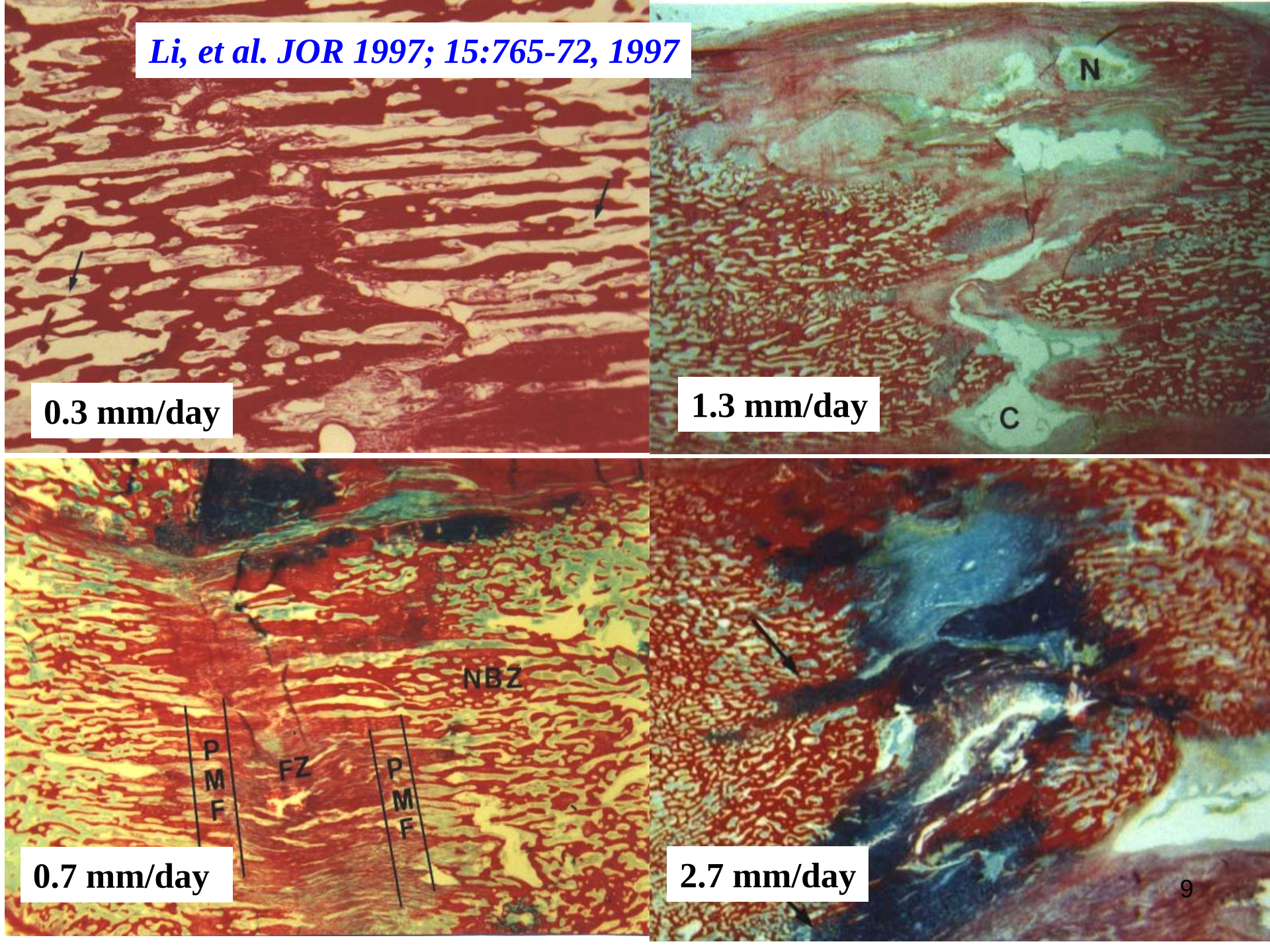
Rapid bone formation and remodeling

Li, et al. JOR 1997; 15:765-72.

The definition of the zones in the regenerate



Li, et al. JOR 1997;15:765-72.


Li, et al. JOR 1997; 15:765-72, 1997
0.3 mm/day
N
C
1.3 mm/day
NBZ
PMF
FZ
PMF
0.7 mm/day
2.7 mm/day

Effect of lengthening rate on cell proliferation

Li, et al. JOR 1997; 15:765-72, 1997.

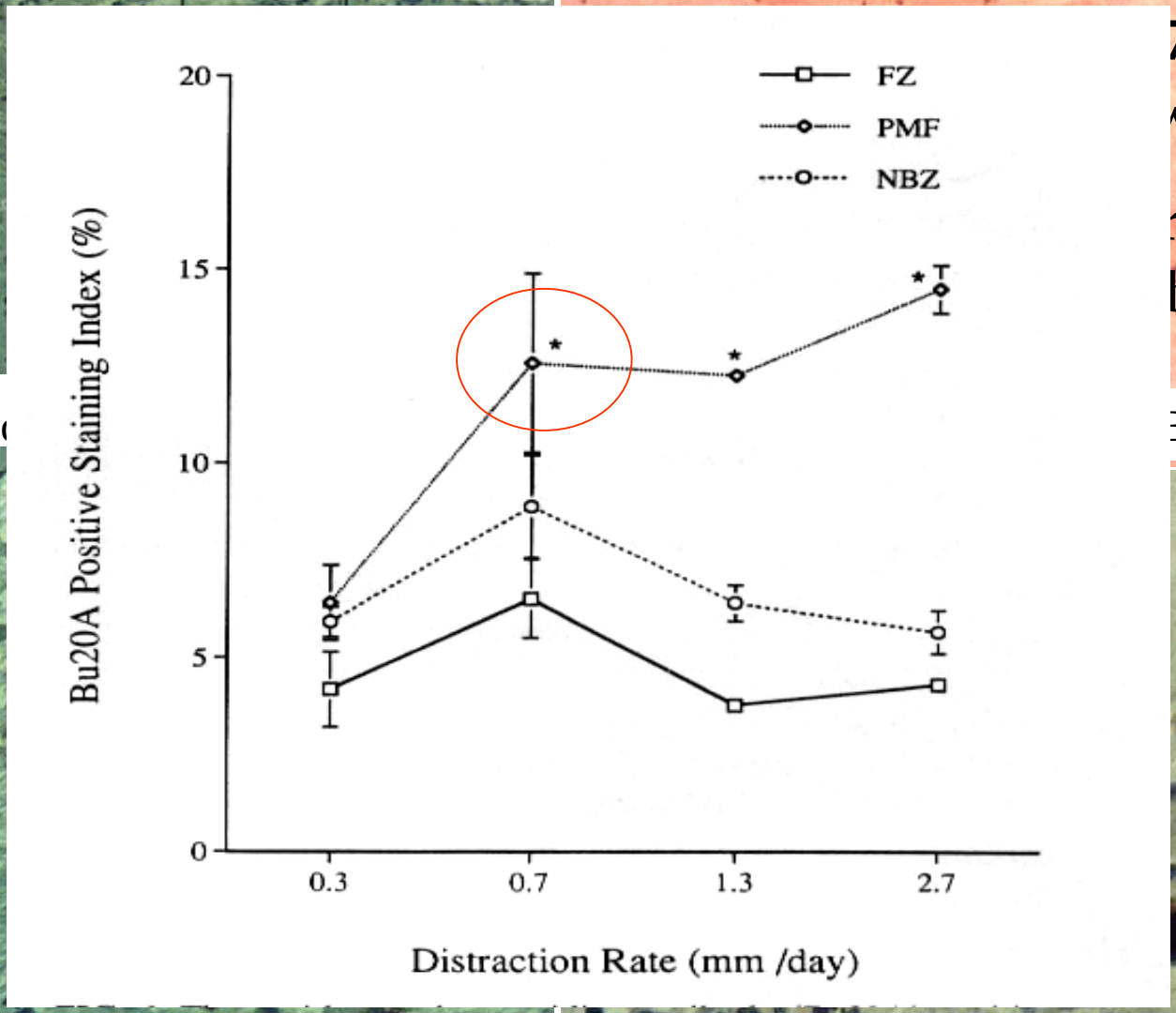
Rate:

7mm/day

vice/day

rdUrd

beling



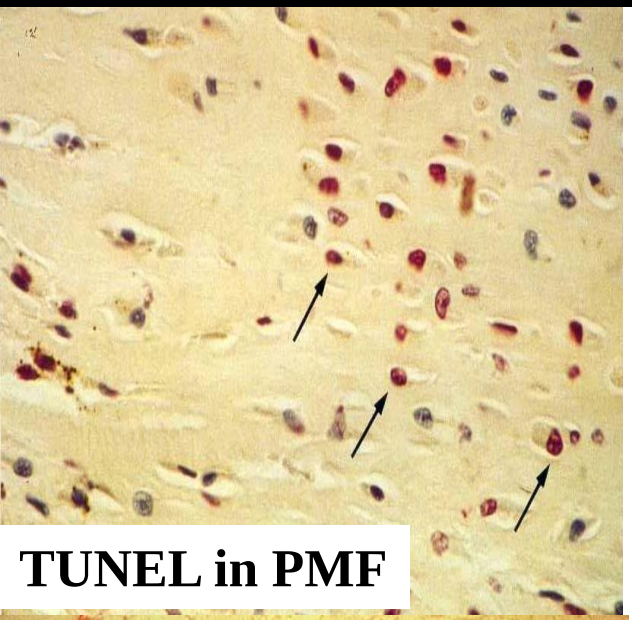
Cell proliferati

BZ, X 100

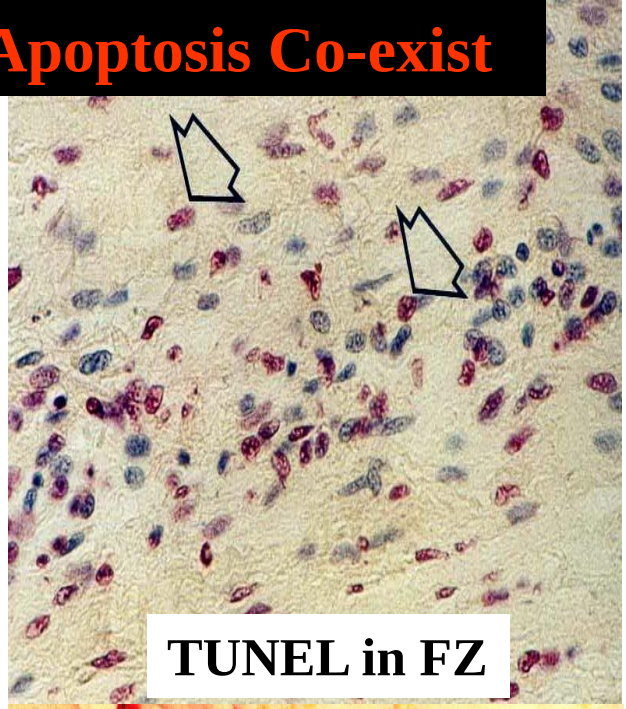
Cell proliferation in the PMF, X 400

Cell proliferation in the NBZ, X 400

Cell Proliferation and Apoptosis Co-exist

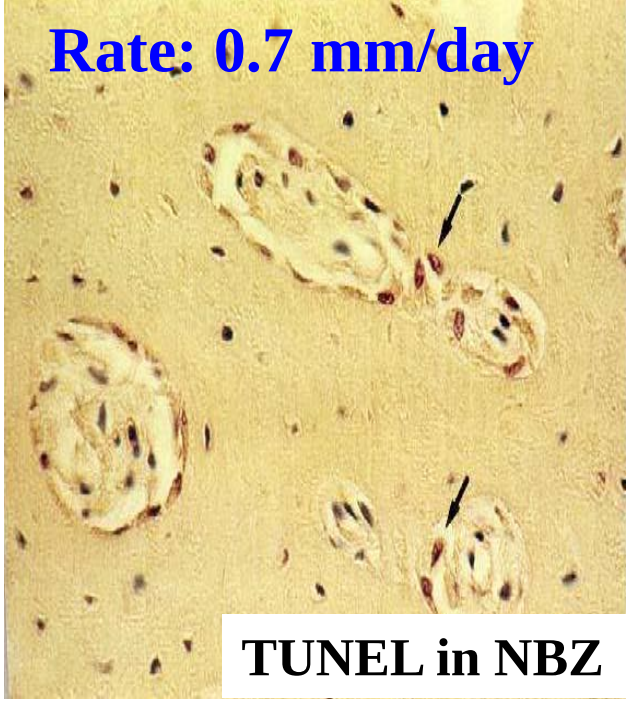


TUNEL in PMF



TUNEL in FZ

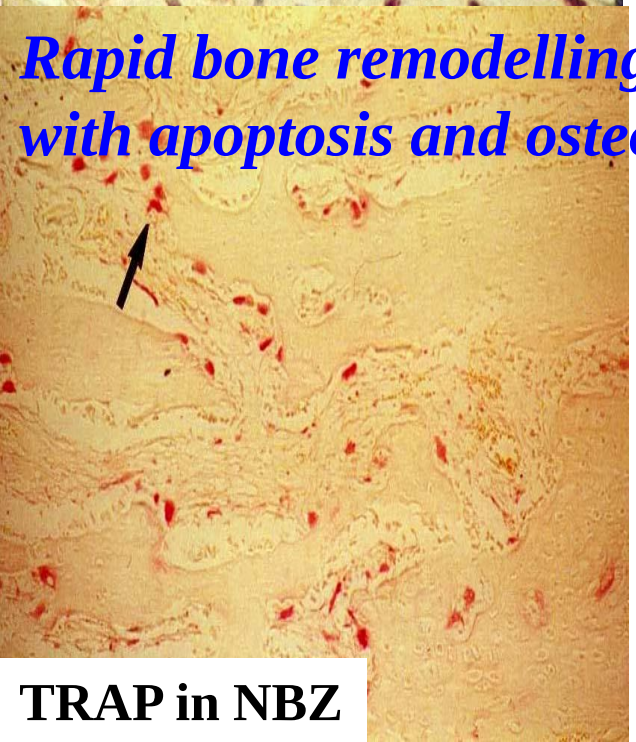
Rate: 0.7 mm/day



TUNEL in NBZ

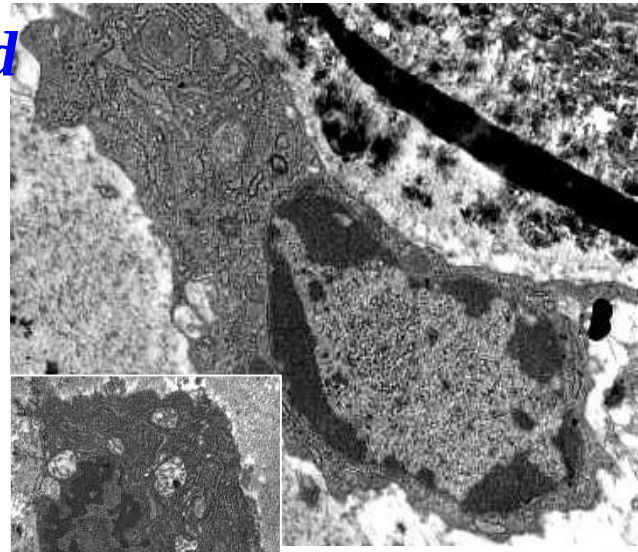
Rapid bone remodelling during DO is associated with apoptosis and osteoclastic activities.

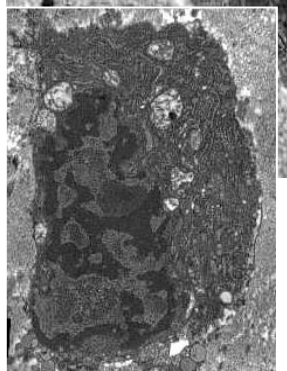
Li, et al, JOR 2003; 21:94-101.



TRAP in NBZ

TRAP





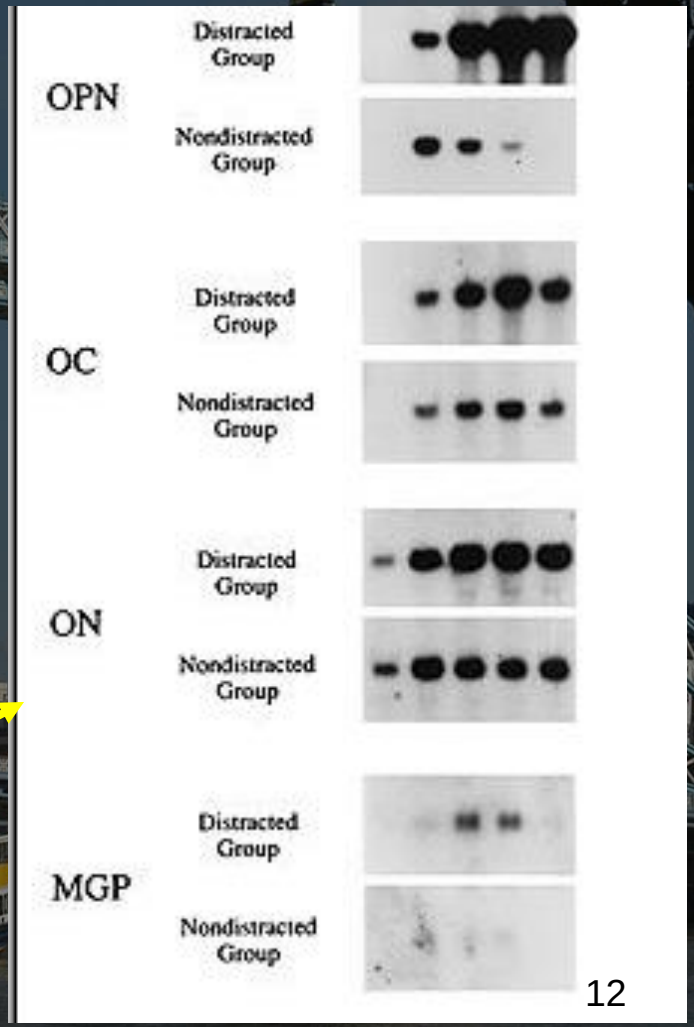
TEM apoptotic changes

Changes of Gene Expression during DO

- *Turn on genes associated with tissue repair (BMPs, VEGFs, etc.)*

The expression of BMP-4 is up-regulated in the newly formed tissues during DO.

