

Fractures – current view

Rozkydal, Z.

I. Orthopaedic clinic

Medical faculty Brno

1. The strength of bone
2. Diagnosis
3. Healing
4. Problem of osteoporotic fx
5. Secondary prevention
6. Medication and healing of fx

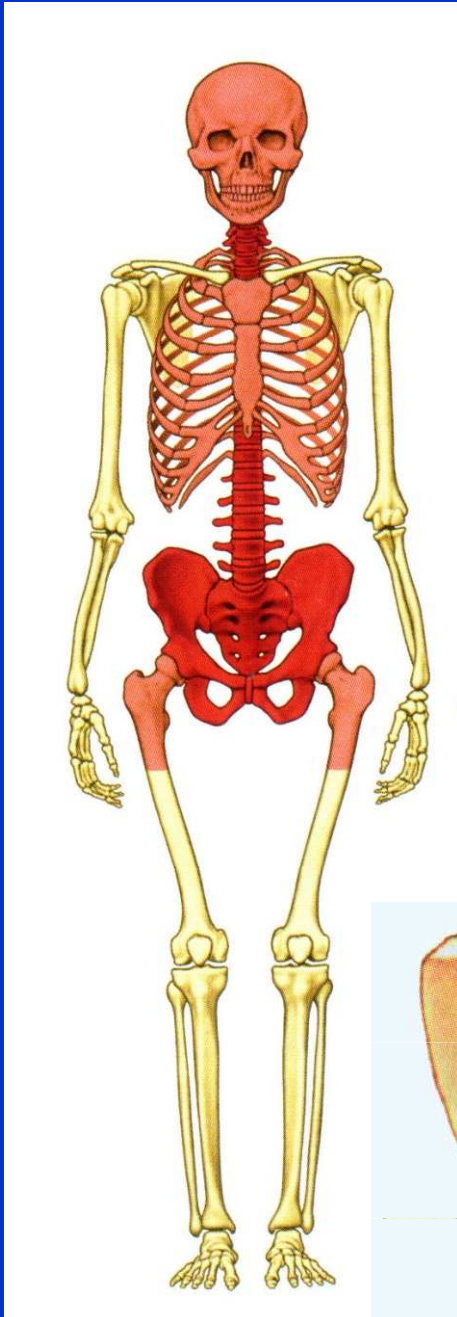
1. The strength of bone

Skeleton

15 % of body weight

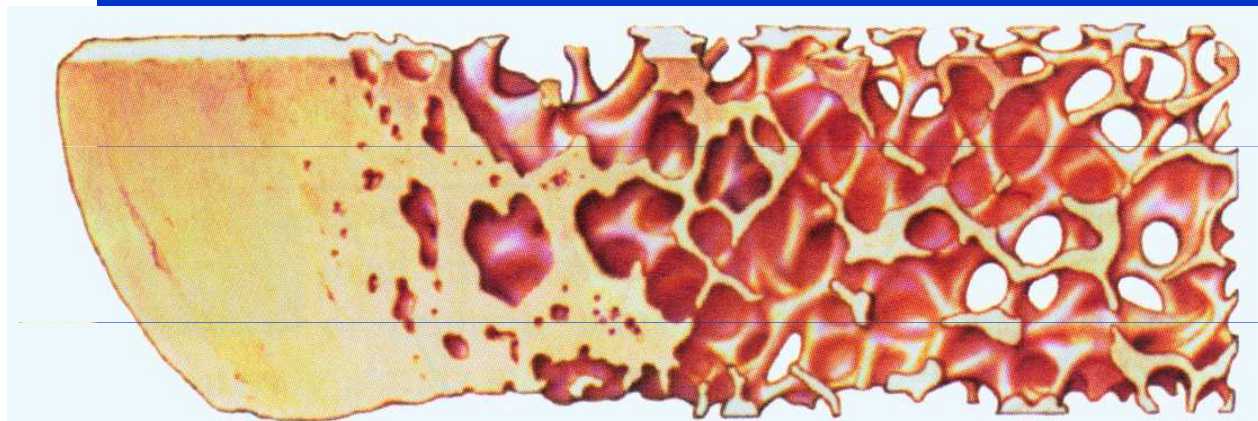
Cortical bone 80 %

Trabecular bone 20 %



80 %

20 %



Cortical bone, Havers systems, osteon

Tvar válce

Průměr 200 μm

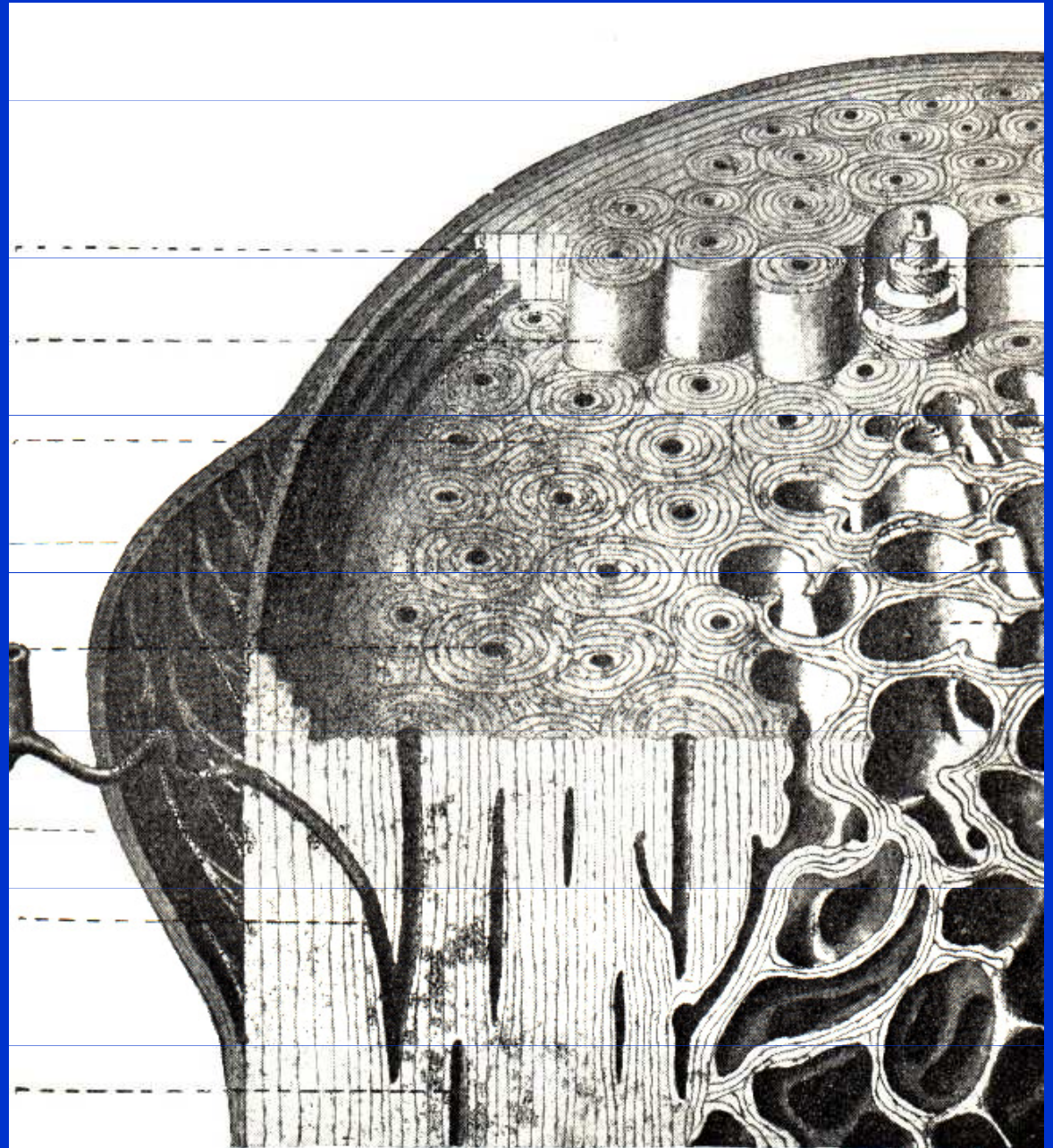
Délka několik mm

Koncentrické lamely

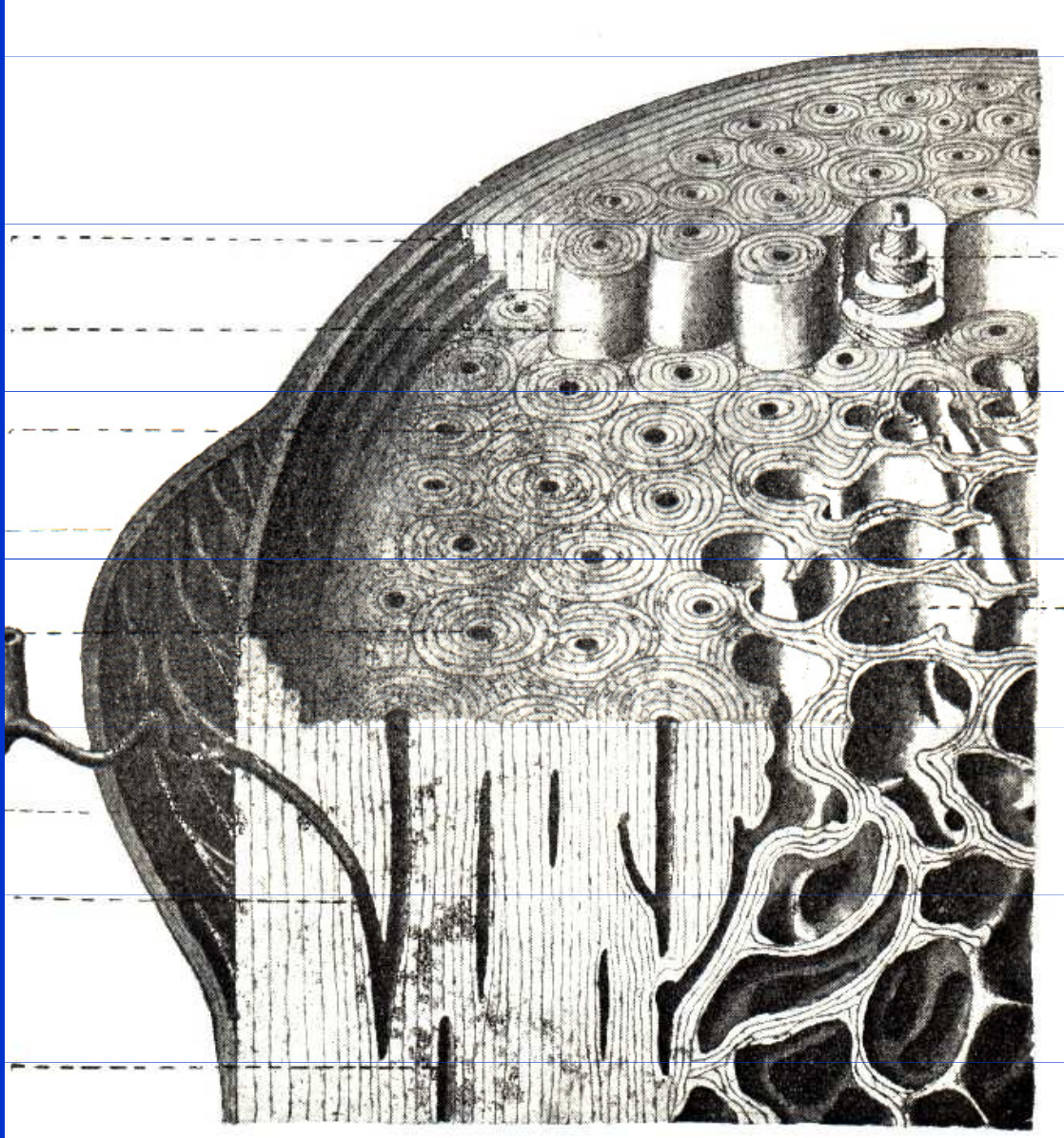
5-20 lamel

Centrální kanál

Orientován ve směru
podélné osy kosti



Cortical lamels



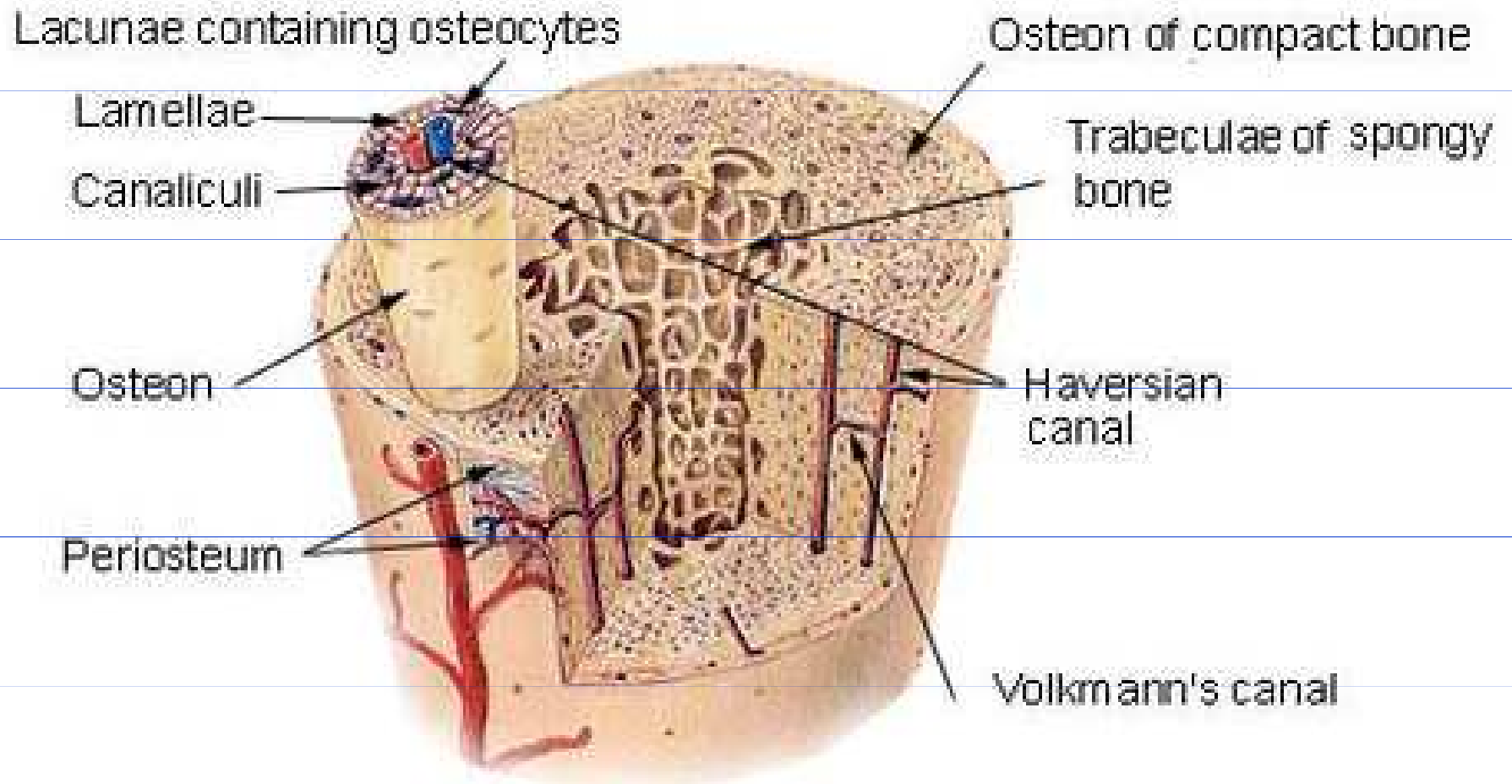
Lamely Haversovy

Lamely vmezeřené

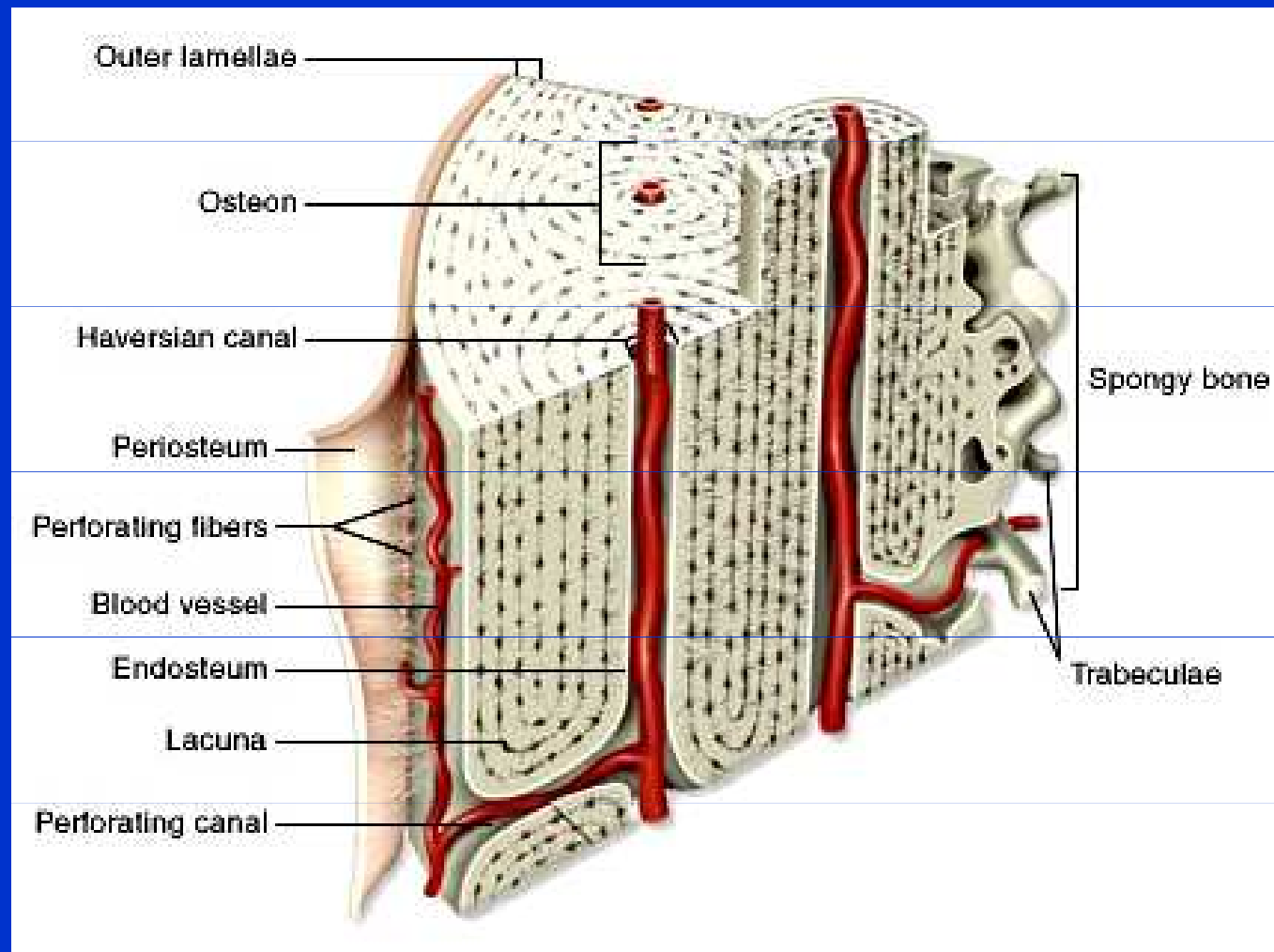
Lamely povrchové

Osteon je obklopen