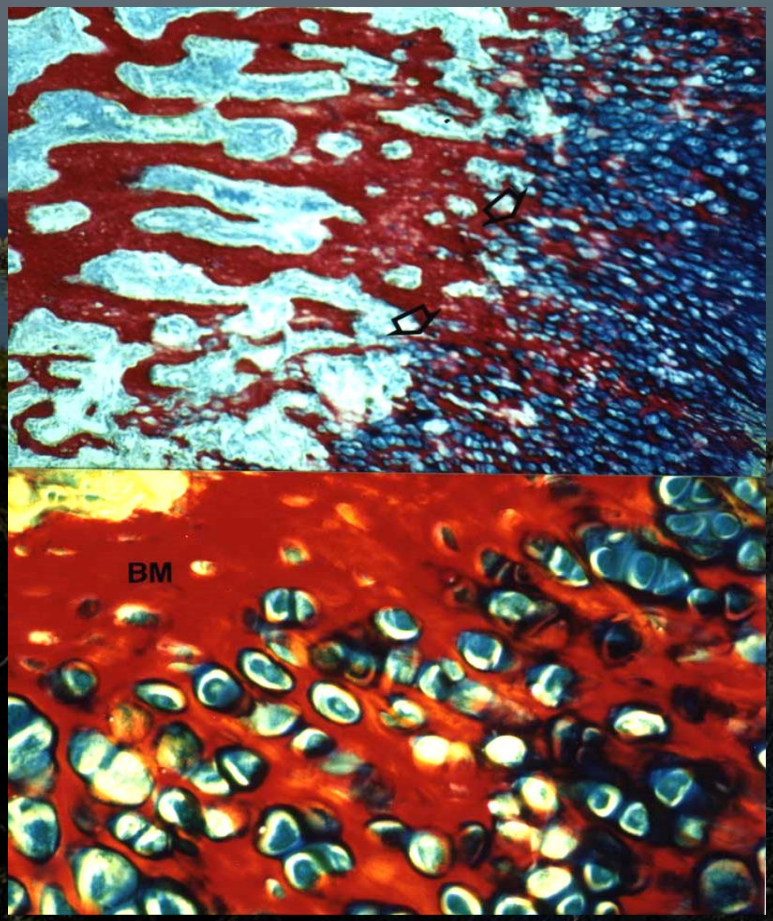
Li, et al. Acta Orthop Scand 1998; 69:420-425.

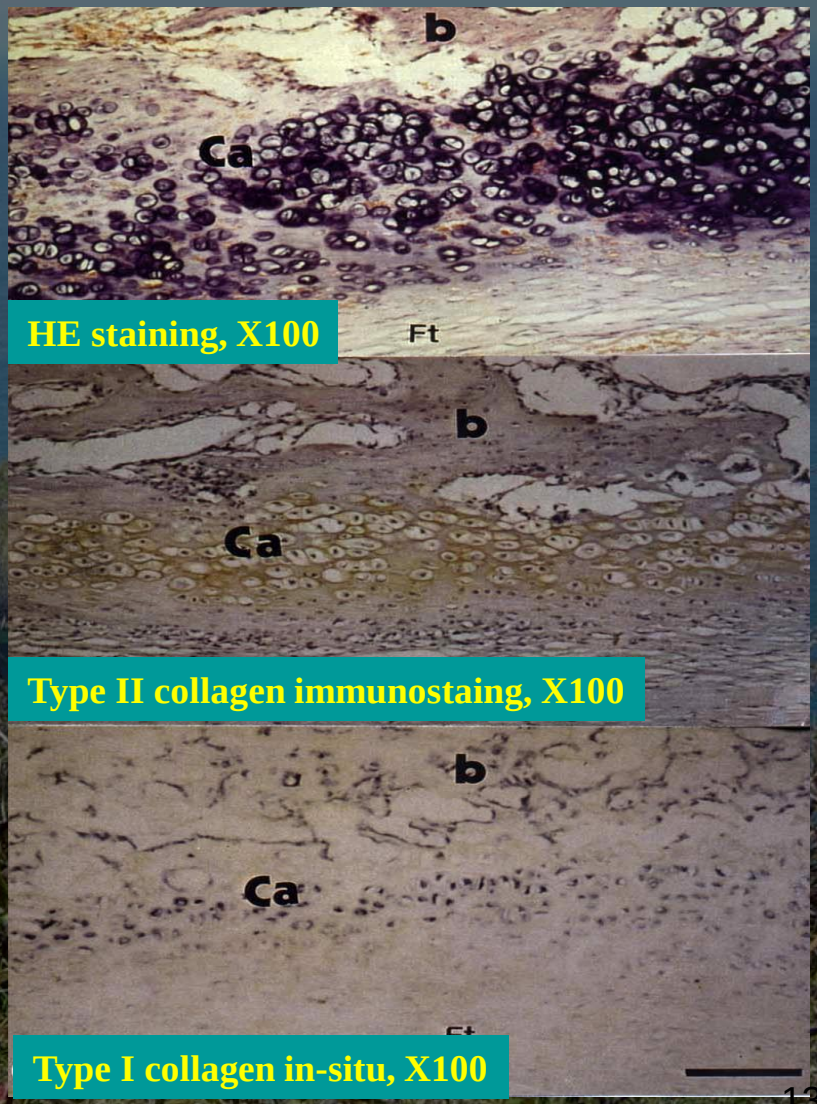


Expression of bone matrix proteins mRNA during DO. ***Sato, et al. JBMR 1998; 13(8): 1221-8.***

Changes of cellular behaviors during DO

Chondrocyte de-differentiation



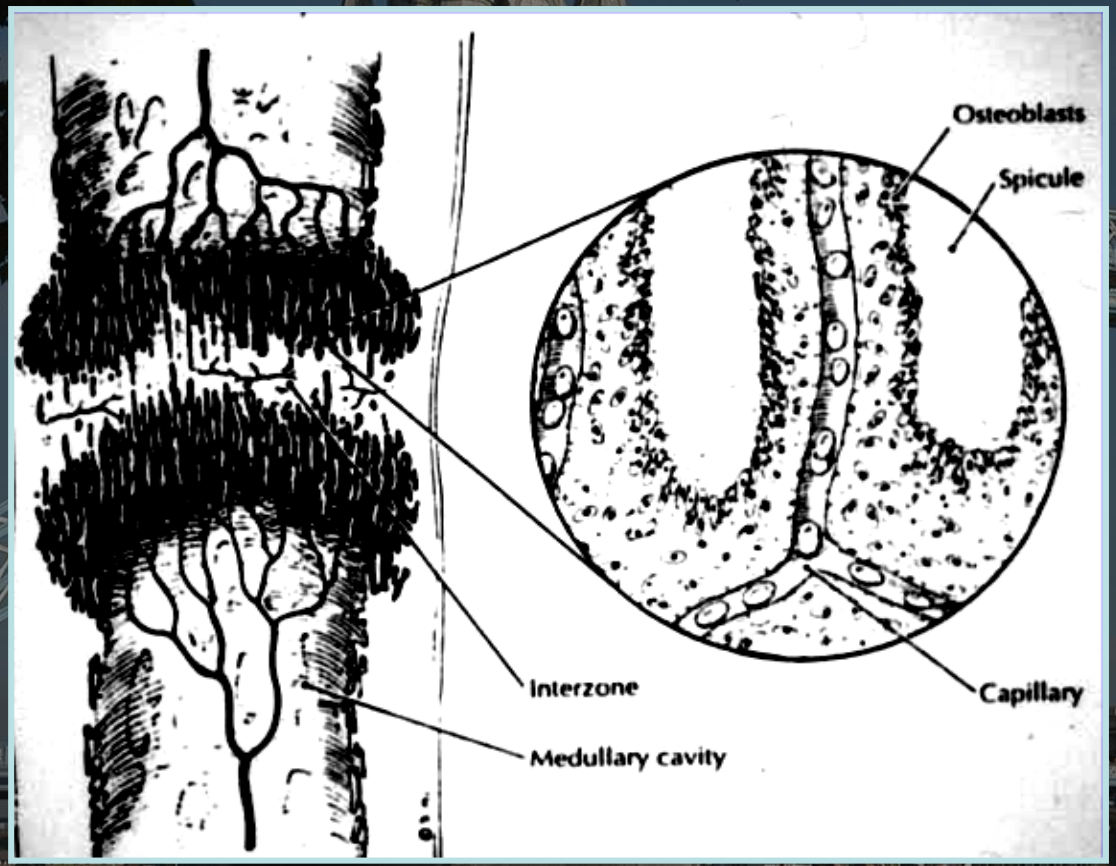


- **Ossification via chondroid bone**
  Yasui, et al. JBJS(Br), 1997; 79.
- **Chondrocyte dedifferentiation?**
  Roach and Scammell, JBMR, 1996; 11.

Li, et al. Calcif Tissue Int 1999; 64:310-17.

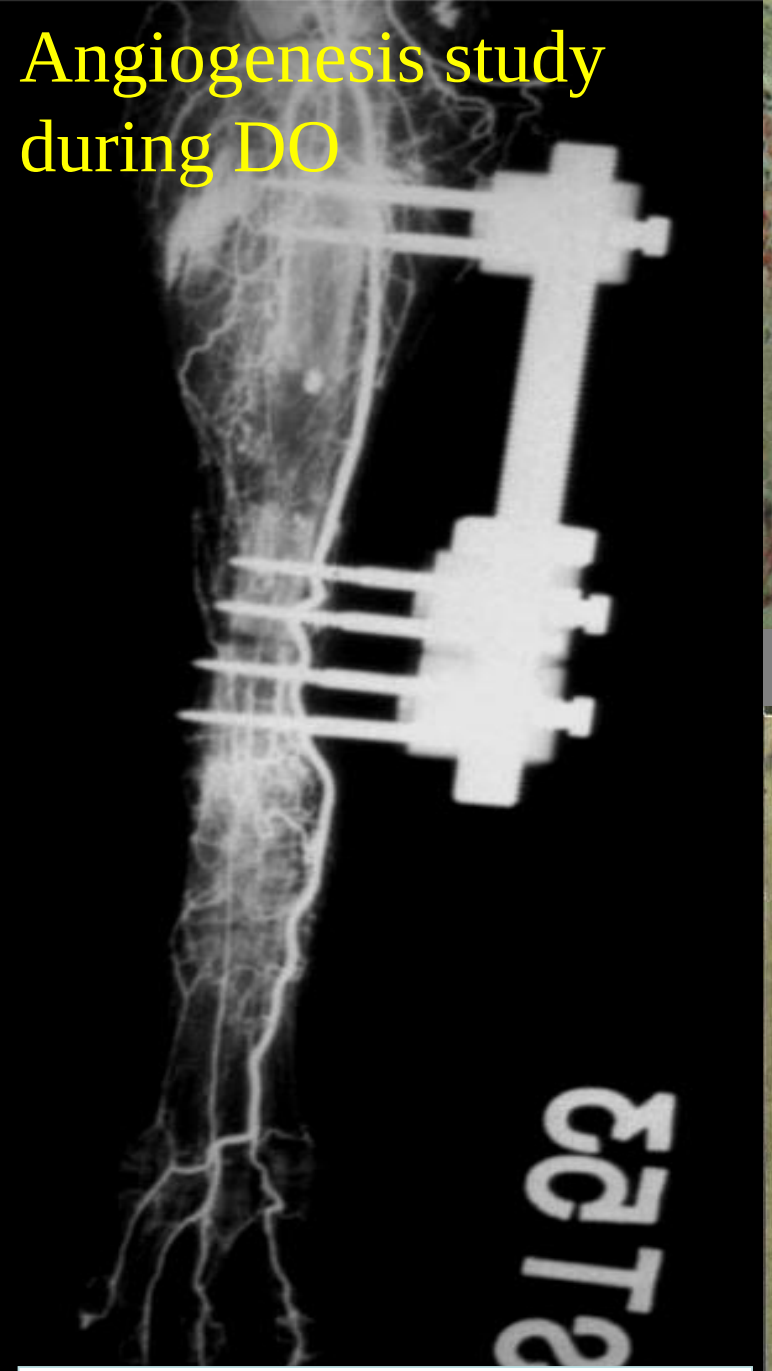
Angiogenesis in Distraction Osteogenesis

- *Angiogenesis plays a key role in DO.*

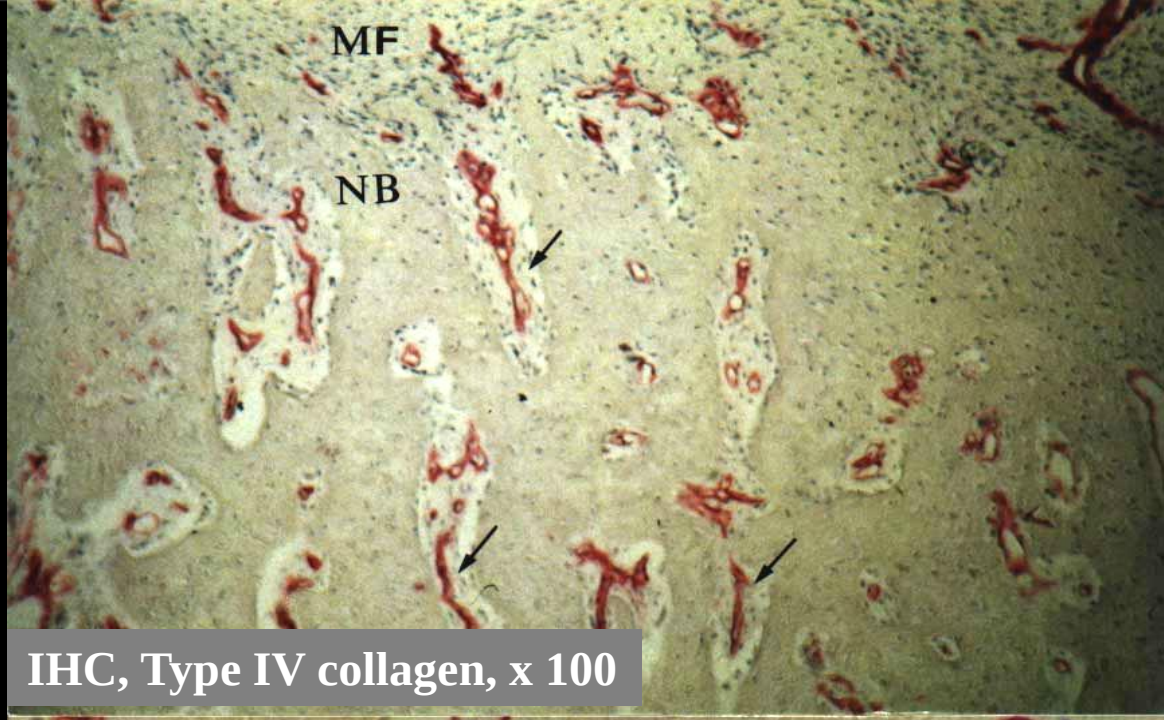


Angiography showing new vessels in the regenerate.

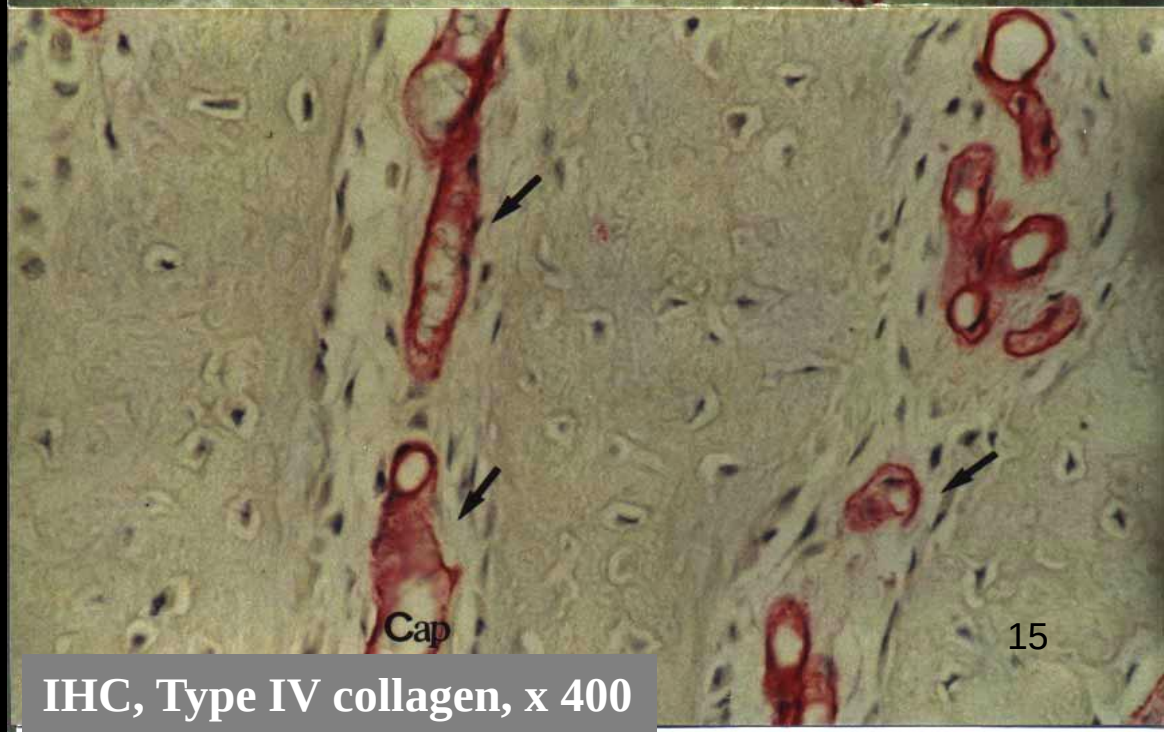
Angiogenesis study during DO



Li, et al. J Orthop Res 1999; 17:362-7.