mineralizovanou matrix

Osteon



Osteon



Volkmannovy kanálky jsou příčné

Přivádějí cévy a nervy z periostu k H. kanálkům a k endostu

Osteon

Haverský kanál

Lamely kostní

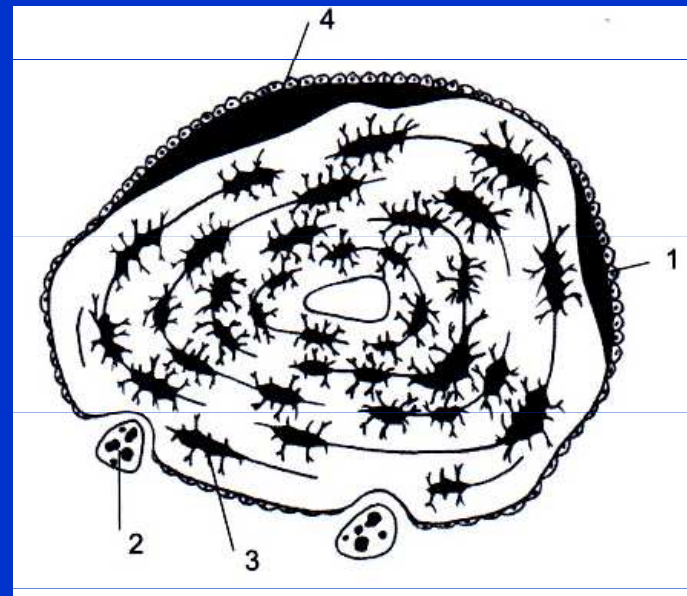
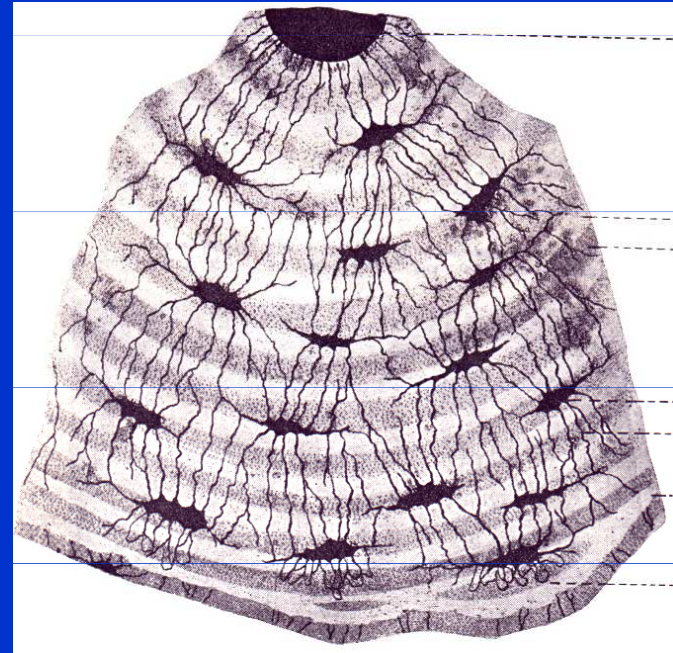
Canaluculi ossium

Osteoblasty

Osteoklasty

Osteocyty

Kostní matrix



Periosteum

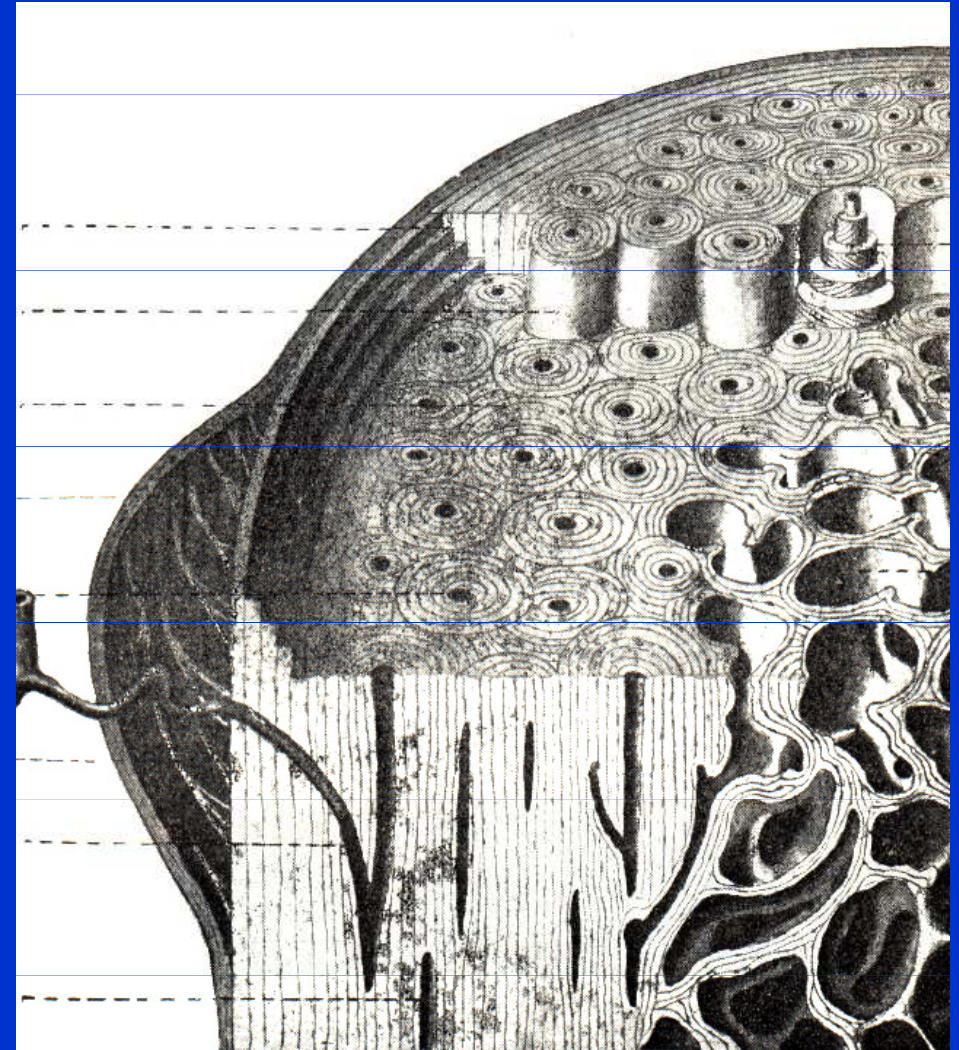
Zevní plášt'ové lamely
probíhají rovnoběžně s povrchem

Periost:

Zevní vrstva fibrózní- tuhé vazivo

Vnitřní vrstva - fibroelastická

Kambiová vrstva- osteoblasty



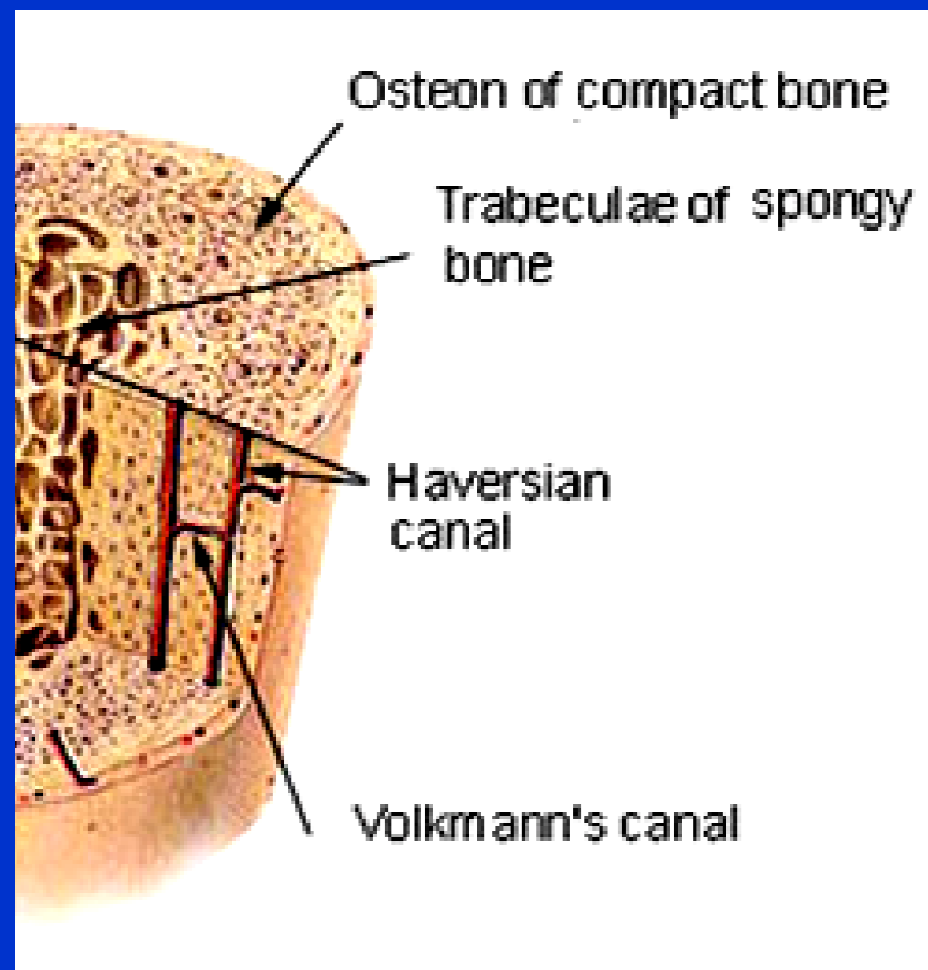
Endosteum

Vnitřní plášťové lamely
ohraničují proti kostní dřeni

Endost:

- tenká vrstva
- zhuštěná vrstva stromatu
kostní dřeně

Obsahuje buněčné elementy



Trabecular bone

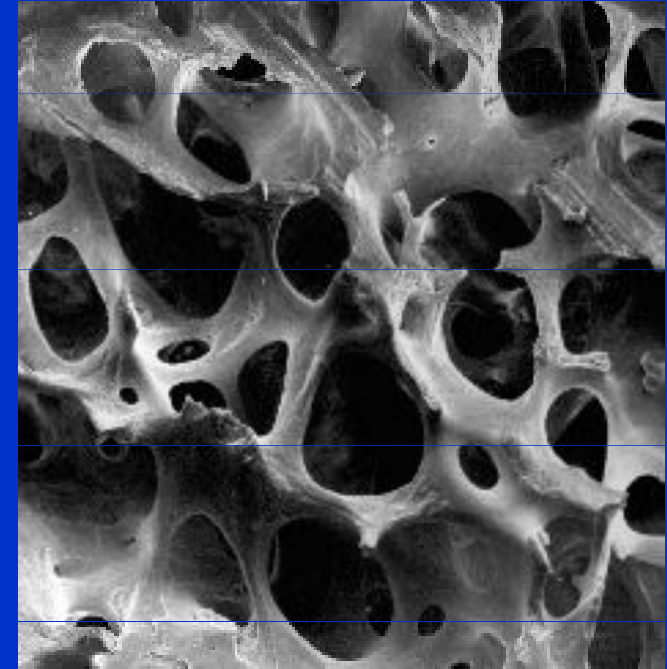
Základní jednotka:

Kostní ploténky (trámce)