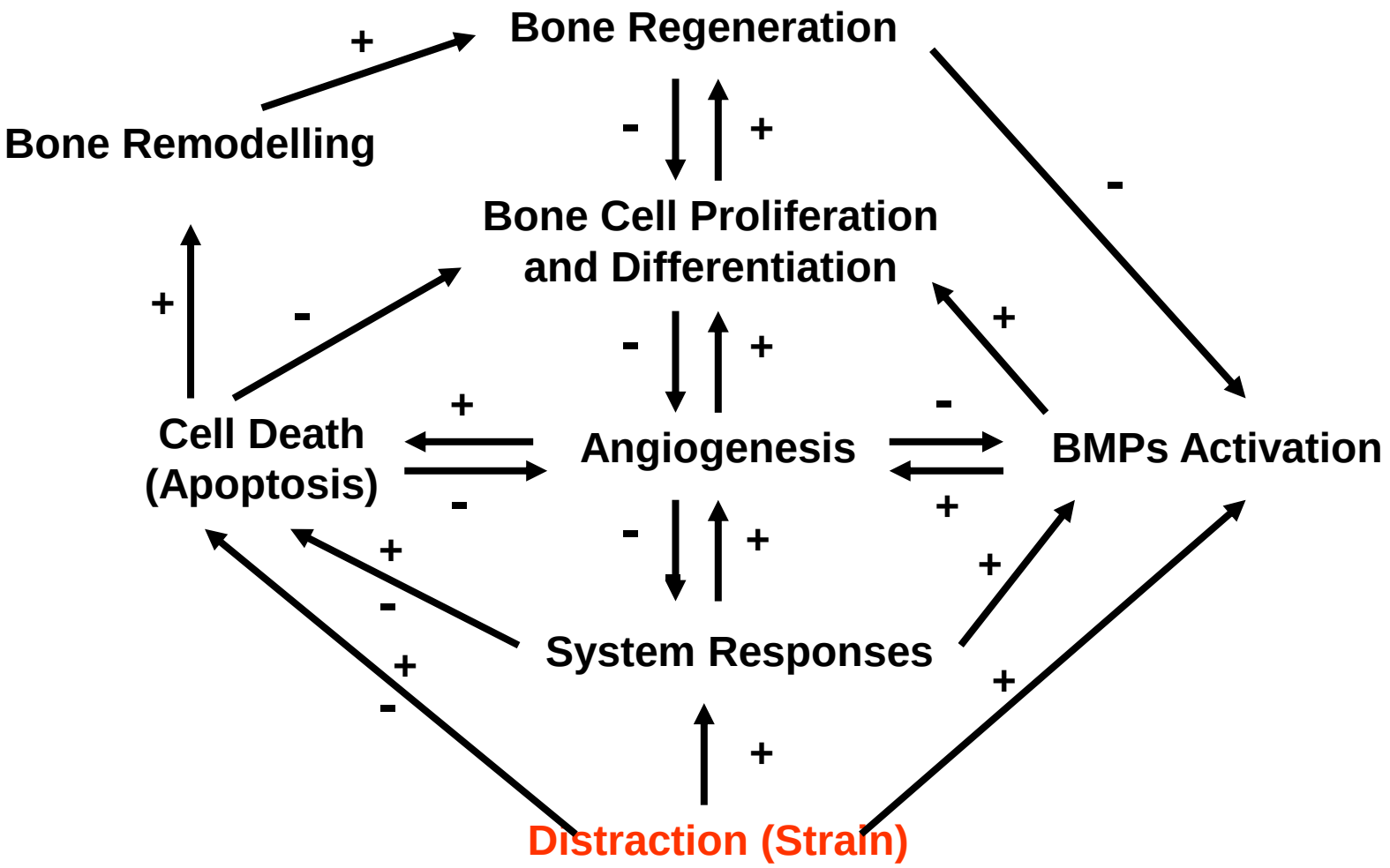


IHC, Type IV collagen, x 100



IHC, Type IV collagen, x 400

Possible Biological Mechanisms of DO

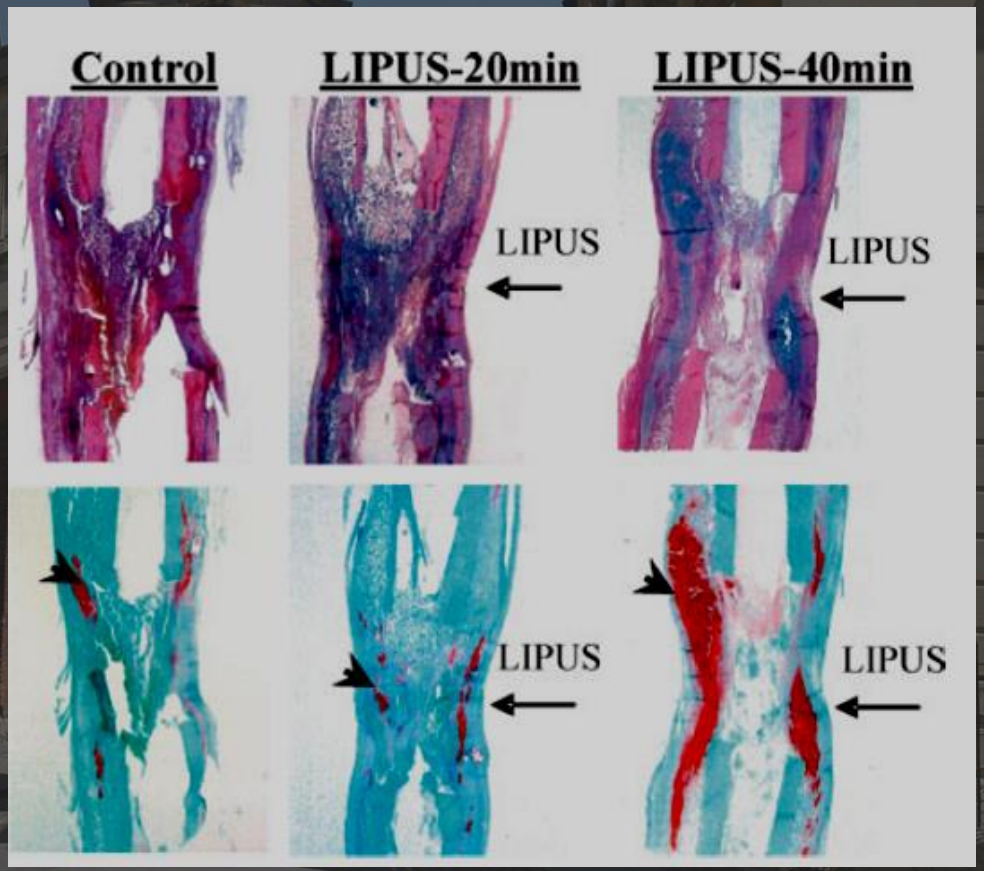


G Li, Current Opinion in Orthopaedics, 2004; 15: 325-30.

Enhancement Bone Formation During DO

- *Physical stimulation*
  - *Weight-bearing exercise*

- *Physical stimulation*
  - *Ultrasound*



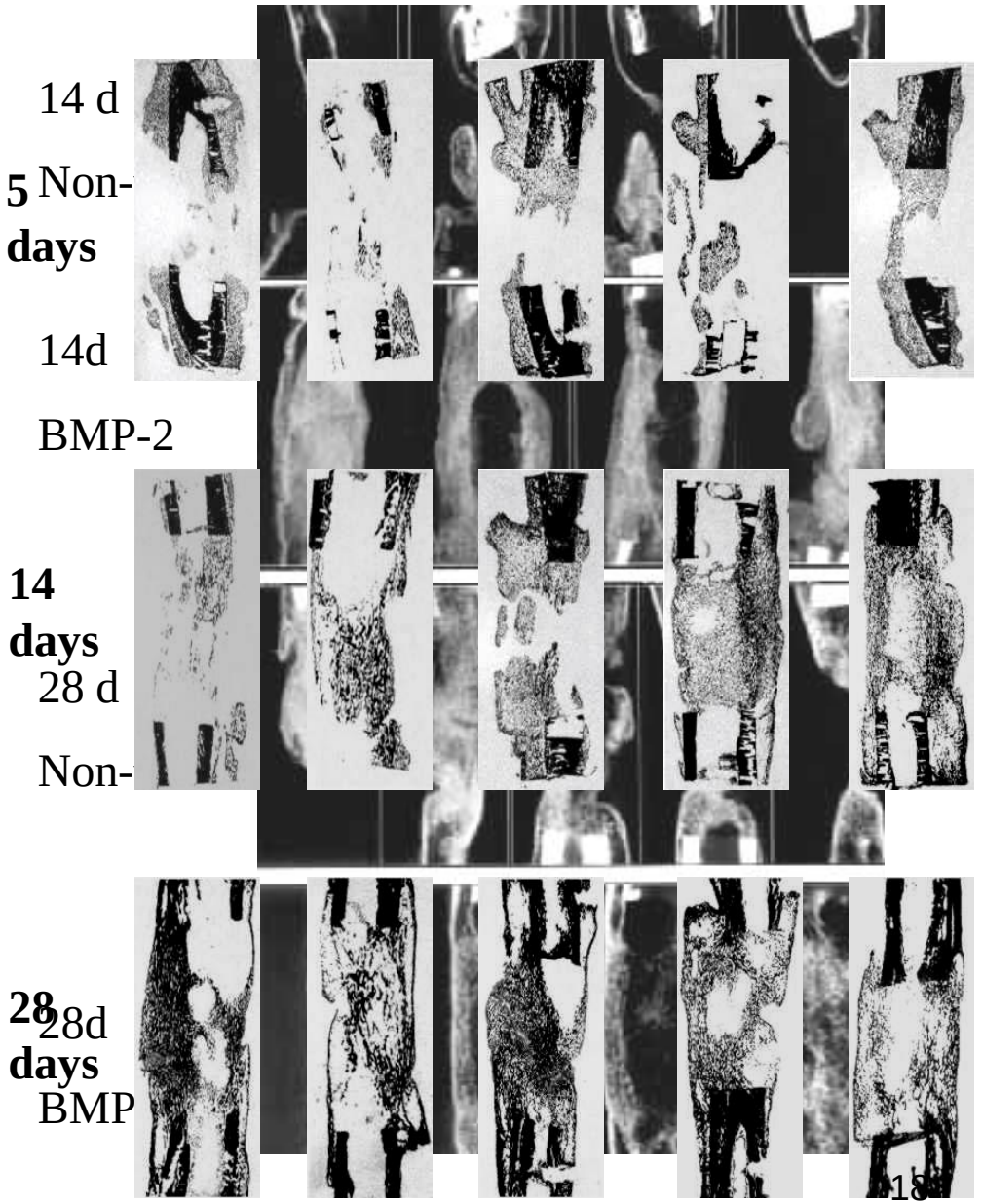
Chan, et al. Dose-depent effect of low-intensity pulsed ultrasound on callus formation during rapid DO. J Orthop Res 2006; 24:2072–9.

Enhancement Bone Formation During DO

- ***Molecular Therapy***
  - ***•rhBMP-2***

- **A latency period 7 days**
- **Tibiae lengthened 2 cm over a period of 10 days**
- **Rate: 2 mm/day**
- **Rhythm: 2 increments/day**
- **rhBMP-2 (75 µg) was administrated to the gap**
- **Placebo controls**

Li, et al. rhBMP-2 in Distraction Osteogenesis. JOR 2002; 20: 658-67.

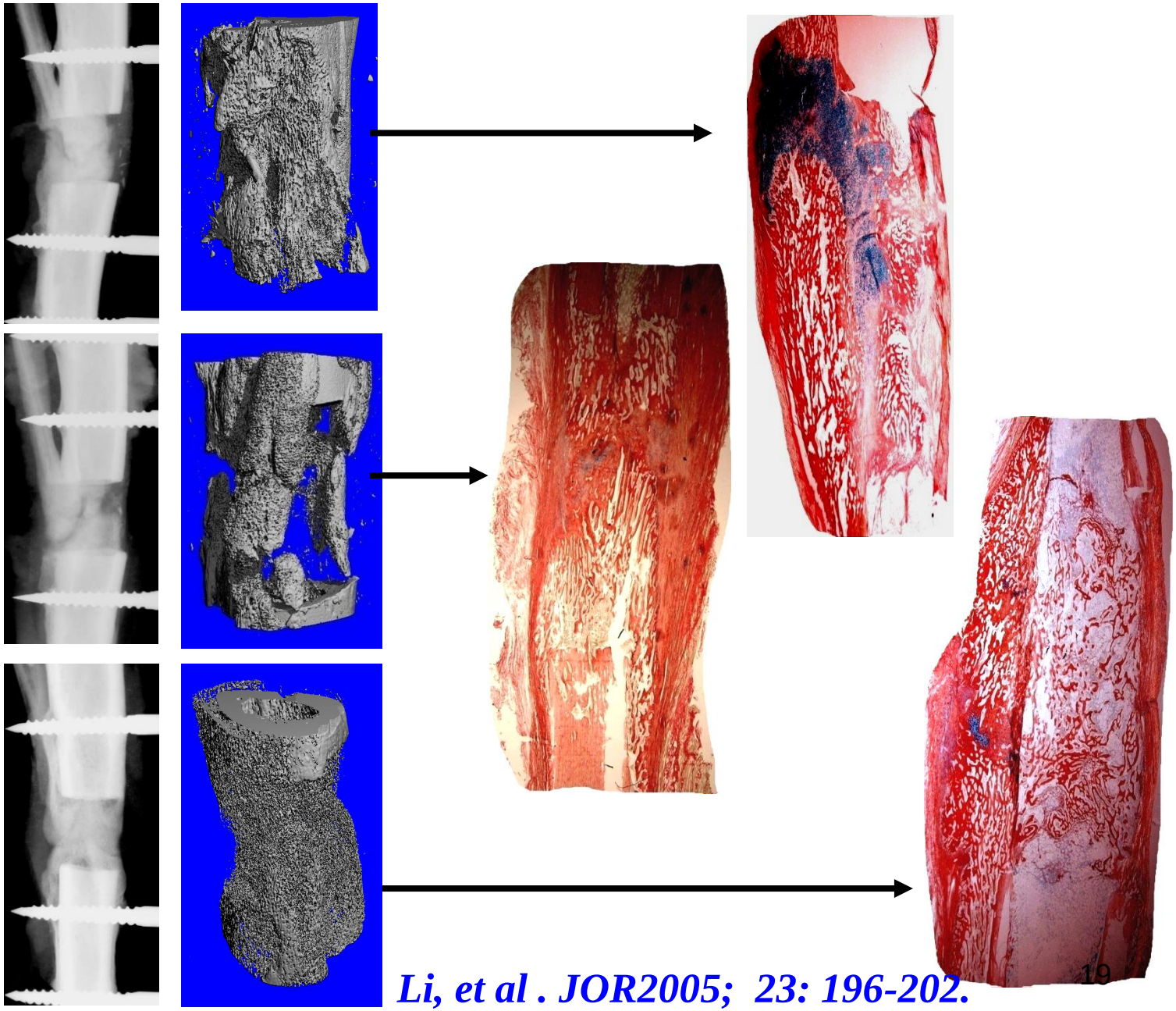


Thrombin-related peptide TP508 enhanced bone consolidation

TP508 300 µg injection twice

Dextran gel Inject Control

Dextran gel with microspheres 300 µg TP508 injection once



Li, et al . JOR2005; 23: 196-202.

Clinical Applications of Distraction Osteogenesis Techniques

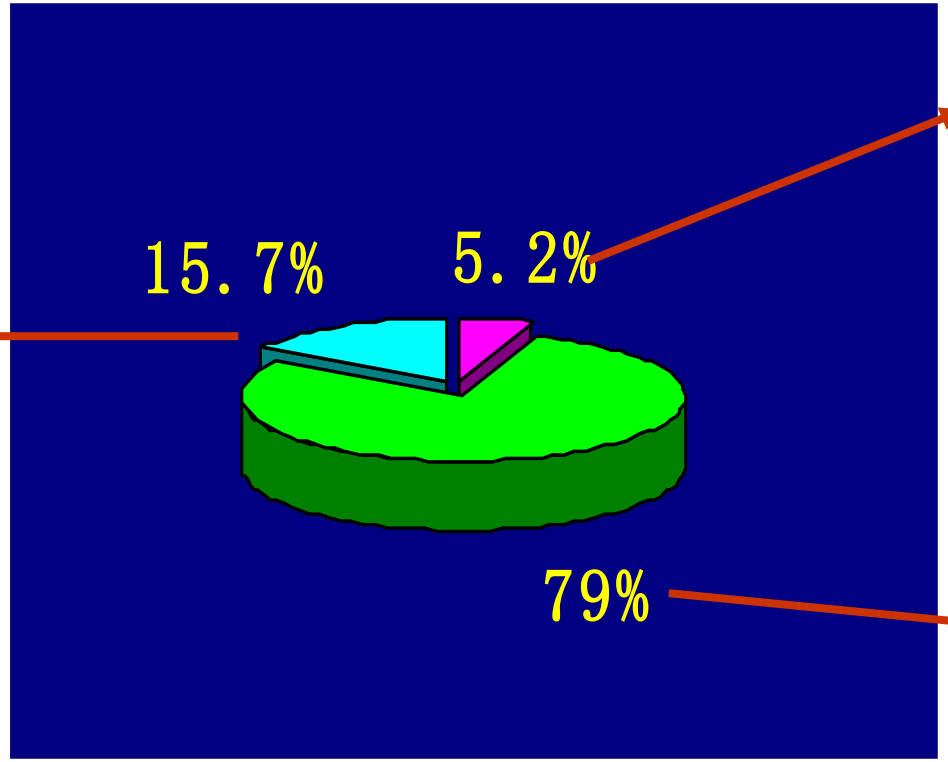
- Limb reconstructions…
- Cosmetic lengthening
- Spine deformity correction
- Vascular diseases managements
- Others…

北京骨外固定技术研究所所长,北京广济医院院长 夏和桃 主任医师

Dr. Xia He-Tiao, MD, Director of Beijing Institute of External Fixation Technology, Chief of Beijing Guangji Orthopaedic Hospital

Over 16,000 patients underwent leg lengthening surgery in Guangji Hospital by Dr. Xia's team over the last 10 years, overall successful rate for cosmetic lengthening is 99%.

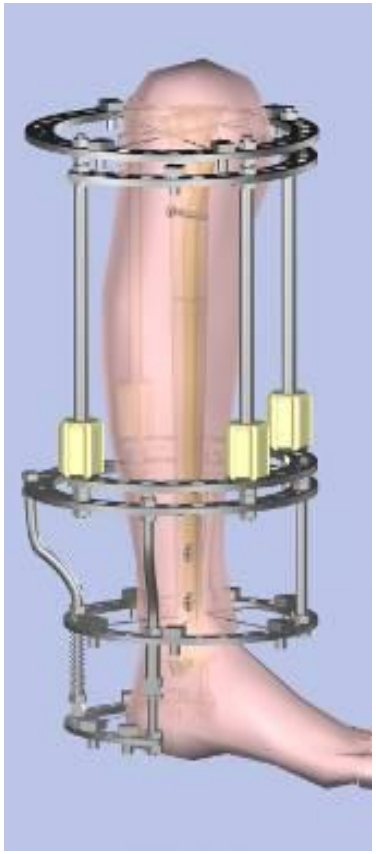
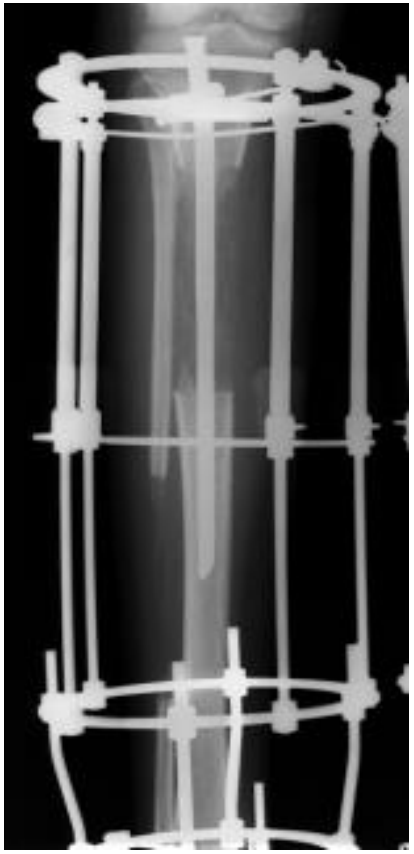
Cosmetic



Dwarf

Short Stature

Modified Ilizarov lengthener combined with interlocking nails

www.leg-lengthening.com

Functional Exercise

www.leg-lengthening.com

Functional Exercise

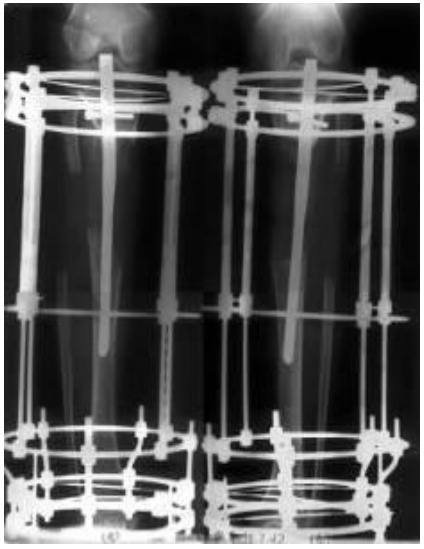
Case 1: **Male. 21 years, height 1.20 m、bilateral tibial lengthening for 18 cm.**

Before Treatment

After First Treatment
18 cm tibial lengthening

After 2nd Treatment
8 cm femoral lengthening

Case 2： **Short stature with knee inversion. Body height was 146 cm before increasing height 9 cm . Deformity was corrected, patient was followed up two years after treatment with good leg function.**



Case 3：　Short stature with knee inversion and body height 146 cm before lengthening 9cm . Deformity was corrected and leg function is satisfactory .