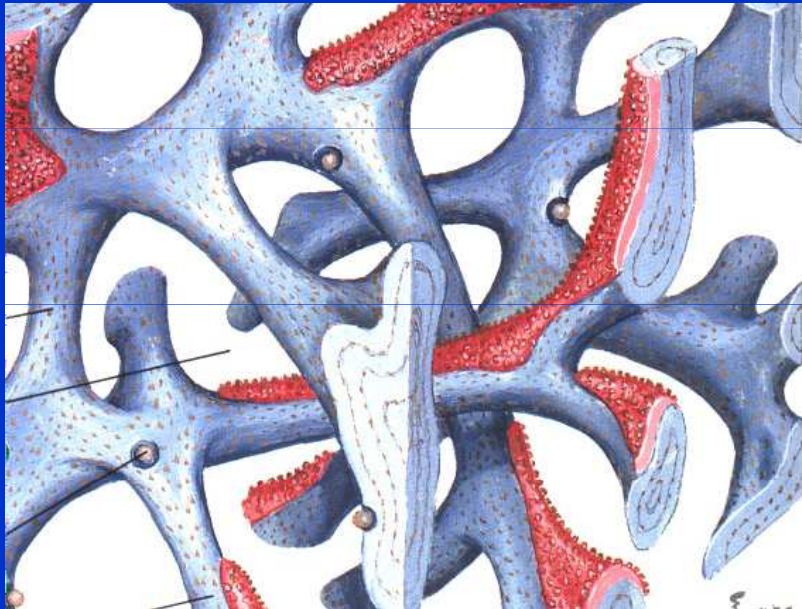
Délka 1mm

Šířka 50 μm

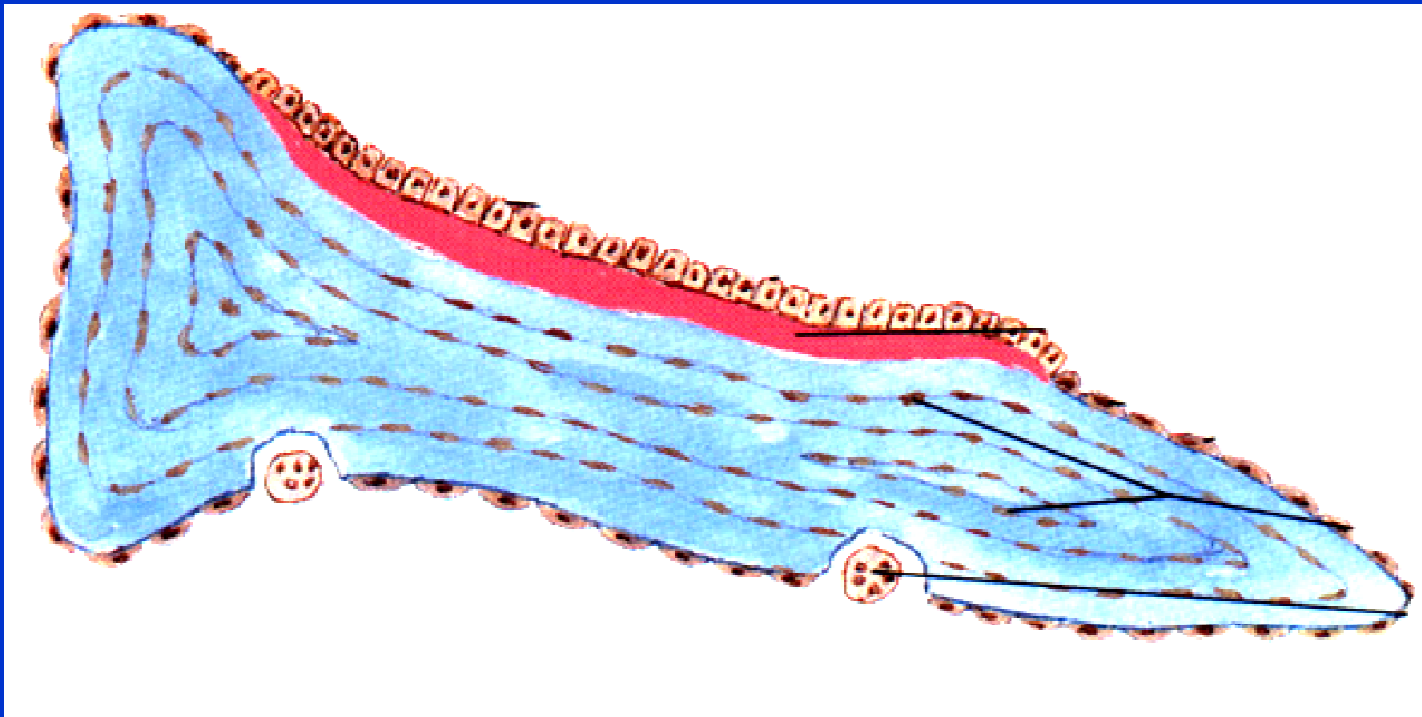
Trámce obsahují
paralerně uspořádané lamely



Trabecular bone



Kostní trámce:
Osteoblasty
Osteocyty
Osteoklasty
Kostní matrix

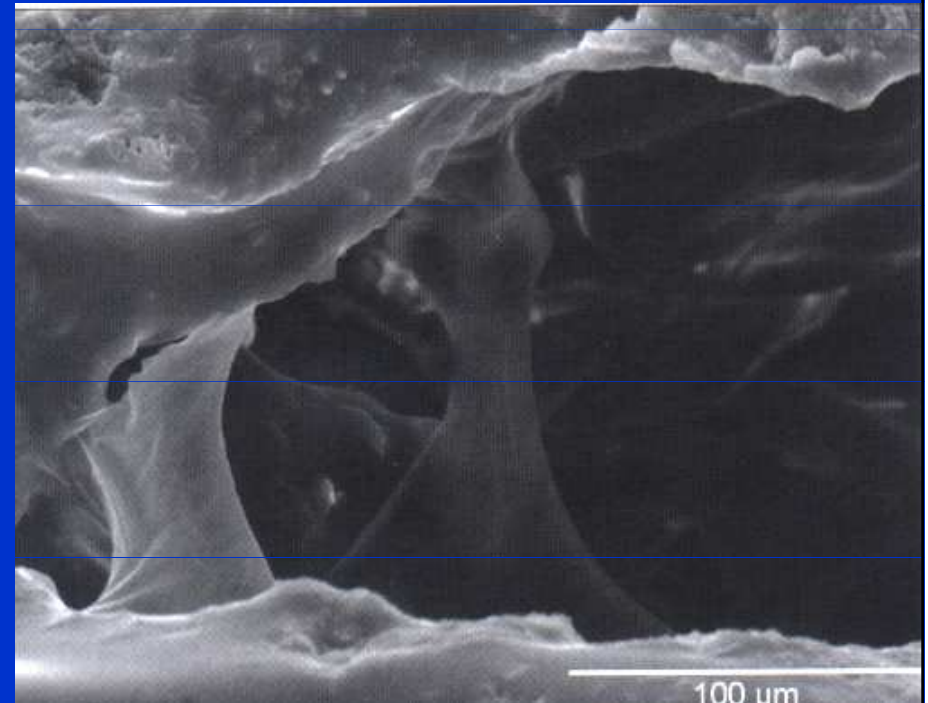


Trabecular bone

Trámce jsou spojené
příčnými destičkami a tyčkami

Mezi nimi je intersticiální
trabekulární kost

Orientace- paralelně k liniím zátěže



SEM

Obrázky v prezentaci převzaty z: Medicographia, Vol. 34, No. 2, 2012
A journey into Bone: Les laboratoires Servier, 2011.

4 stages of bone architecture

1.

2.

3.

4.

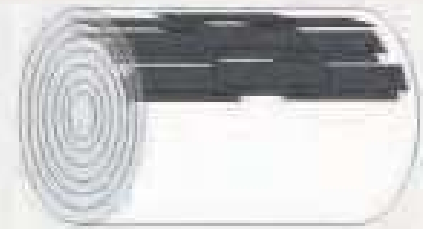
Bone composite material

Collagen
mineral

Mineralized
collagen fibril

Lamellar
organization

Bone packets



10 nm

200 nm

20 μm

200 μm

1. Collagen

Kolagen typ I.

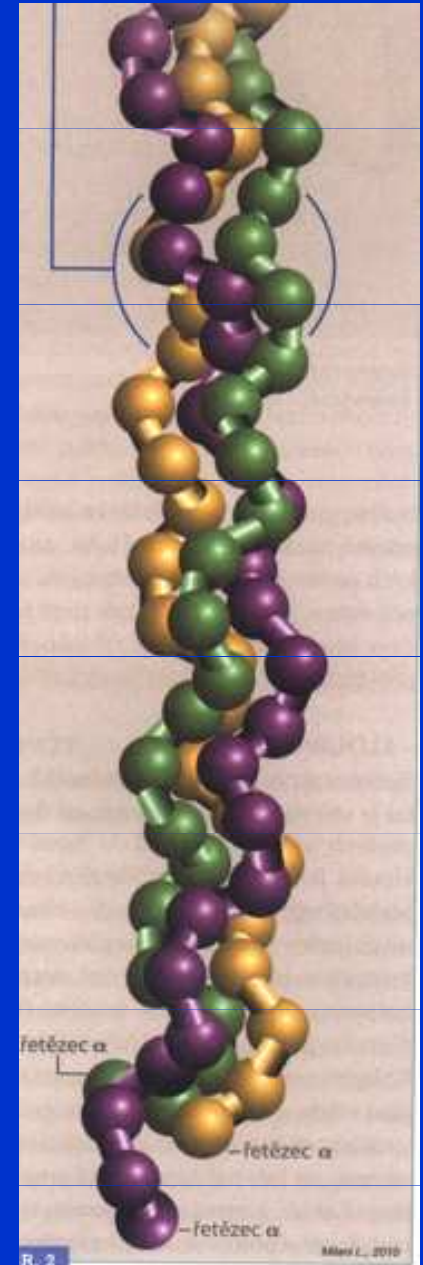
Dva $\alpha 1$ řetězec
Jeden $\alpha 2$ řetězec

Pravotočivý triple helix

Tropokolagen \rightarrow kolagen \rightarrow fibrily \rightarrow vlákna

Kolagenní matrix vytváří síť pro kostní minerál

Určuje elasticitu a ohebnost kosti



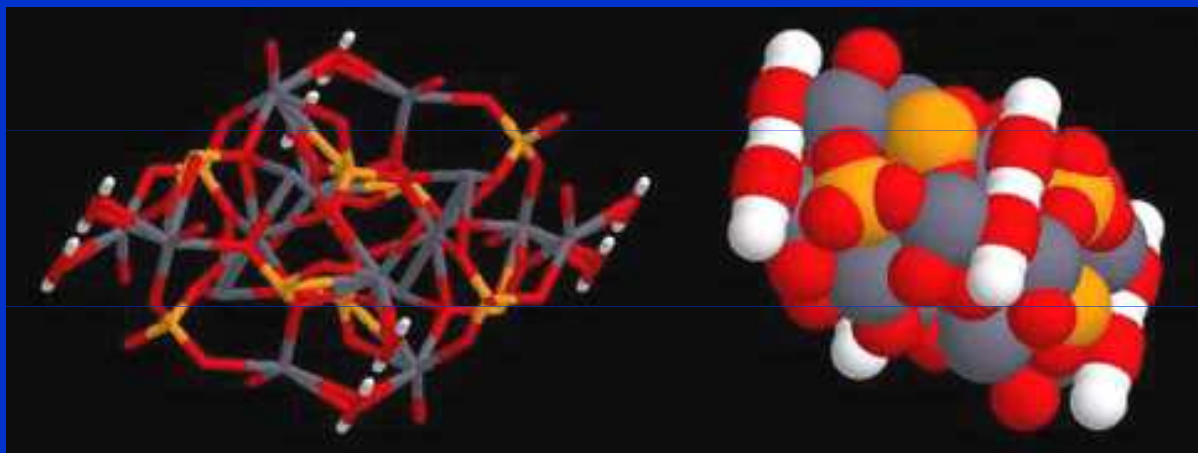
Bone mineral

Octacalcium crystal

Karbonovaný hydroxyapatit

Krystaly se tvarují do destiček

Určuje pevnost a lomivost kosti



Bone mineral



Destičky:

Tloušťka 1- 10 nm

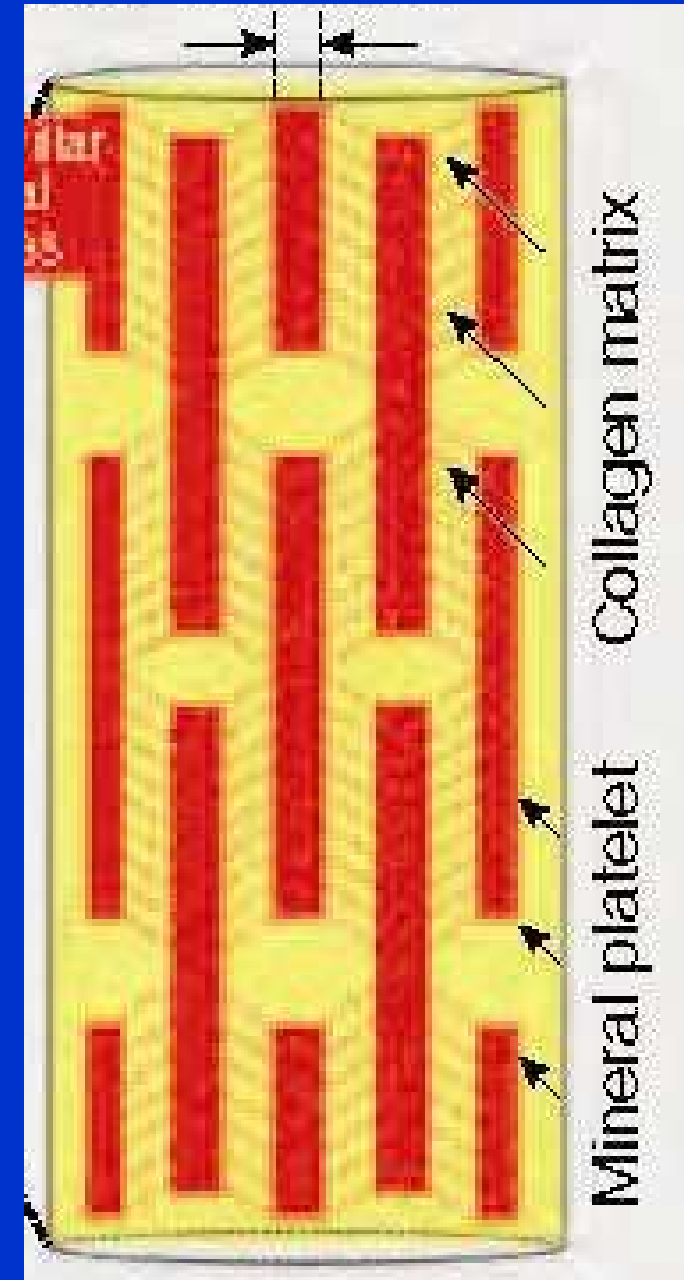
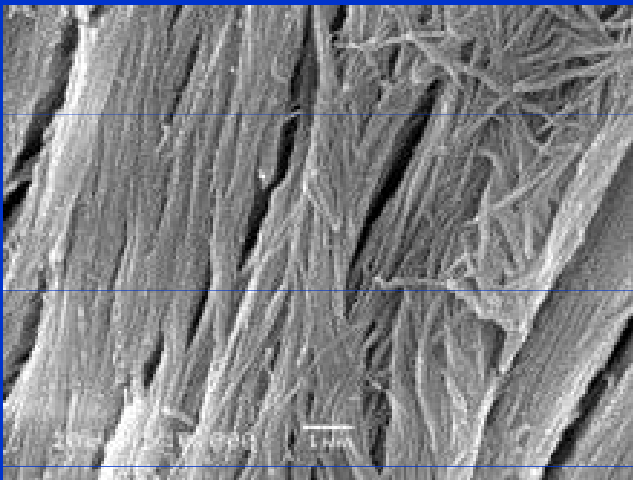
Délka 60 nm (15 – 200)

Destičky jsou tvrdé a křehké

Síla kosti je dána:

- krystalinitou apatitu
- obsahem Ca a P
- zralostí destiček

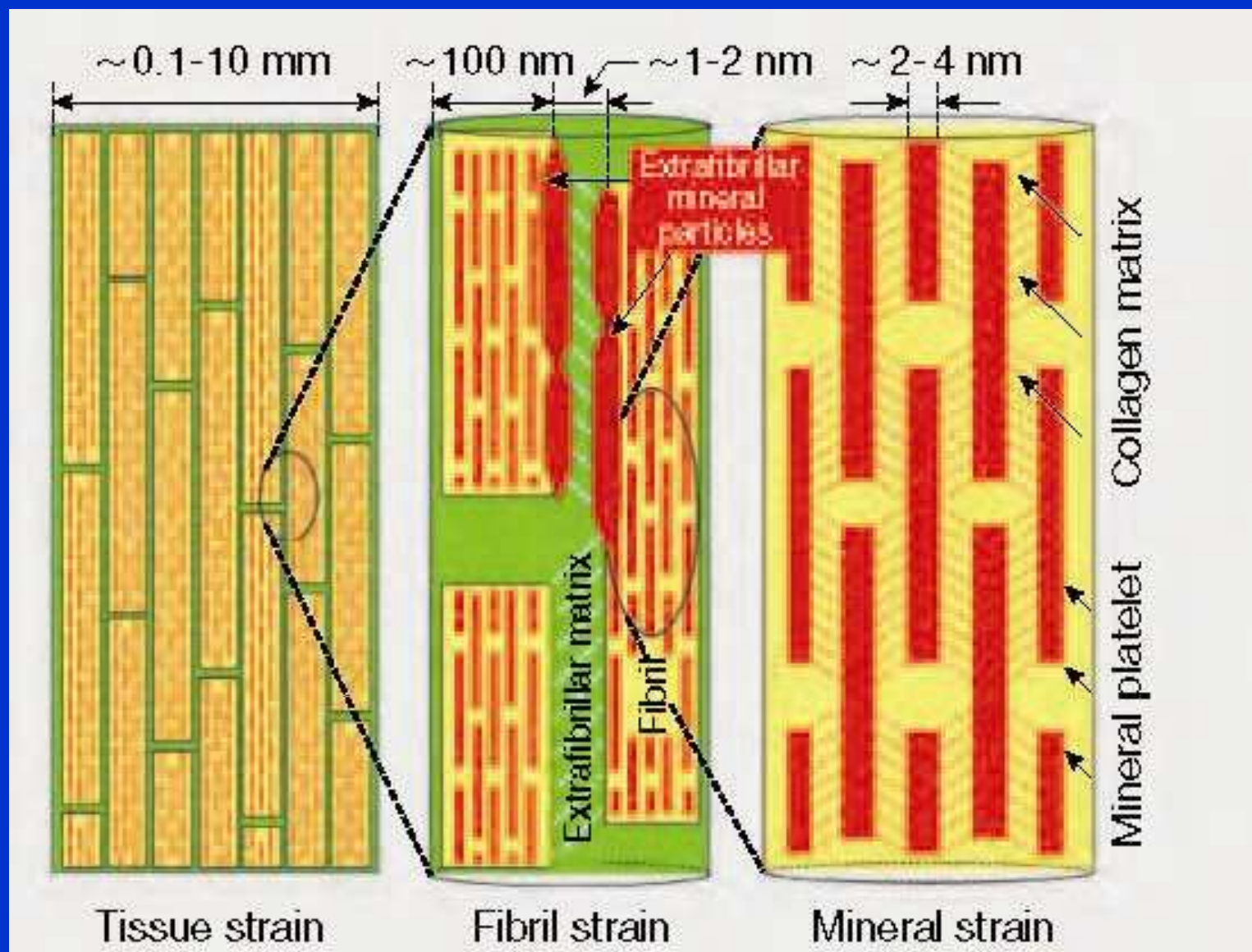
2. Mineralised collagen fibres



Fibrily- průměr 200 nm

Mezi kolagenní matrix jsou gapy 35- 67 nm

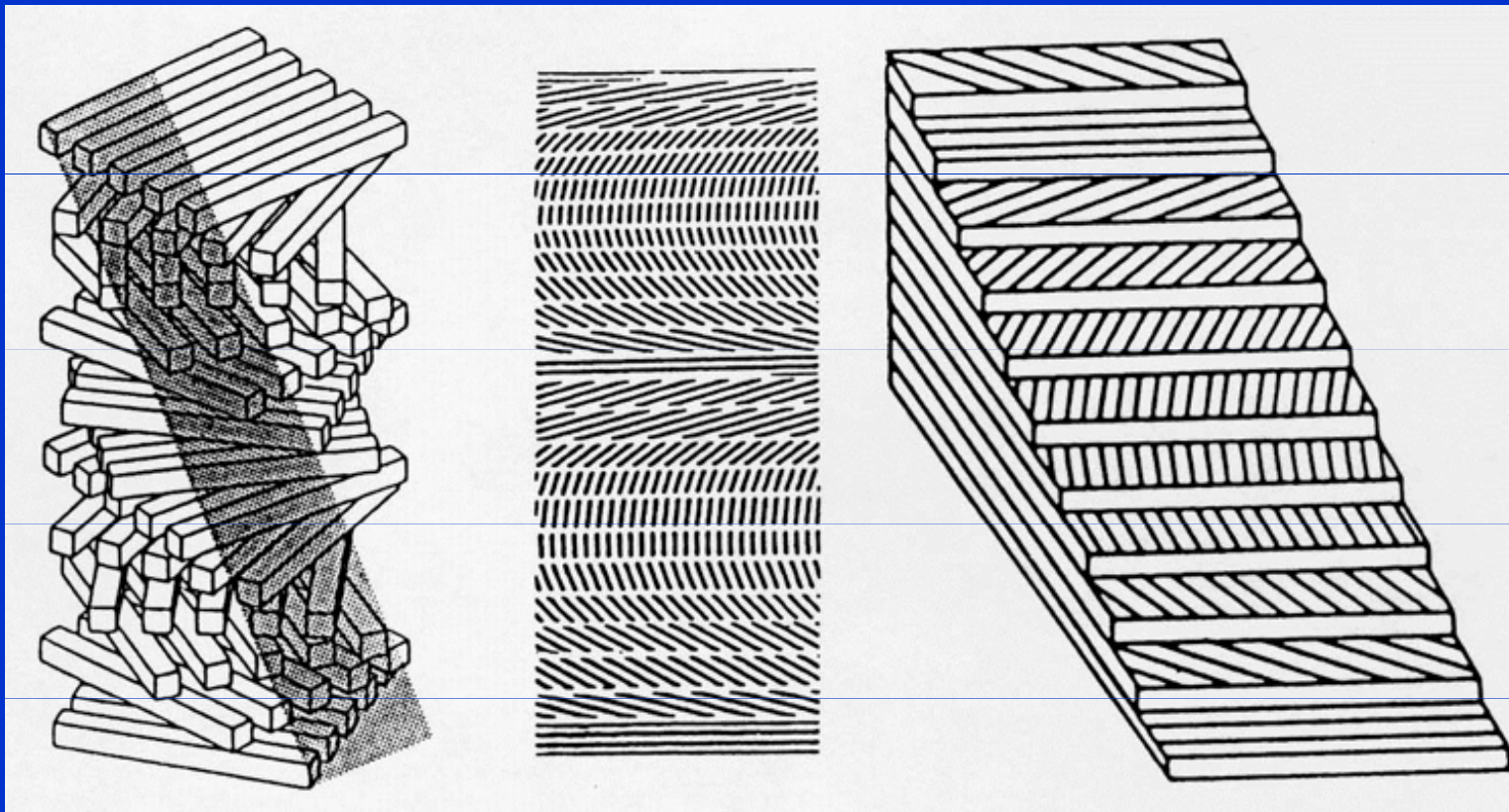
Do nich se ukládají krystaly
jako ploché destičky k sobě paralelně
a v podélné ose kolagenní fibrily



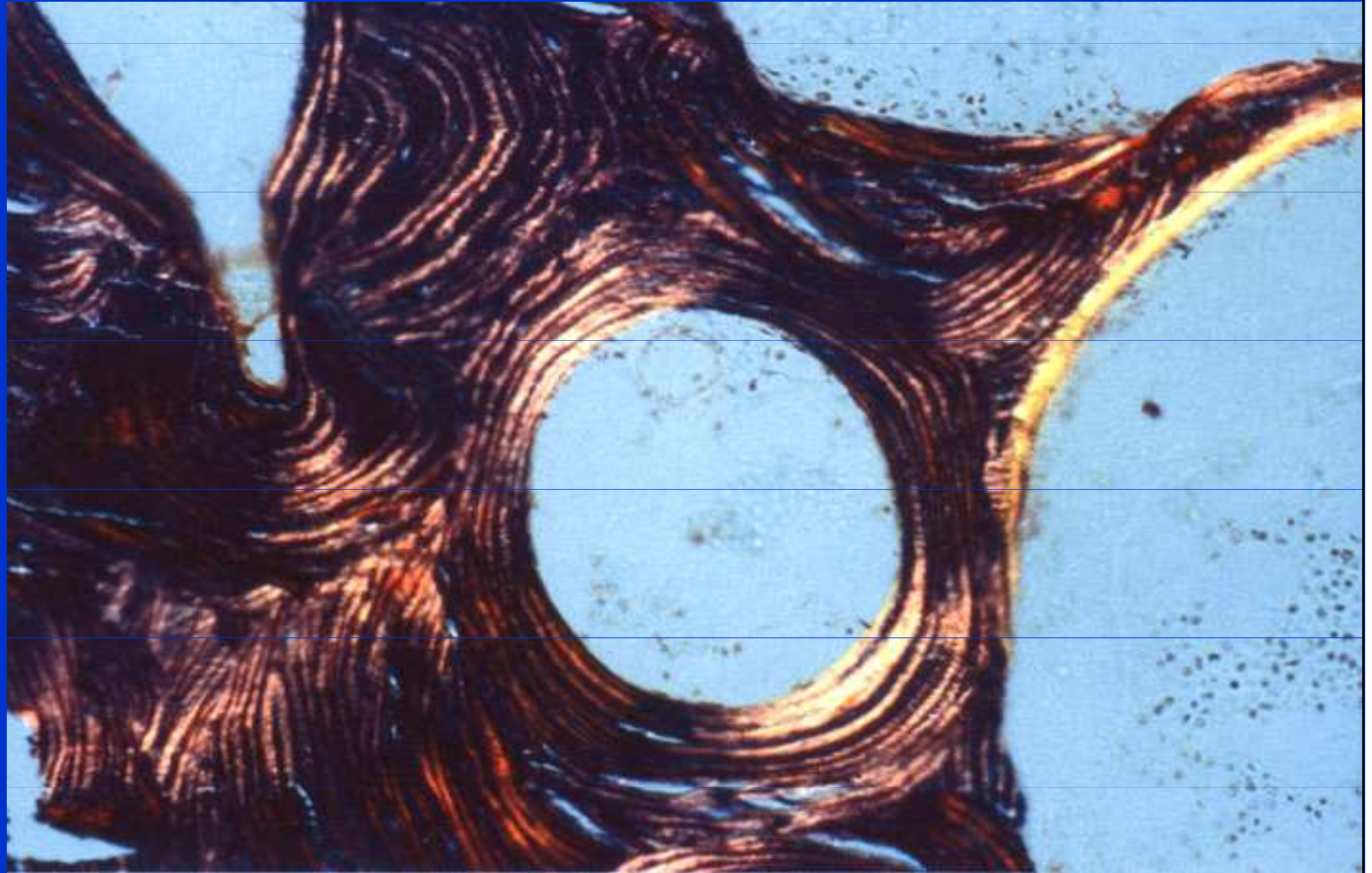
Kost- komposit kolagenních vláken a kostního minerálu
 „ mineralizované kolagenní fibrily“.

3. Lamellar architecture

Mineralizované kolagenní fibrily se spojují do lamel.
Další vrstva má vždy opačné uspořádání
jako překližka – pevnost při torzi.



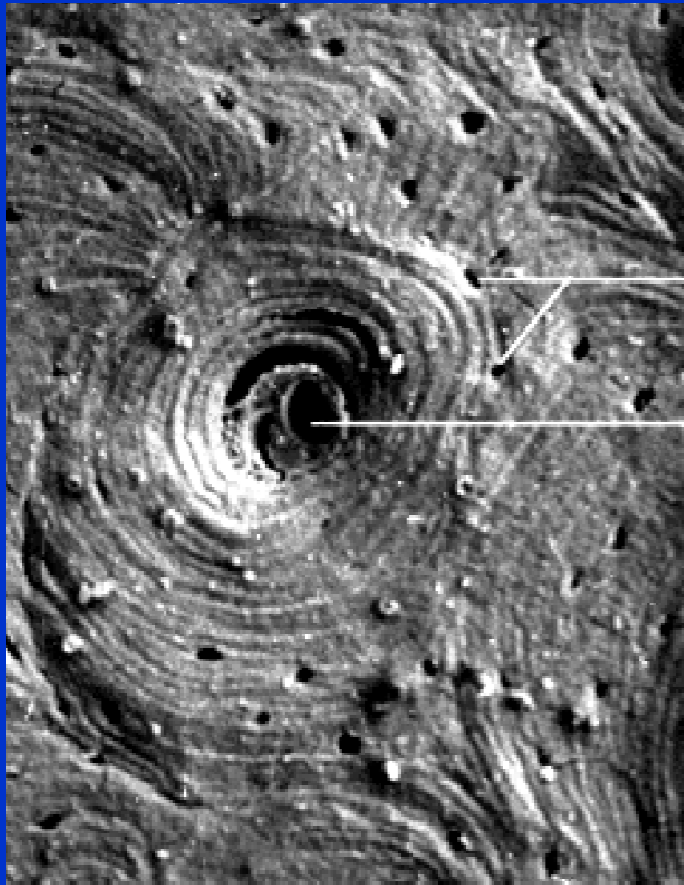
Lamelae



Trabekulární lamely - paralelně, v polooblouku (hemiosteon)

Kortikální lamely - koncentricky (osteon)

Lamellar bone



Lépe organizovaná, mechanicky pevná
Tvoří se pomalu- depozice kolagenních vláken 1-2 $\mu\text{m}/\text{den}$
- určuje rychlost tvorby kostní matrix

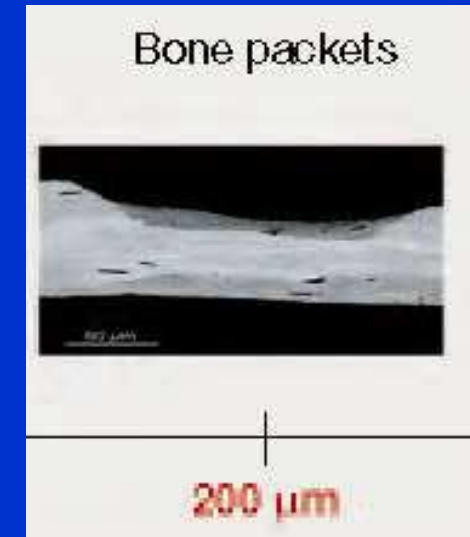
Woven bone



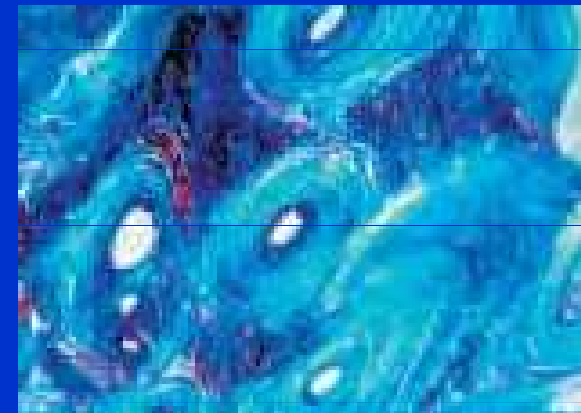
Nahodilé uspořádání kolagenních vláken
Mechanicky je slabá
Tvoří se rychle, např. při hojení zlomenin

4. Bone packets

BSU- Basic structural unit



Kortikální kost- osteony



Trabekulární kost- trabekulární svazky
„trámce nebo hemiosteony“



Composition of bone

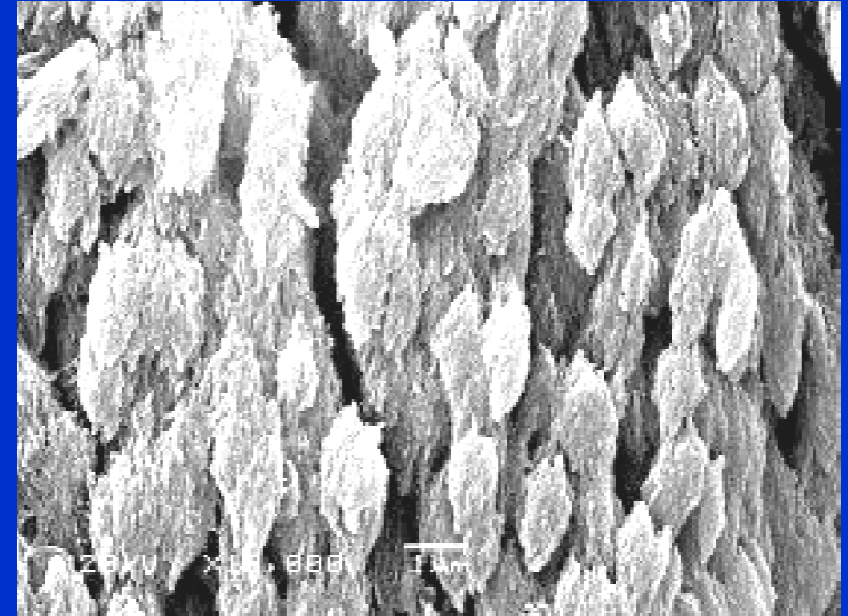
Bone matrix

Anorganic part - 50 %
(bone mineral)

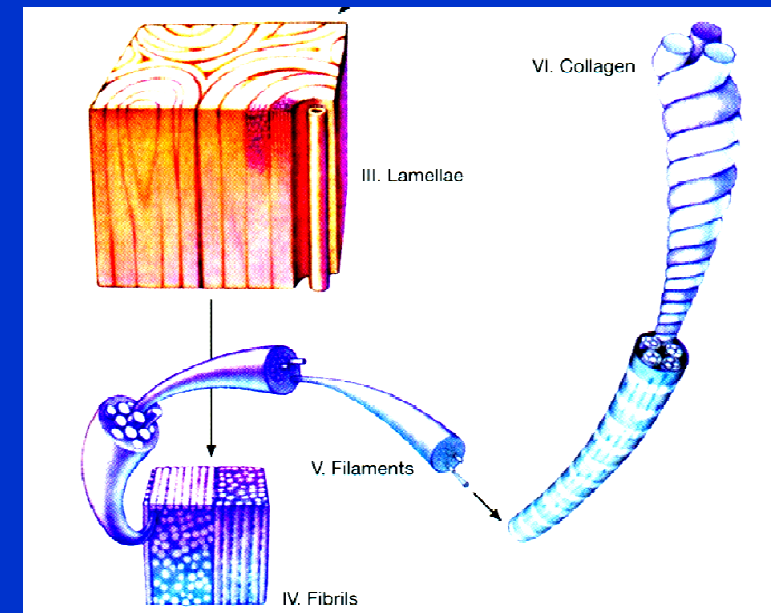
Organic part - 25 % (osteoid):
90 % collagen type I
10 % other proteins

Cells

Water binding on collagen
and mucopolysacharids- 25 %



HA krystaly



Kolagen typ I.