Case 4：**Leg-lengthening was performed twice in this patient of short stature. 7 cm at first time , 4 cm at second time in the tibiae.**

Case 4. The new bone at second lengthening was formed very well at the regenerate following the first lengthening.

Case 5: Ms. Dong Mei, Female, 22 years, "man-made beauty" of South-East China. She was 148 cm, had received tibial lengthening of 12cm to 160 cm.

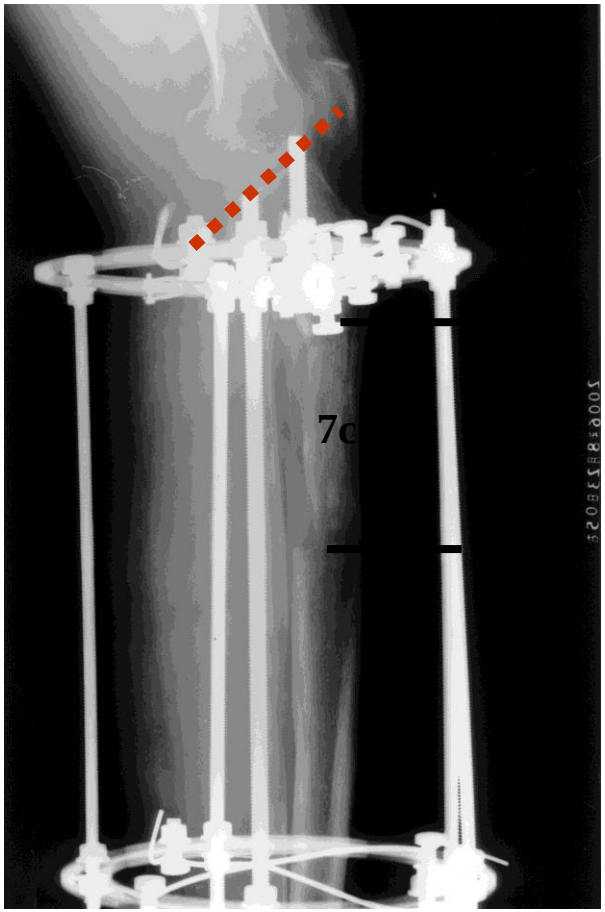
www.leg-lengthening.com

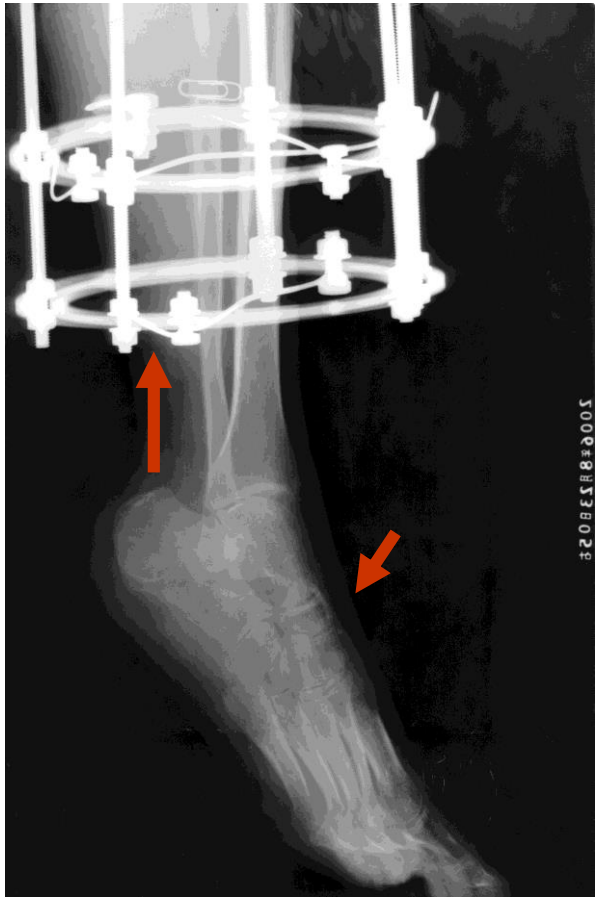
Bilateral tibial lengthening 12 cm after the external fixators were removed.

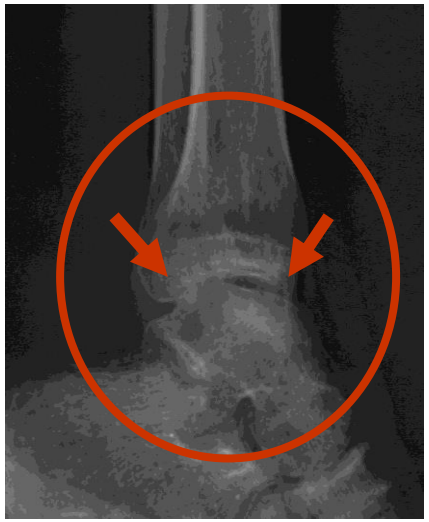
Functions were fully recovered after 1.5 years.

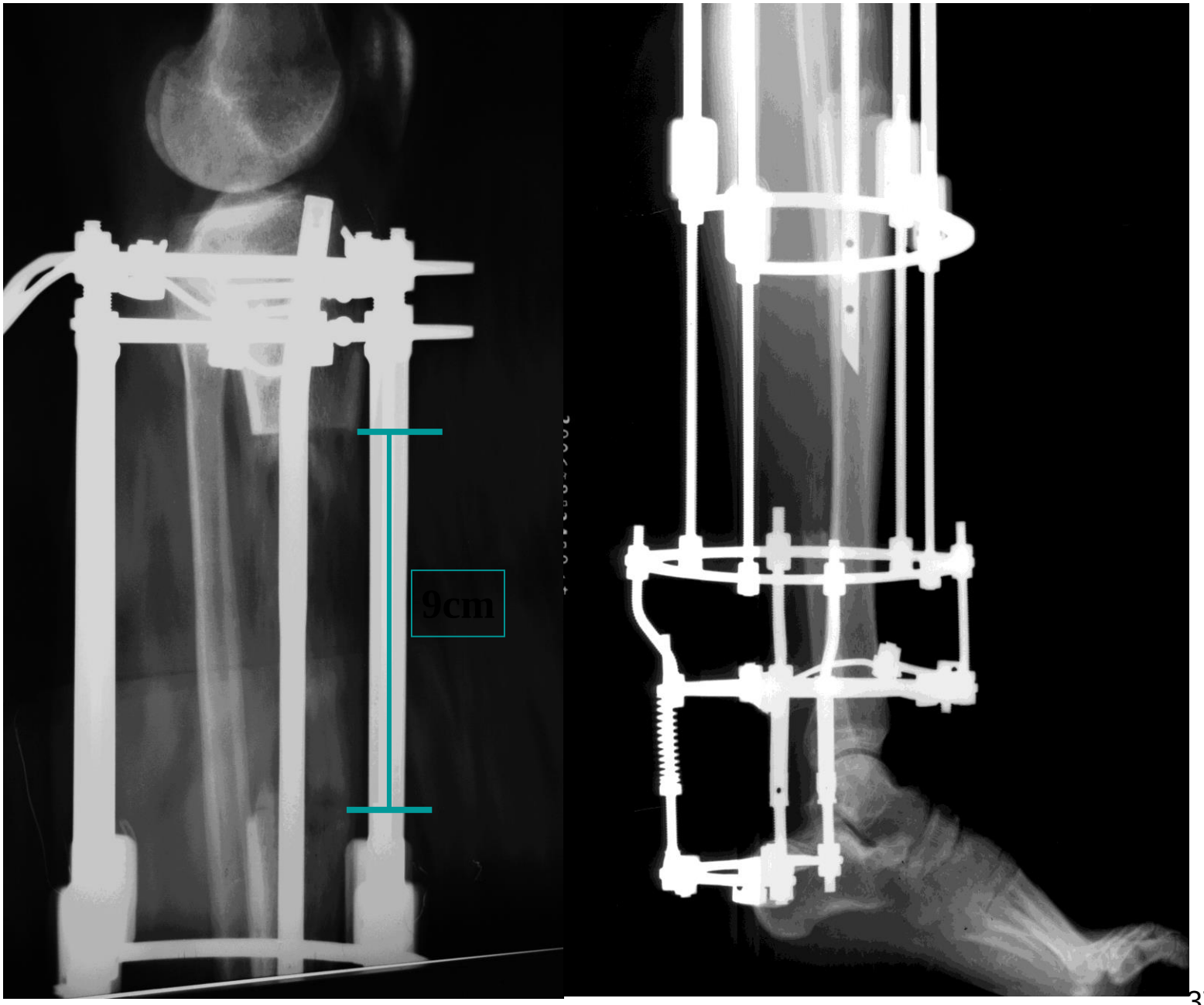
www.leg-lengthening.com

The common problems encountered using classical Ilizarov techniques for leg-lengthening over 5 cm: Foot dropping and joint cartilage damages.







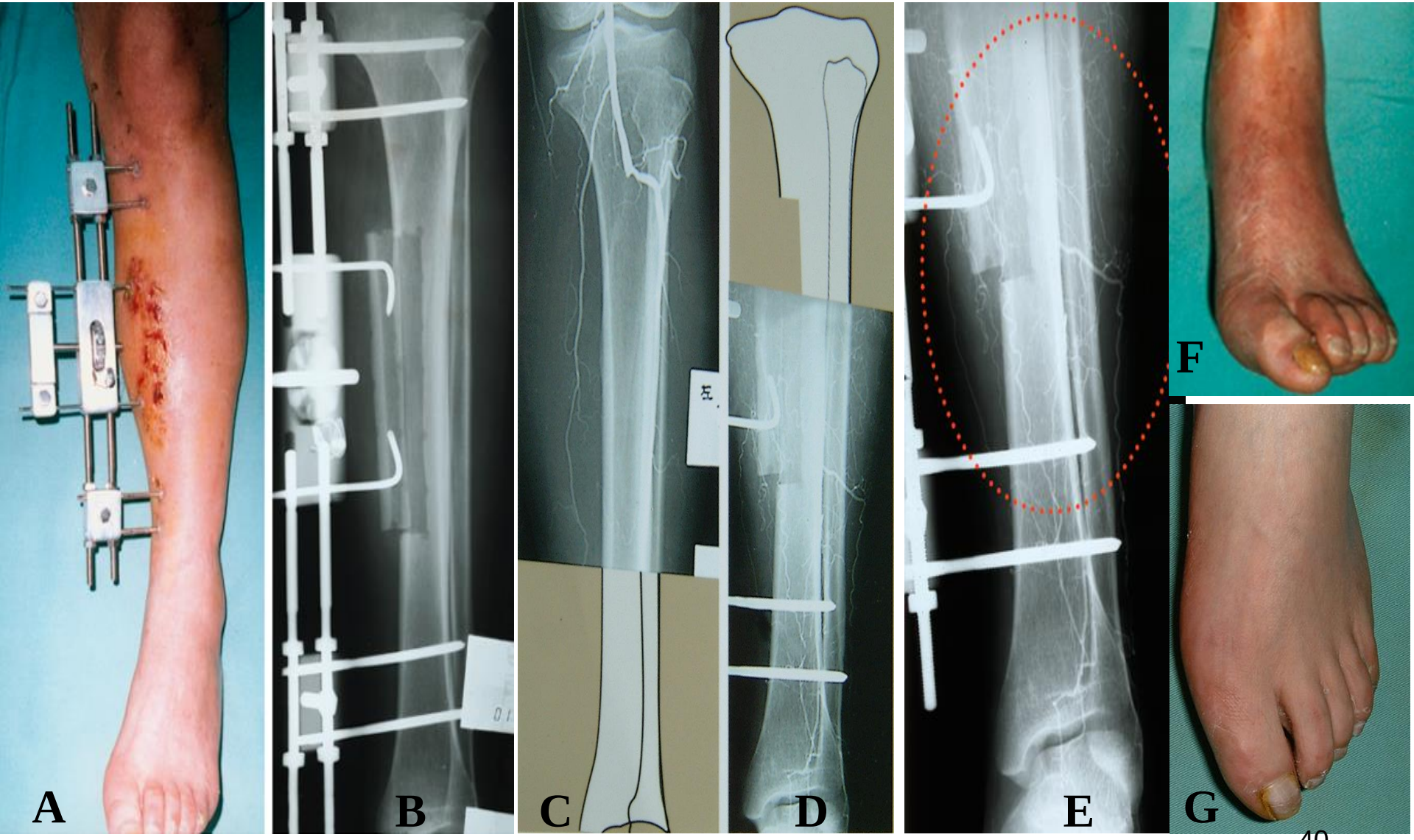

9cm

We can make giants !

New Clinical Applications of DO
Spine Deformity Correction

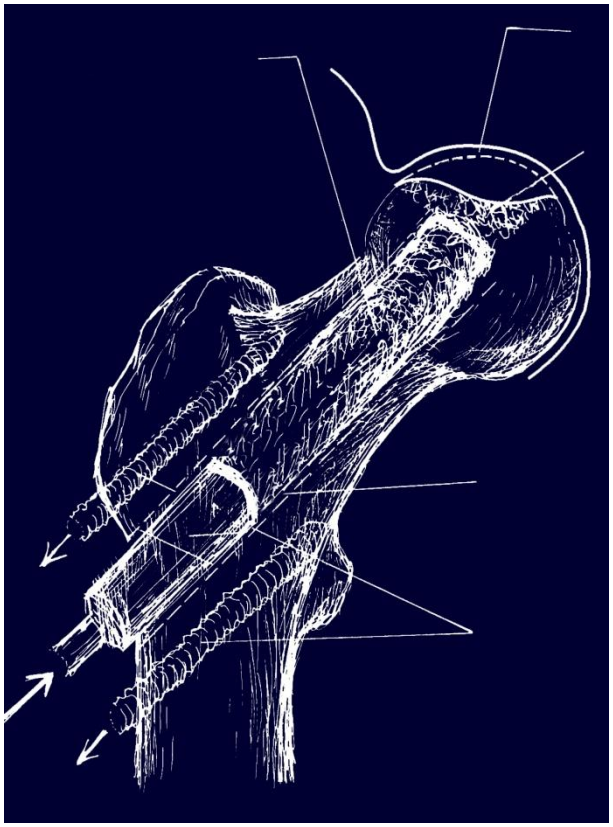
Photograph taken at Russian Kurgan Ilizarov Centre, with permission, by Dr. G Li

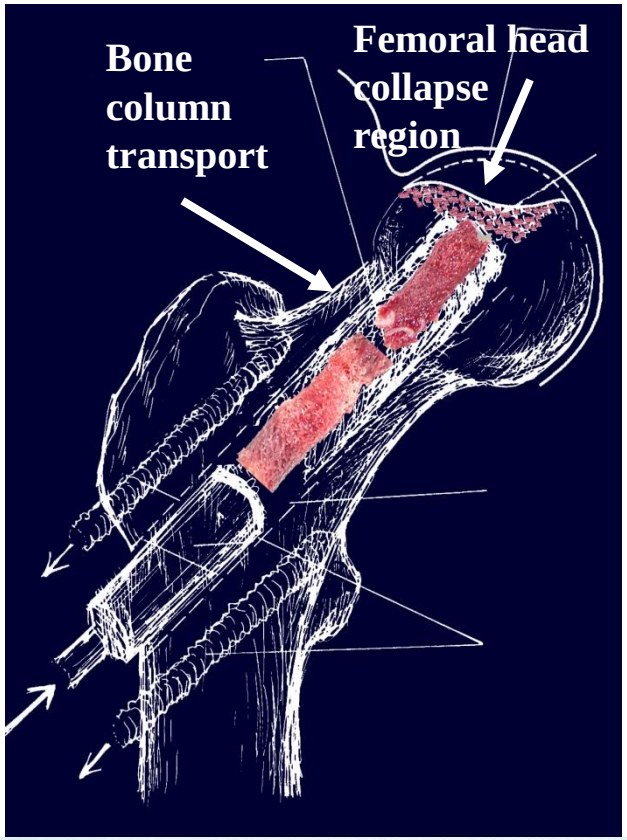
New Clinical Applications of DO
Treatment of Peripheral Vascular Disease



Courtesy of Dr. Long Qu, Beijing Bone Lengthening and Transport Centre, China.

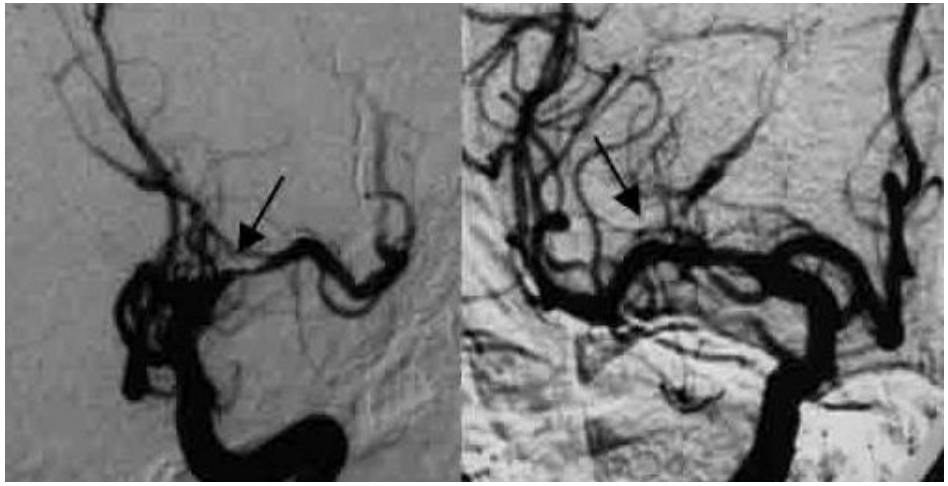
New Clinical Applications of DO
Treatment of Avascular Femoral Head Necrosis





Courtesy of Dr. Long Qu, Beijing Bone Lengthening and Transport Centre, China.

New Clinical Applications of DO
Treatment of Cerebrovascular Disease/Stroke

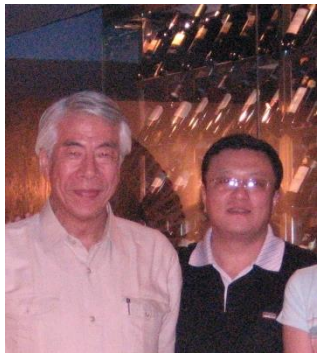


Photograph taken at Russian Kurgan Ilizarov Centre, with permission, by Dr. G Li

People who perfected DH techniques








Italy, Russia, Japan, USA, Germany, China…..