The strength of bone

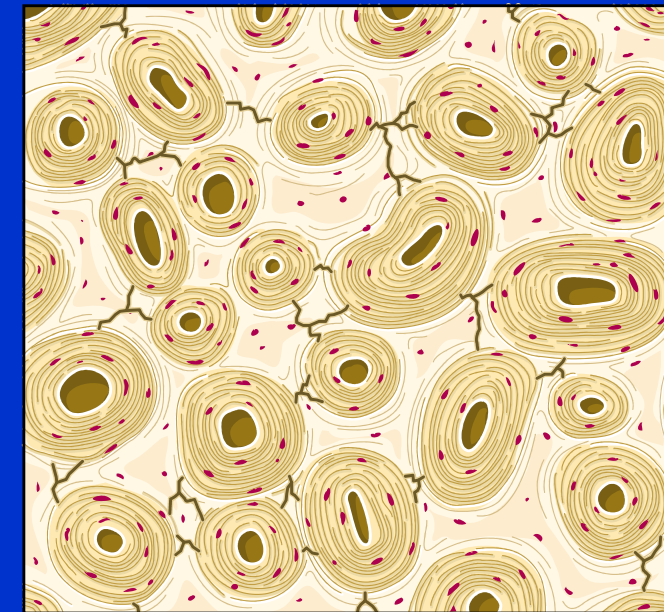
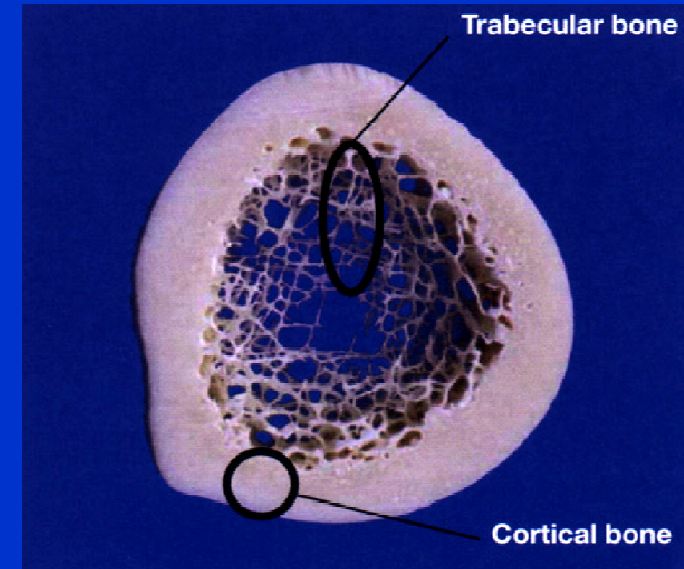
Kvalita kortikální a trabekulární kosti,
kolagenu a kostního minerálu

Denzita podle BMD predikuje
60-75 % mechanické pevnosti kosti

Kumulace mikropoškození
a mikrozlomenin

Remodelace kosti:

- permanentní odstraňování
poškozené a staré kosti
- zabraňuje propagaci mikrocracků
do makrozlomenin



Microcracks

Cortical bone

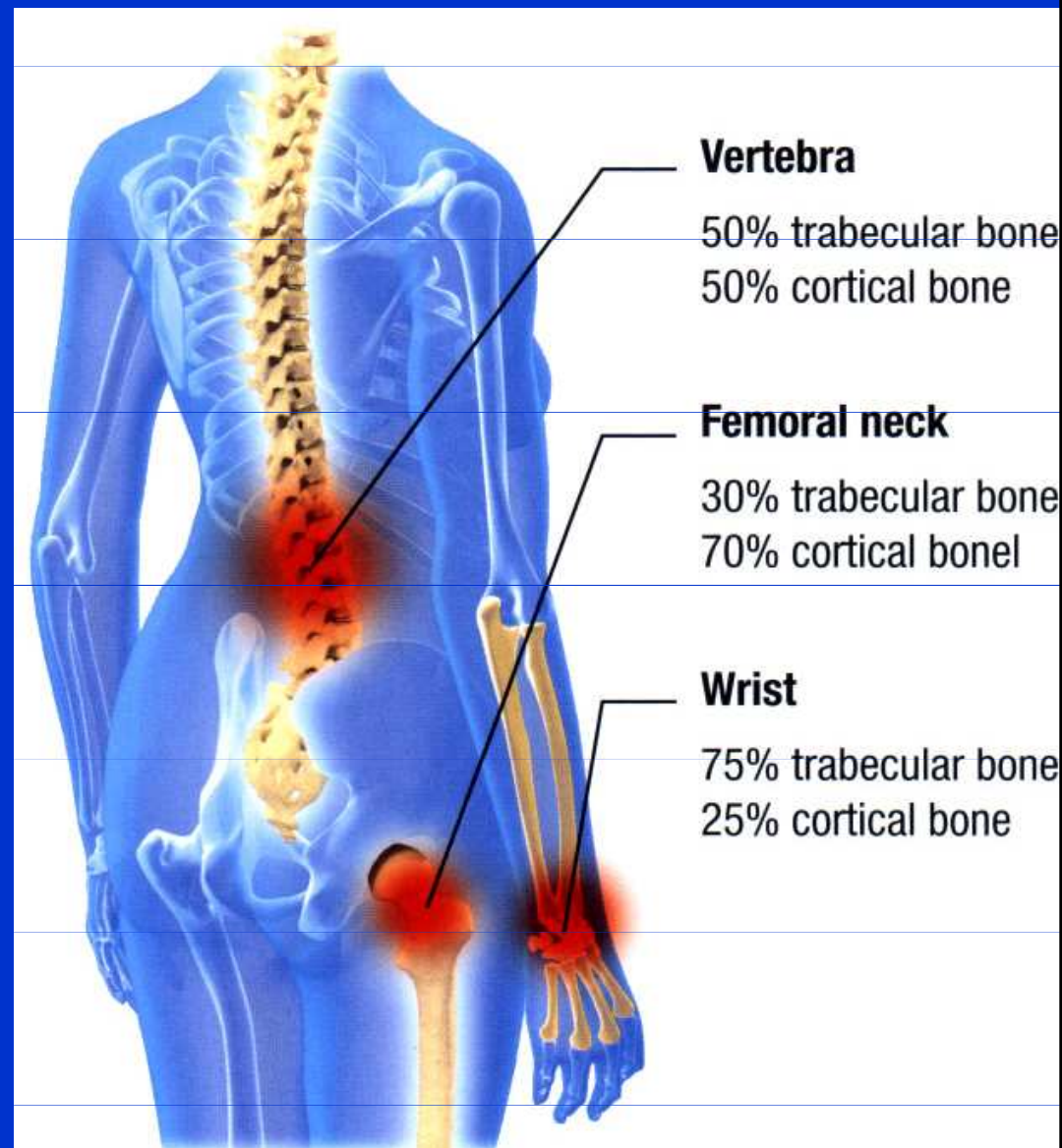
Pevnost

70- 85 % pevnosti kostí celkem

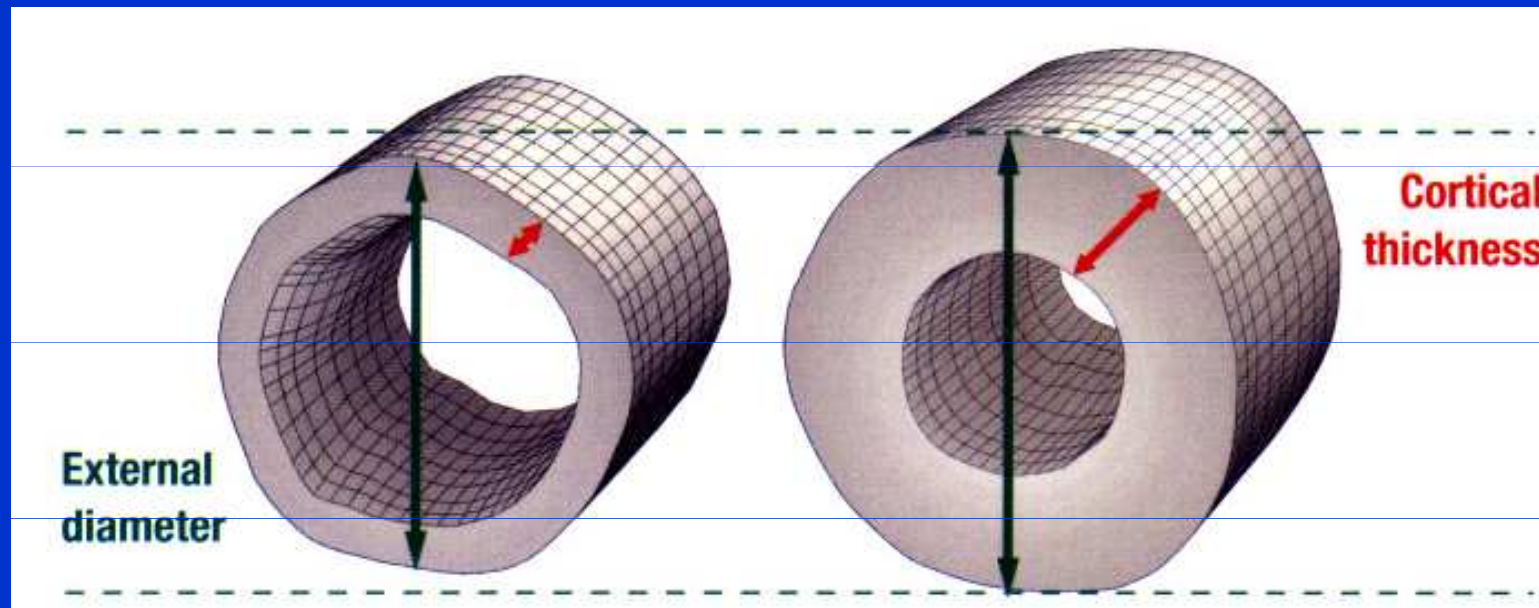
70 % všech zlomenin u seniorů jsou nevertebrální zlomeniny s lokalizací v kortikální kosti

20 % ztráta ve smyslu zeslabení kortiky
- 40 % snížení pevnosti kosti

Složení kosti



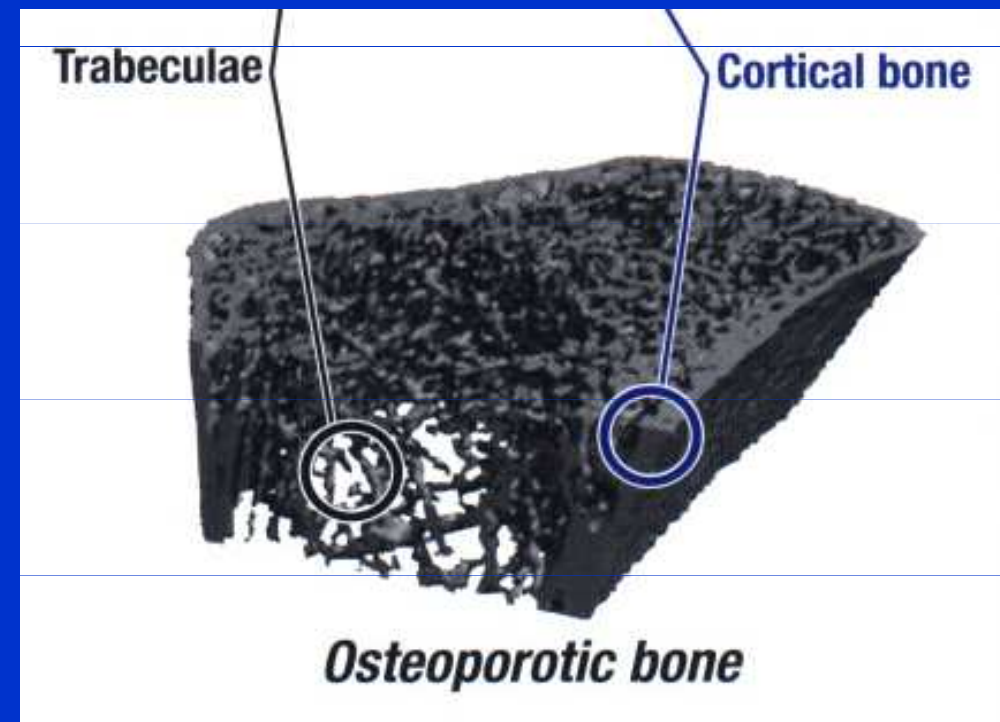
Factors of cortical strength



Průměr kosti

Tloušťka kortikální kosti

Kortikální porozita



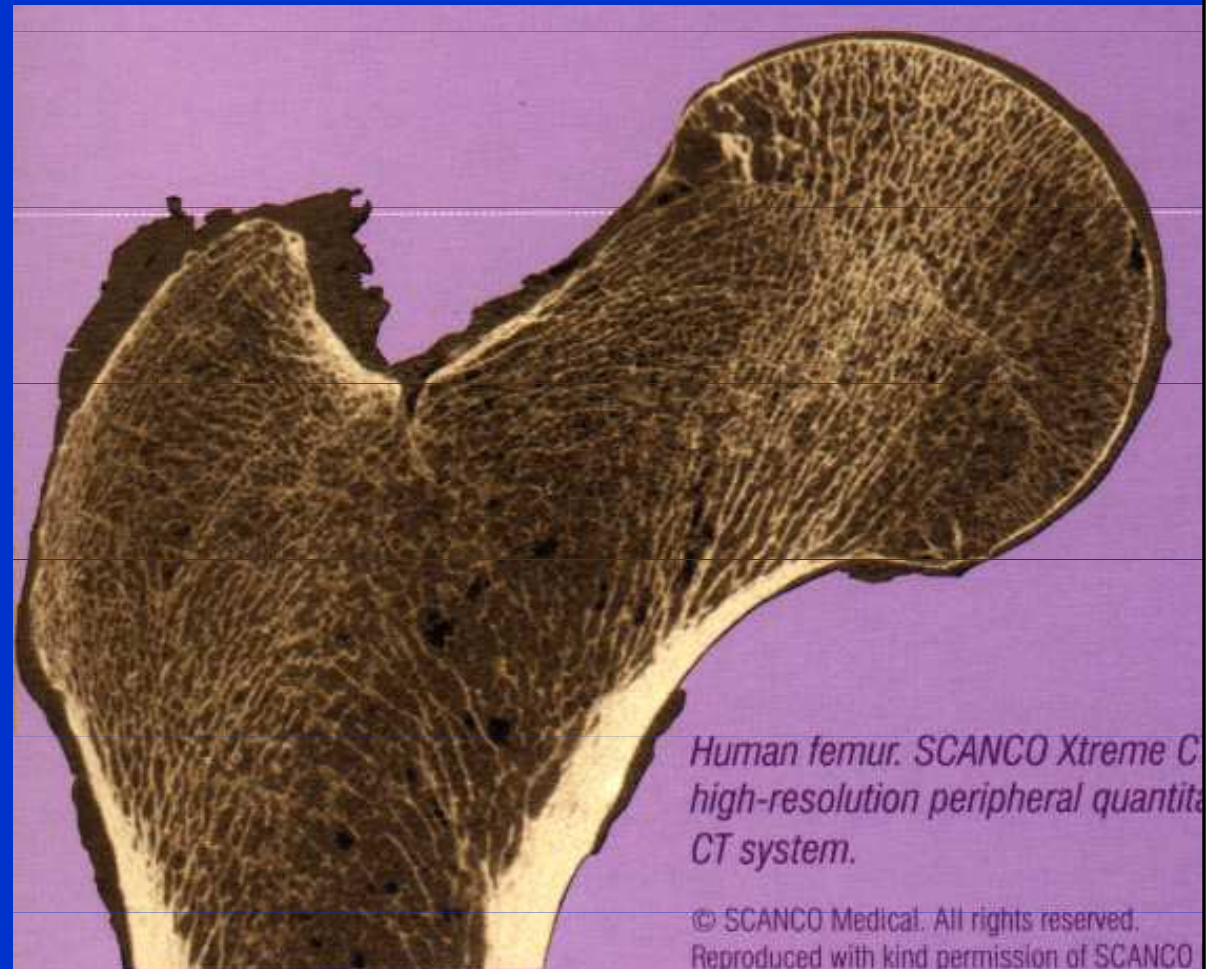
Cortical bone in proximal femur

Zajišťuje 90 % pevnosti krčku femuru

Hlavní faktory pro vznik zlomeniny:

Zeslabení kortiky

Zvýšení kortikální porozity



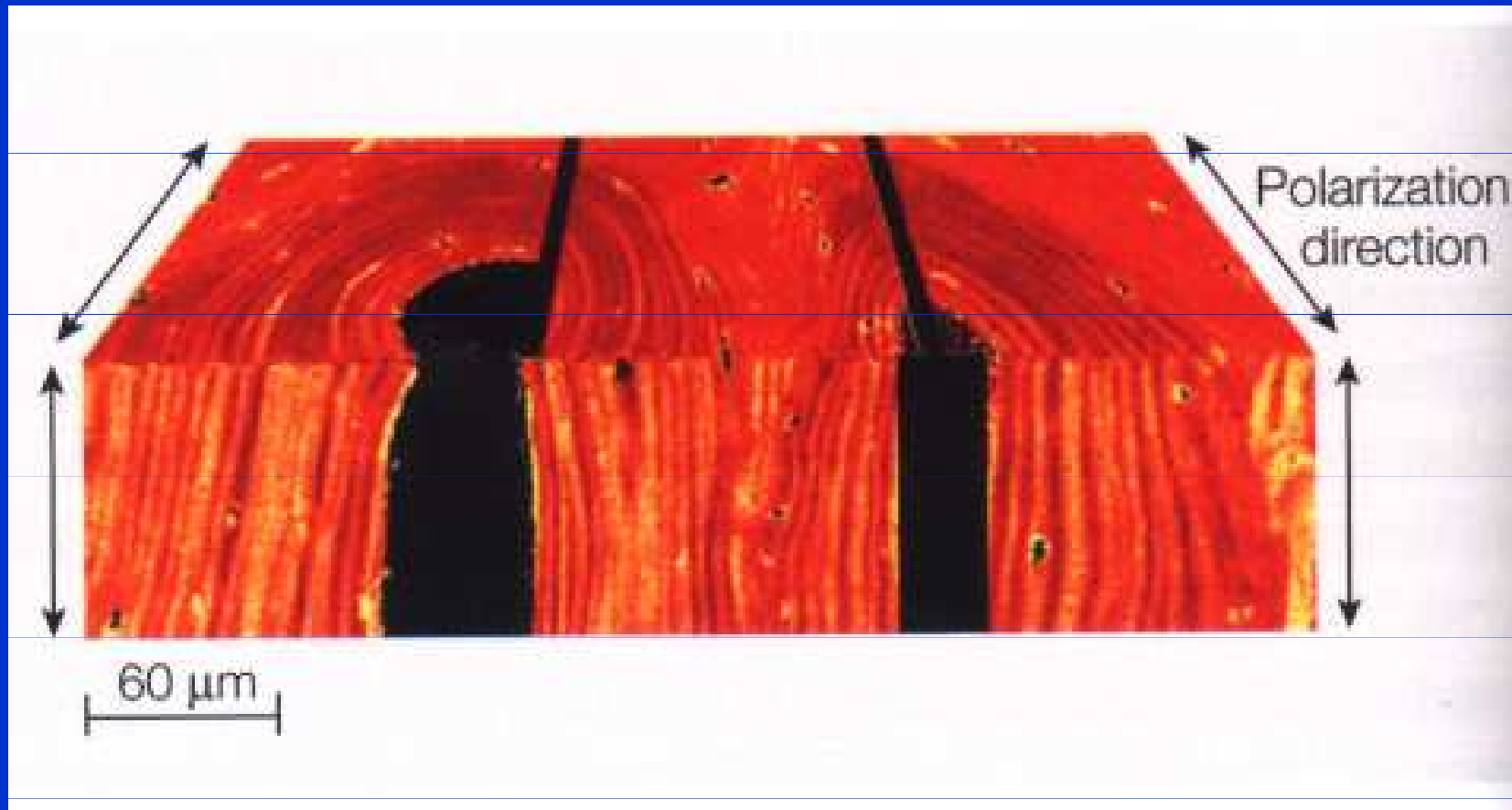
SCANCO Xtreme CT
HR qCT

Cortical porosity

Zvyšuje se po 40 letech věku

Tloušťka kortikalis se snižuje každých 10 let o 6 %

Začíná resorpcí a rozšířením Haversova kanálu



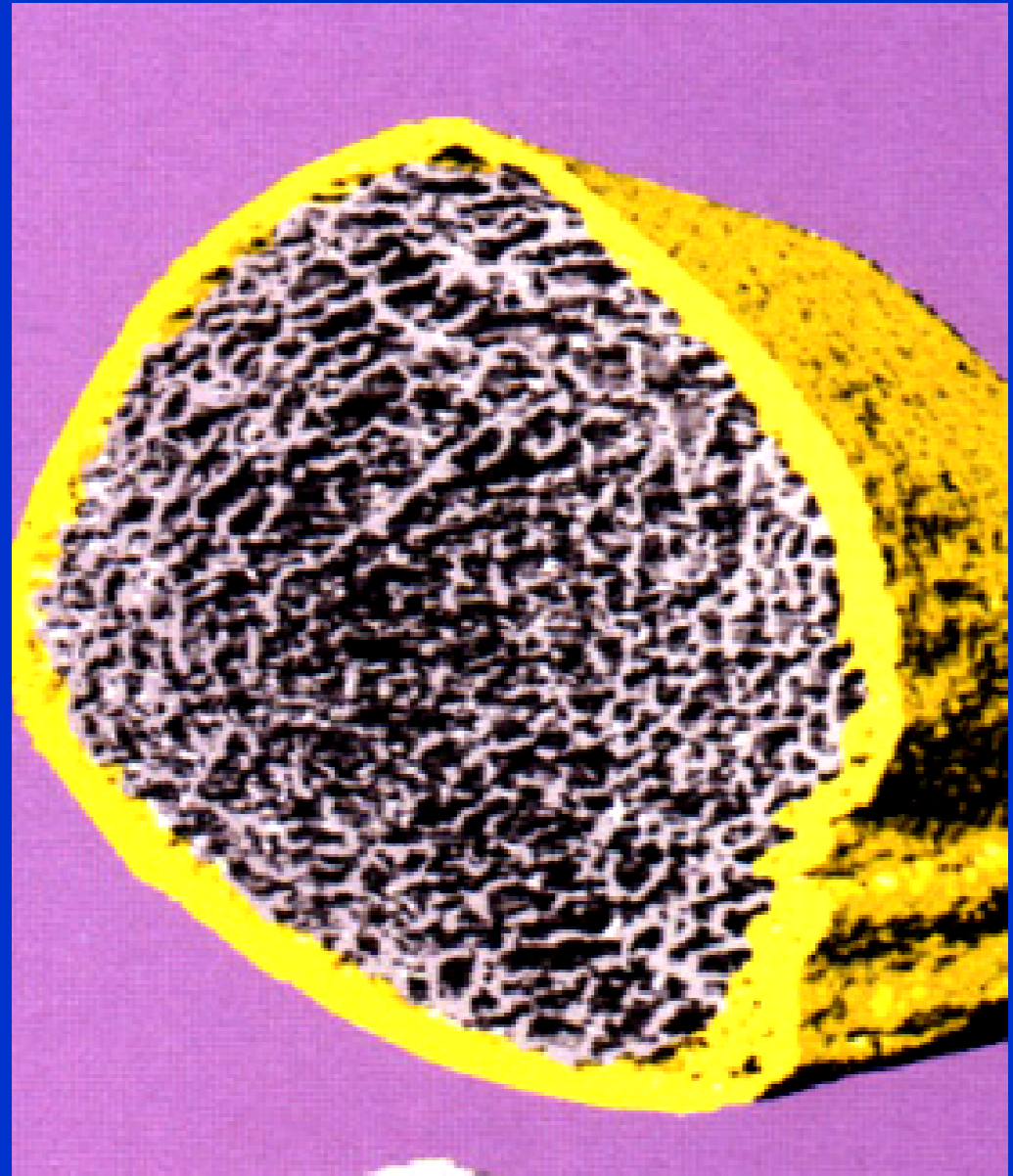
Raman microspectroscopy

Osteoporosis

Ztráta kortikální kosti

Ztenčení kortikalis

Kortikální porozita



Extreme CT: denzita a 3 D mikroarchitektura kosti

Osteoporosis

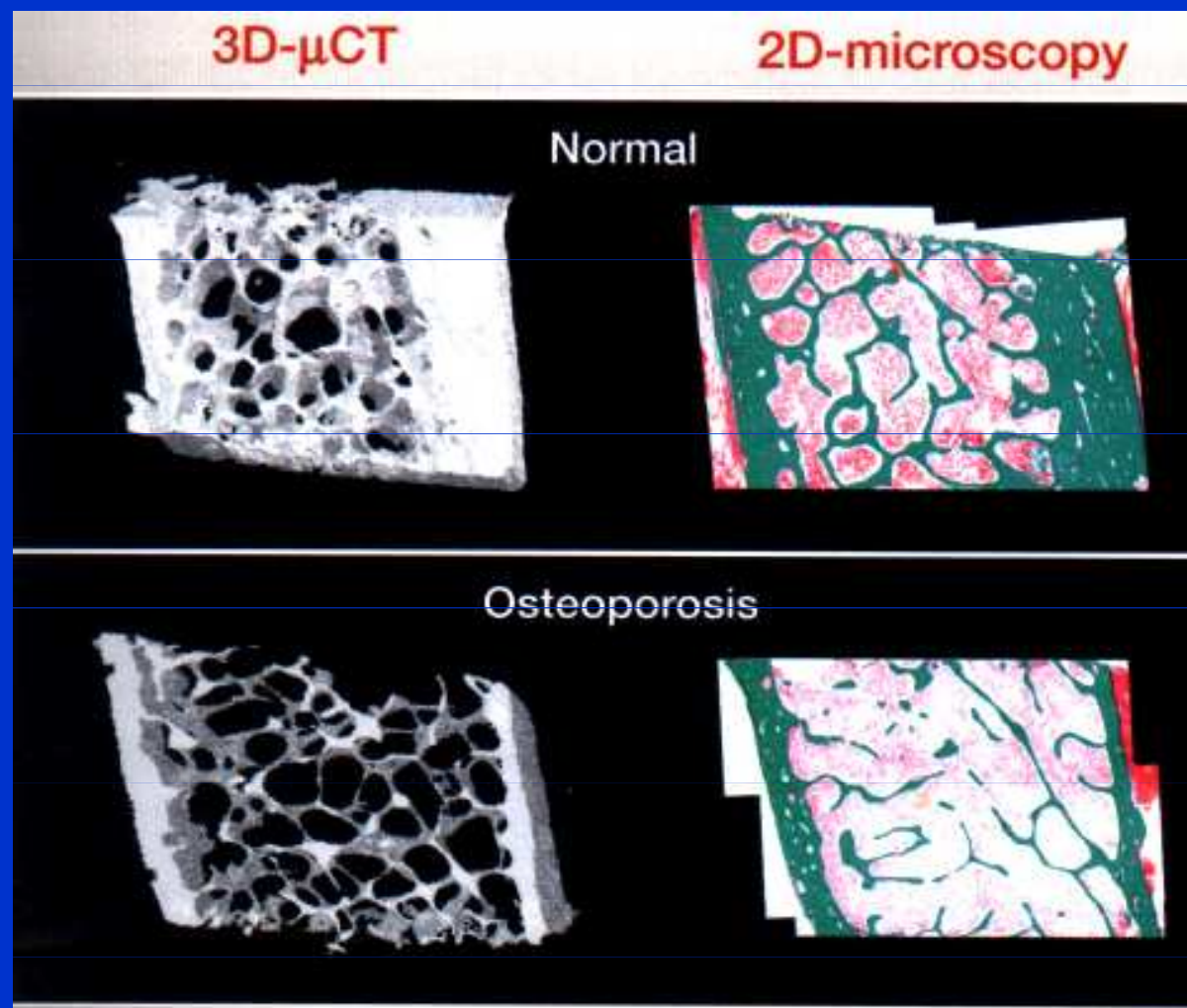
Tvorba nepravidelných obrovských kanálů

Tvorba rezorpčních kavit

Vznik menších osteonů

Snadnější tvorba mikrotrhlin

Nižší hustota osteocytů v intersticiální hmotě



Factors of the strength of trabecular bone

Počet trámců, jejich tloušťka

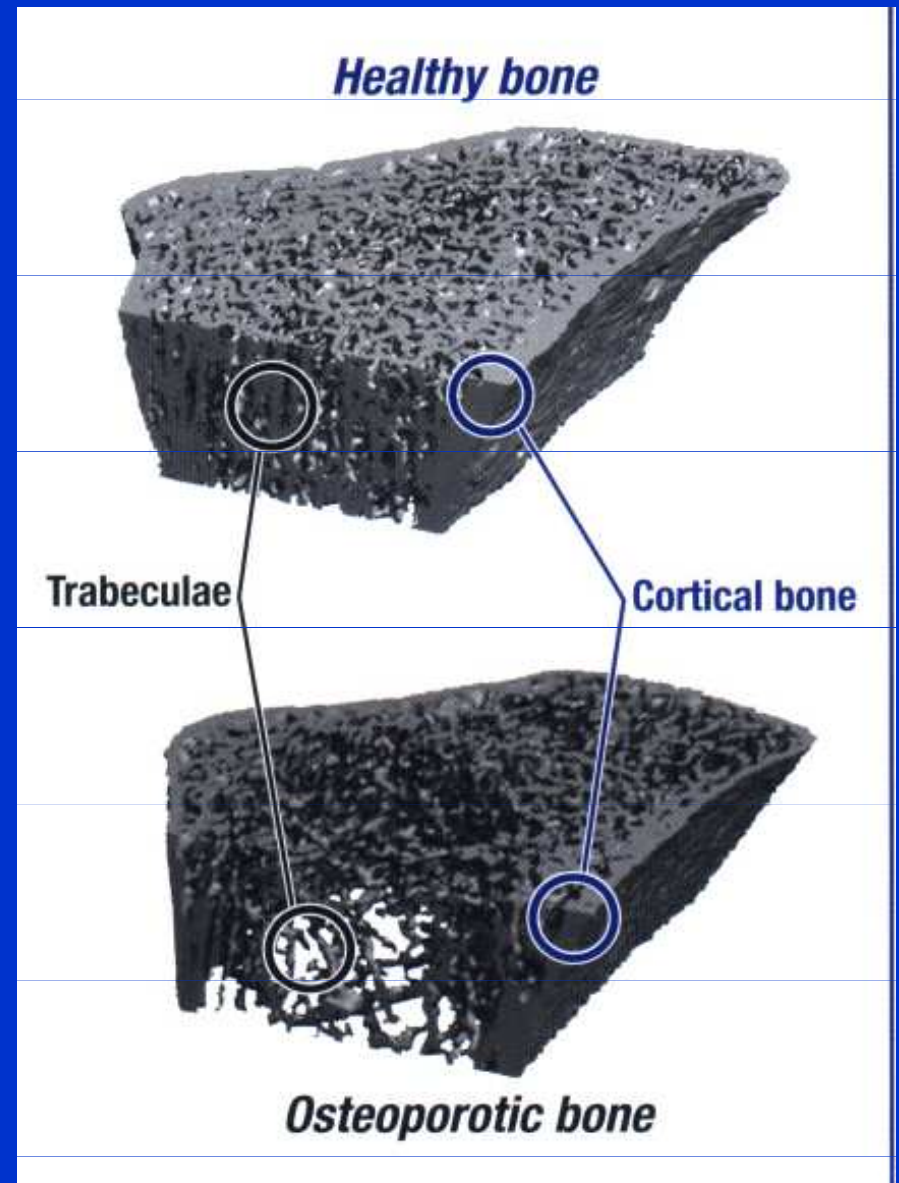
Spojení mezi trámci- interconnectivity

Uspořádání dle siločár

Trabekulární kostní objem

Trabekulární denzita

Intertrabekulární spacing



Trabecular bone

Zdravá kost

Trabekulární kost tvořená převážně
destičkami



Plate like elements

Trabecular bone

Osteoporotická kost

Transformace z destiček na tyčky

Trabekulární kost tvořená převážně tyčkami



Rod like elements

Bone matrix

Kolagen:

Kvalita

Prostorové uspořádání

Orientace fibril, délka fibril

Cross linky:

poměr divalentní- trivalentní vazby

Krystaly:

Velikost

Tvar

Objem

Osové uspořádání

2. Diagnosis of fractures

Diagnosis

Anamnéza, mechanismus úrazu

Low energy trauma- osteoporosis?

Klinické známky zlomenin

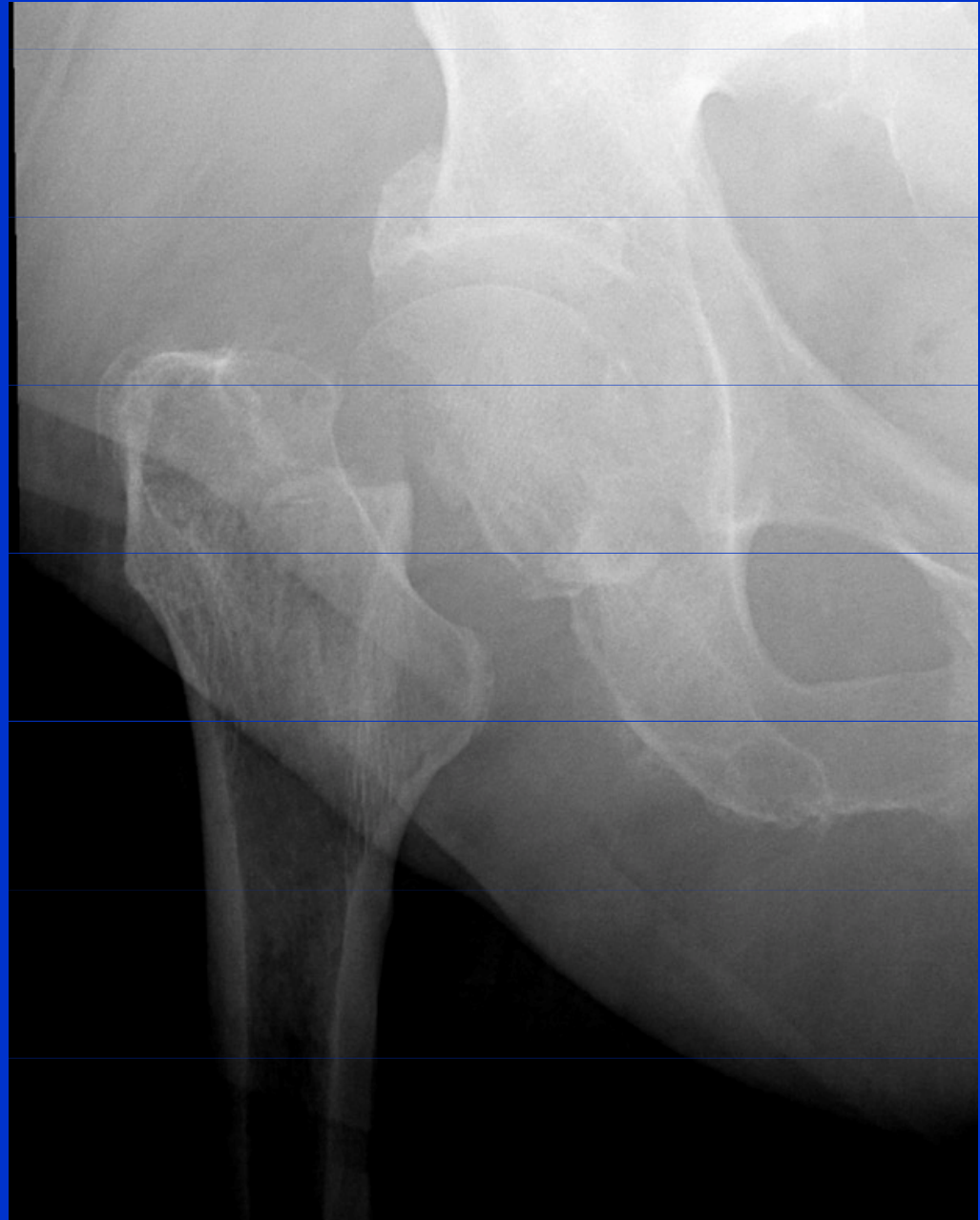
RTG, CT vyšetření

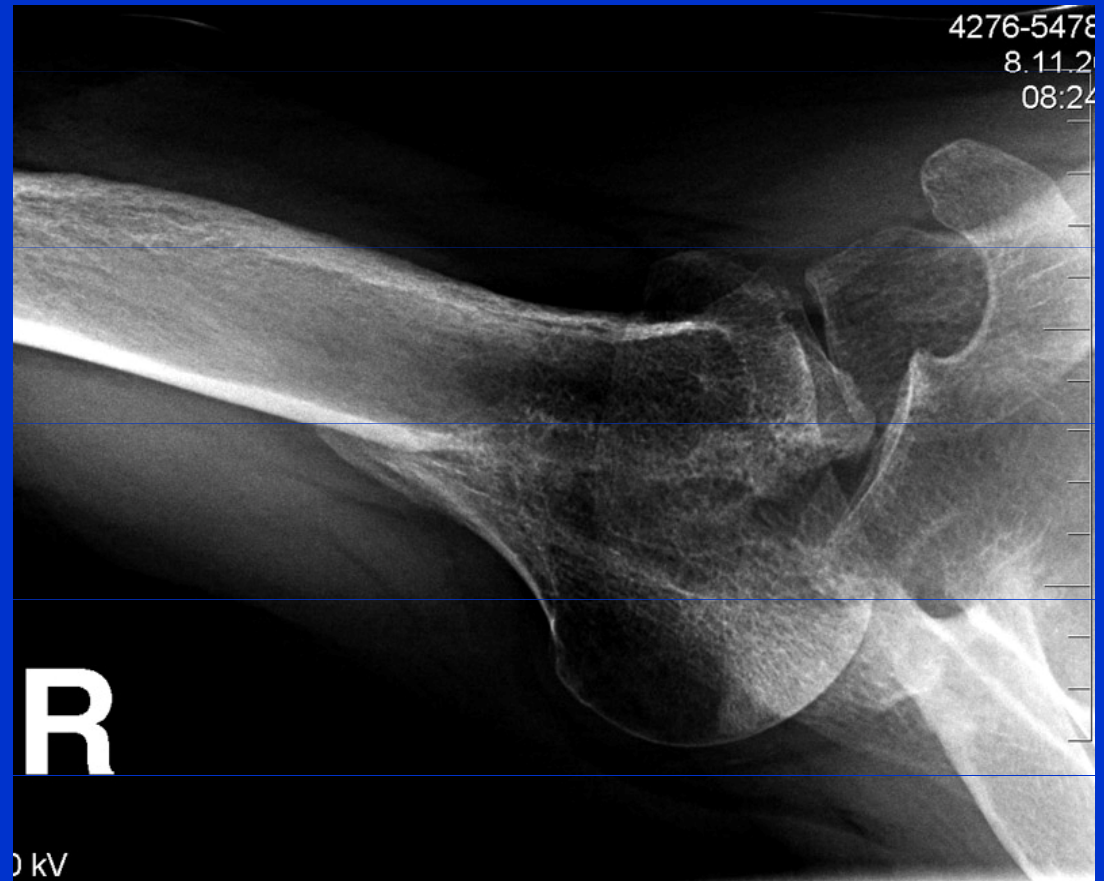
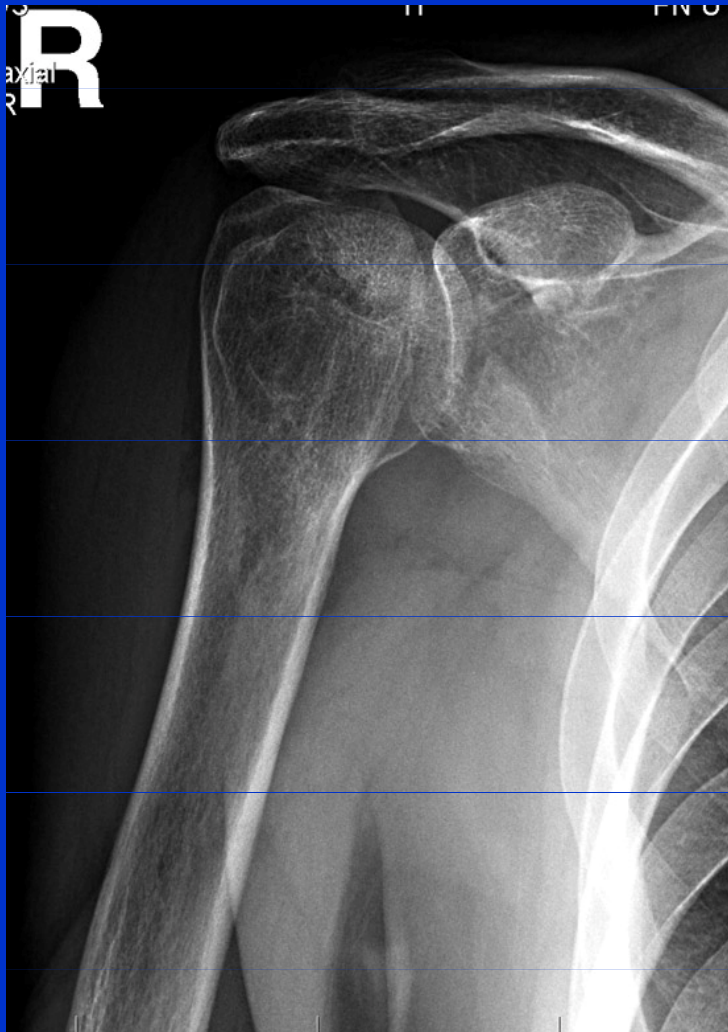
Pečlivé radiologické vyhodnocení

Opakované vyšetření s odstupem 10-14 dnů

Neglected fx

Ž, 59 r., úraz před 6 týdny



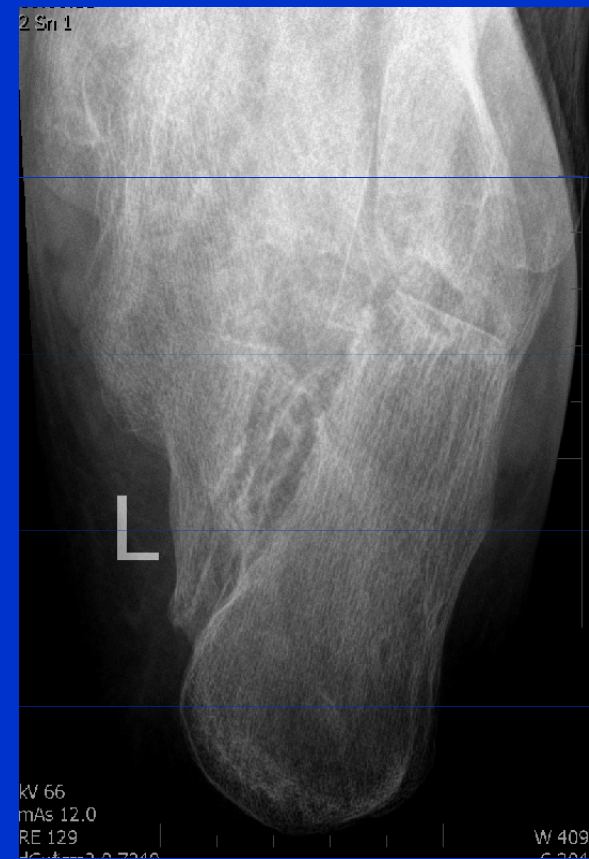
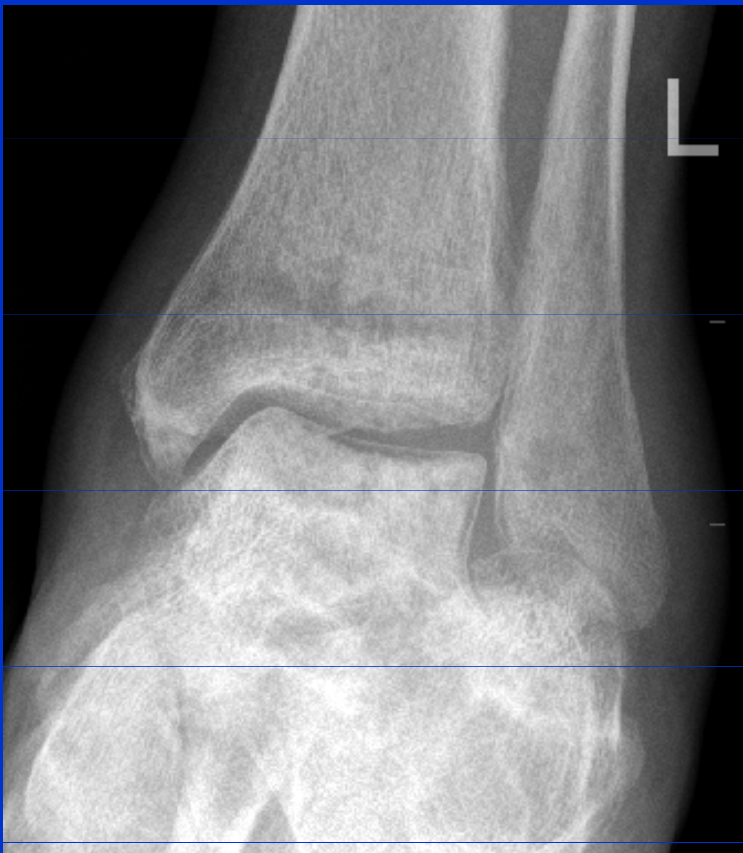


M, 41 r., úraz před 5 měsíci



M, 21 r., úraz před 3 měsíci





M., 47 r., úraz před 6 měsíci

3. Healing of fx

Healing

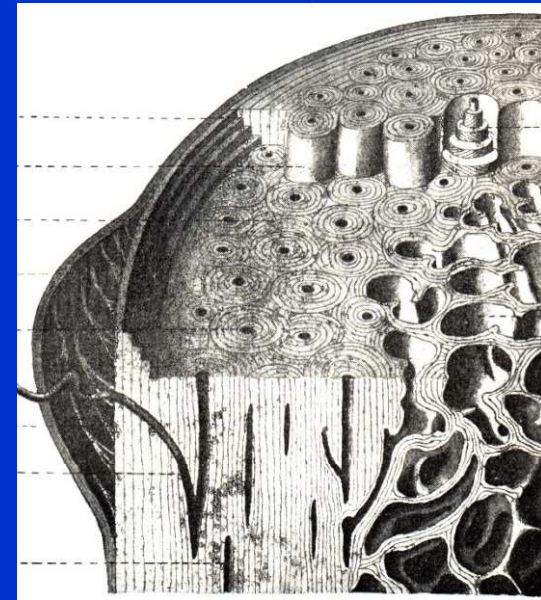
Osteoblasty:

Kortikální kost:

kambiová vrstva periostu a endostu,

Trabekulární kost:

trámce spongiózy epifýz a metafýz



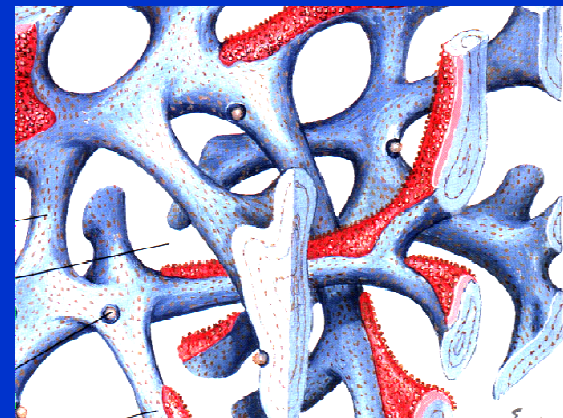
Osteoprogenitorní buňky

Diafýza - málo buněk

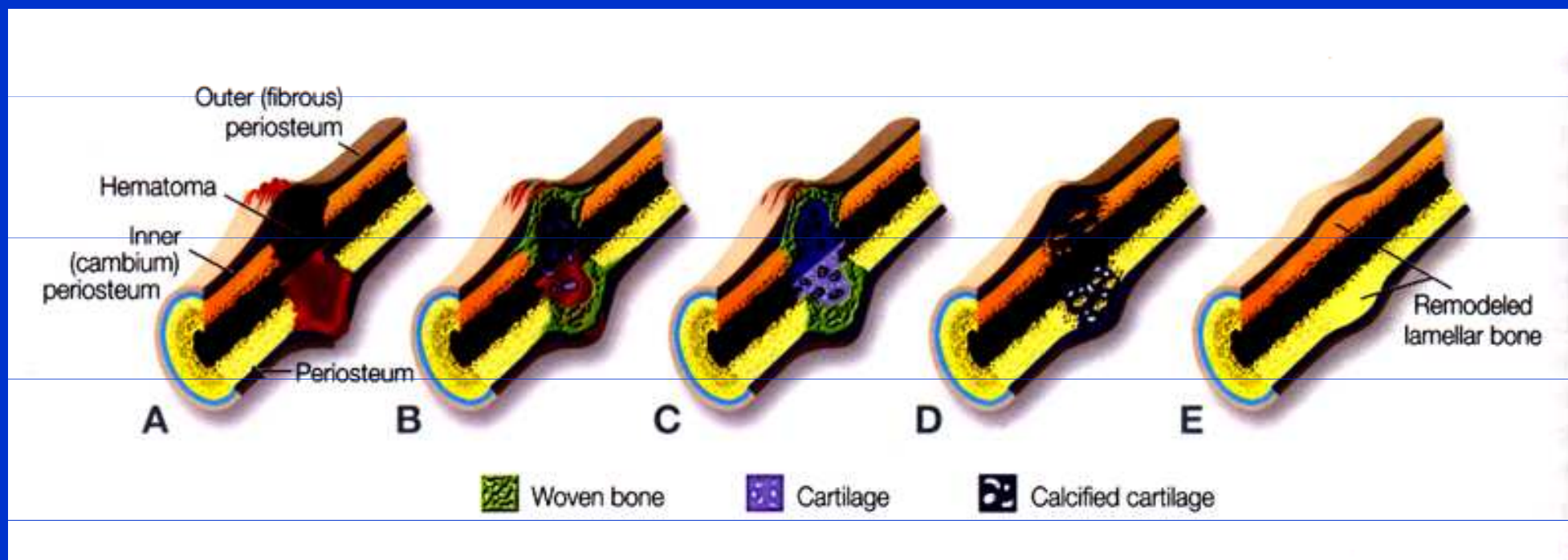
delší doba hojení

Epi a metafýza - hodně buněk

kratší hojení



Indirect healing



A. Hematom

B. Granulační tkáň- zánět

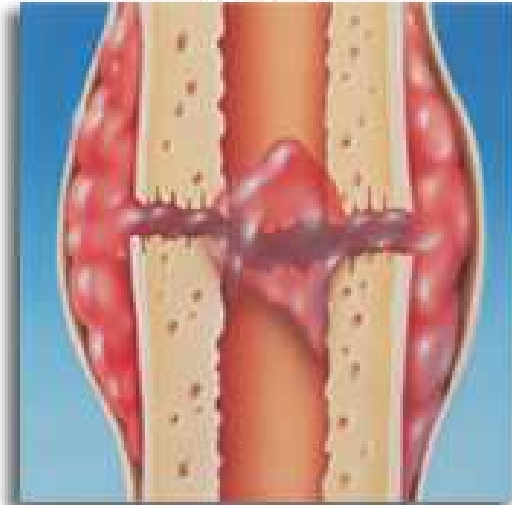
C. Primární kostní svalek (osteoid, pletivová kost, chrupavka, vápenaté soli)

D. Sekundární kostní svalek (nahrazování pletivové kosti kostí lamelární)

E. Remodelace kostního svalku

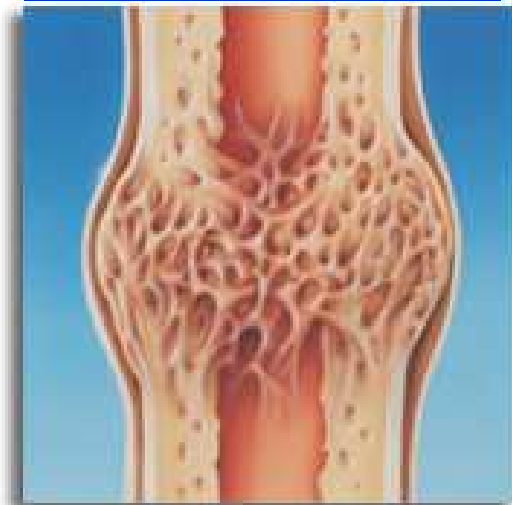
Proces hojení kosti

1. týden



Hematom (nebo záněť)

4.-16. týden



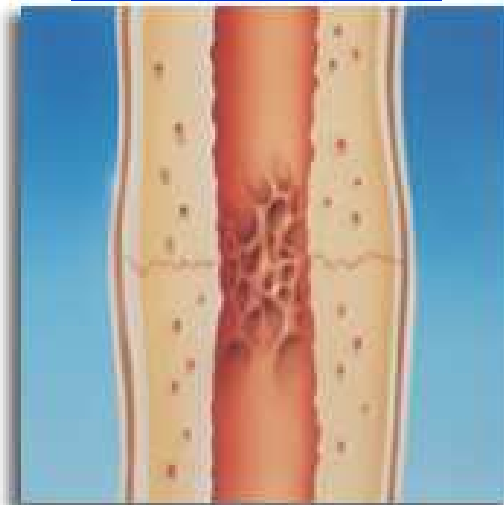
Tvrký svalek

2.-3. týden



Měkký svalek

17. týden a dále



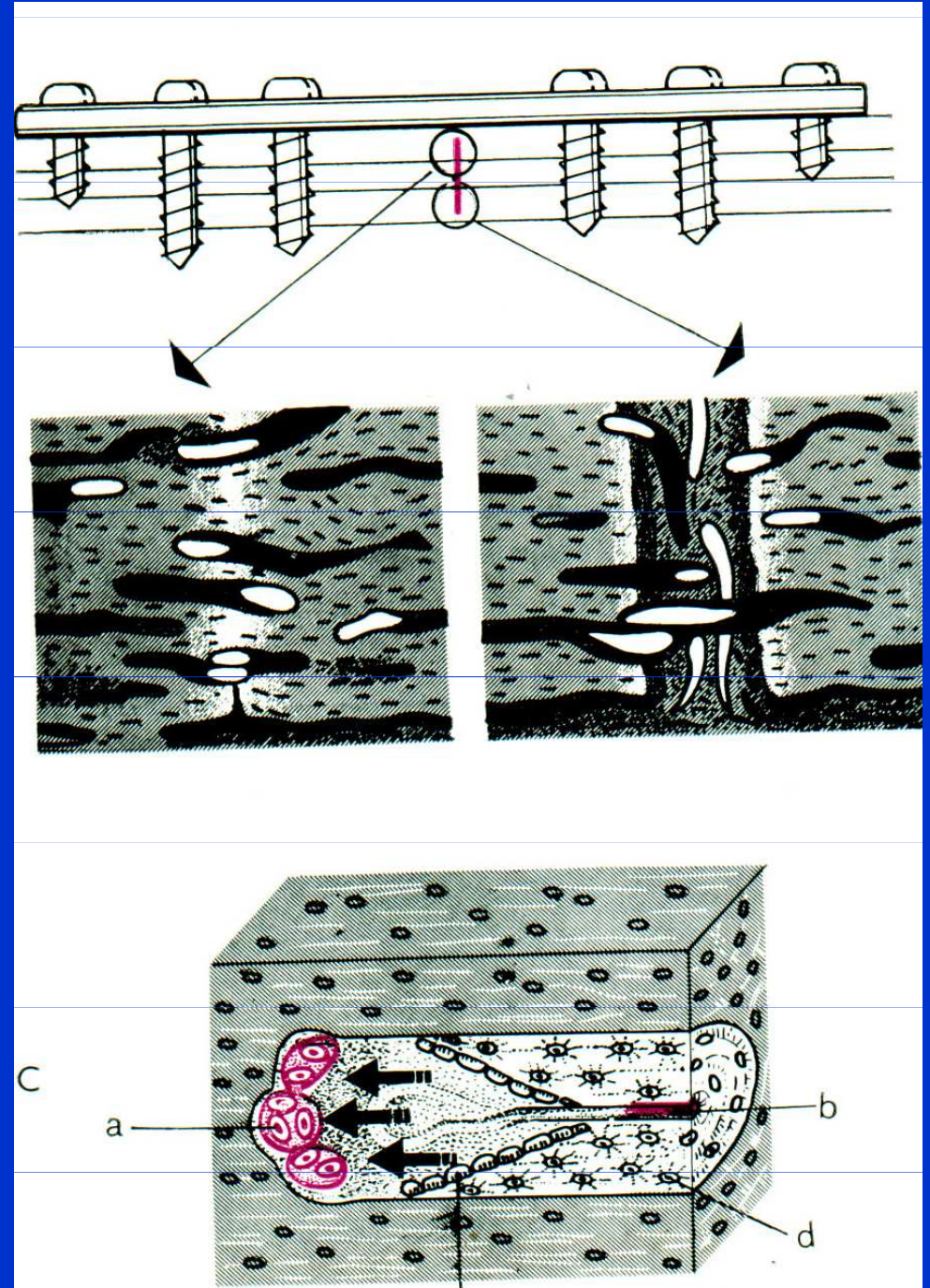
Remodelace

Direct healing

Stabilní fixace, mechanický klid

Hojení interkortikální

Osteon: osteoklasty tvoří rezorpční kanál, za nimi je céva a podél ní osteoblasty.

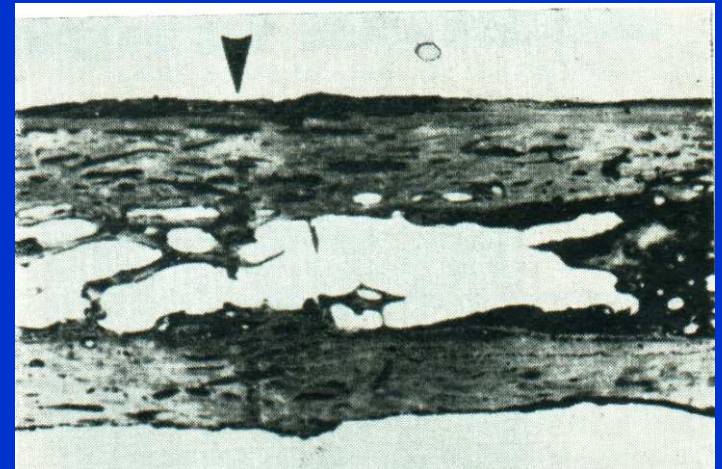


Direct healing

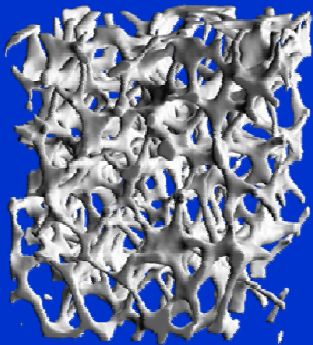
Rychlost osteonů: 0,1 mm/den

Odbourávání a novotvorba

Bez vazivového a chrupavčitého svalku



Osteoporosis



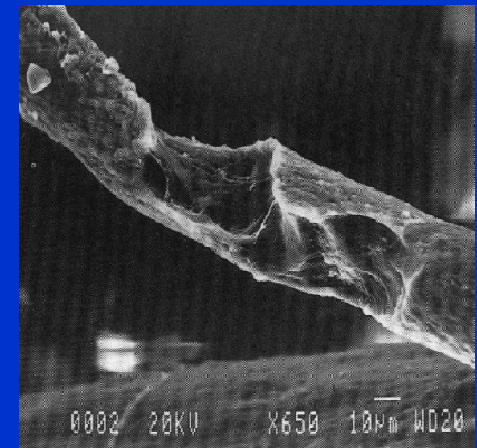
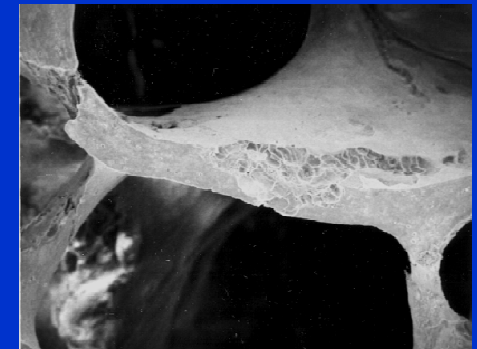
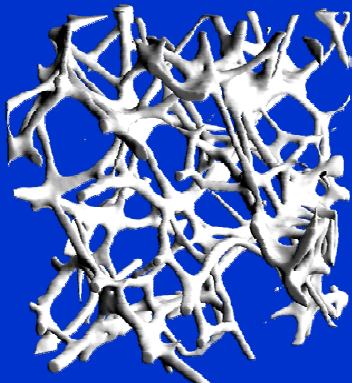
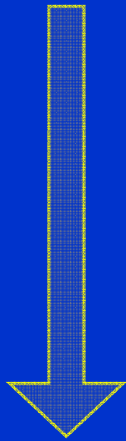
Pokles objemu kostní hmoty

Chátrání trabekulární architektury

Zvýšená kortikální porozita

Zvýšené kortikální ztenčování

Změna kompozice kostní matrix



L. Mosekilde
Tech and Health Care, 1998

Snížená odolnost kosti

Bouxsein. Best Practice in Clin Rheum. 2005 ; 19:897-911

Seeman & Delmas, New England J Med, 2006 ; 354:2250-61

Fragility fractures

Nízká kvalita kosti

Tříštivý charakter zlomenin

Zborcení kosti

Prodloužení času hojení

Vyšší nároky na techniku osteosyntézy

Horší fixace implantátu v kosti

Vyšší riziko pakloubu



Management

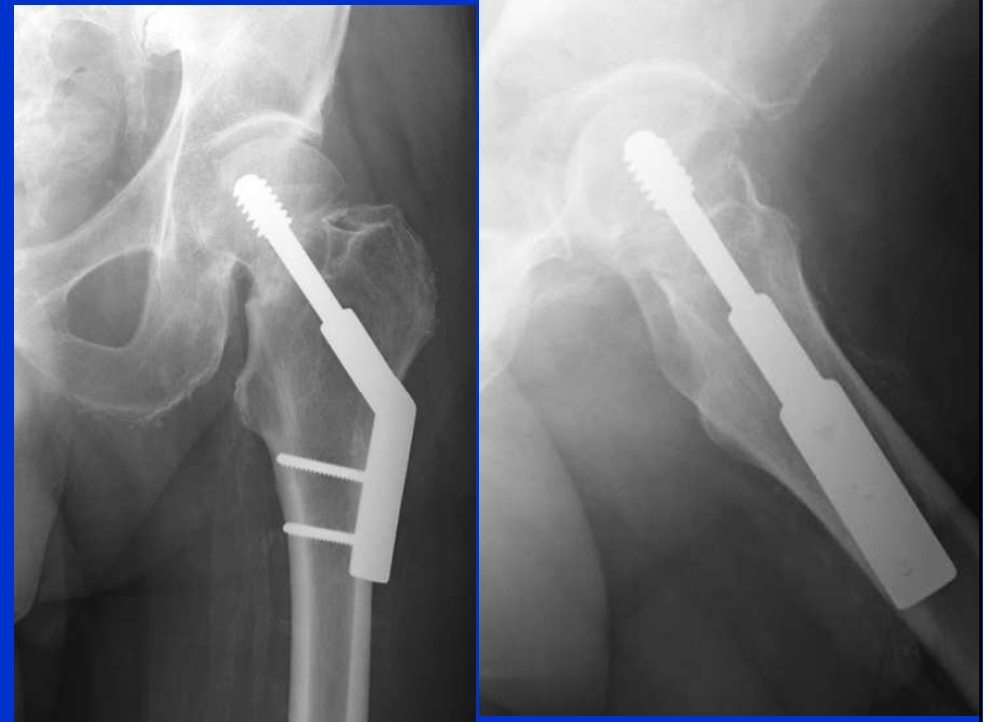
Správné posouzení typu zlomeniny

Správná indikace k léčbě-
konz. postup, OS, alopastika

Výběr implantátu

Korektní repozice

Stabilní fixace



Hemiarthroplasty

Cemented - uncemented

Monoblock - modular type

Unipolar - bipolar

Metal head - ceramic head

Over 80 y.

Higher risk of acetabular erosions



THA

It is preferable versus hemiarthroplasty

In dislocated fx over 65 y.

In fractures with O.A. of the hip

3 - 5 % of dislocation

2 - 4 % of septic complication

Reoperation rate in elderly:

Internal fixation 40 %

Arthroplasty 4,5 %



4. Osteoporotic fractures

Fx of proximal femur

Incidence

USA (280 mil. inhab.) 310 000 / rok

U.K. (60 mil. inhab.) 80 000 / rok

ČR (10 mil. inhab.) 18 000 / rok

Svět 1.8 million / rok

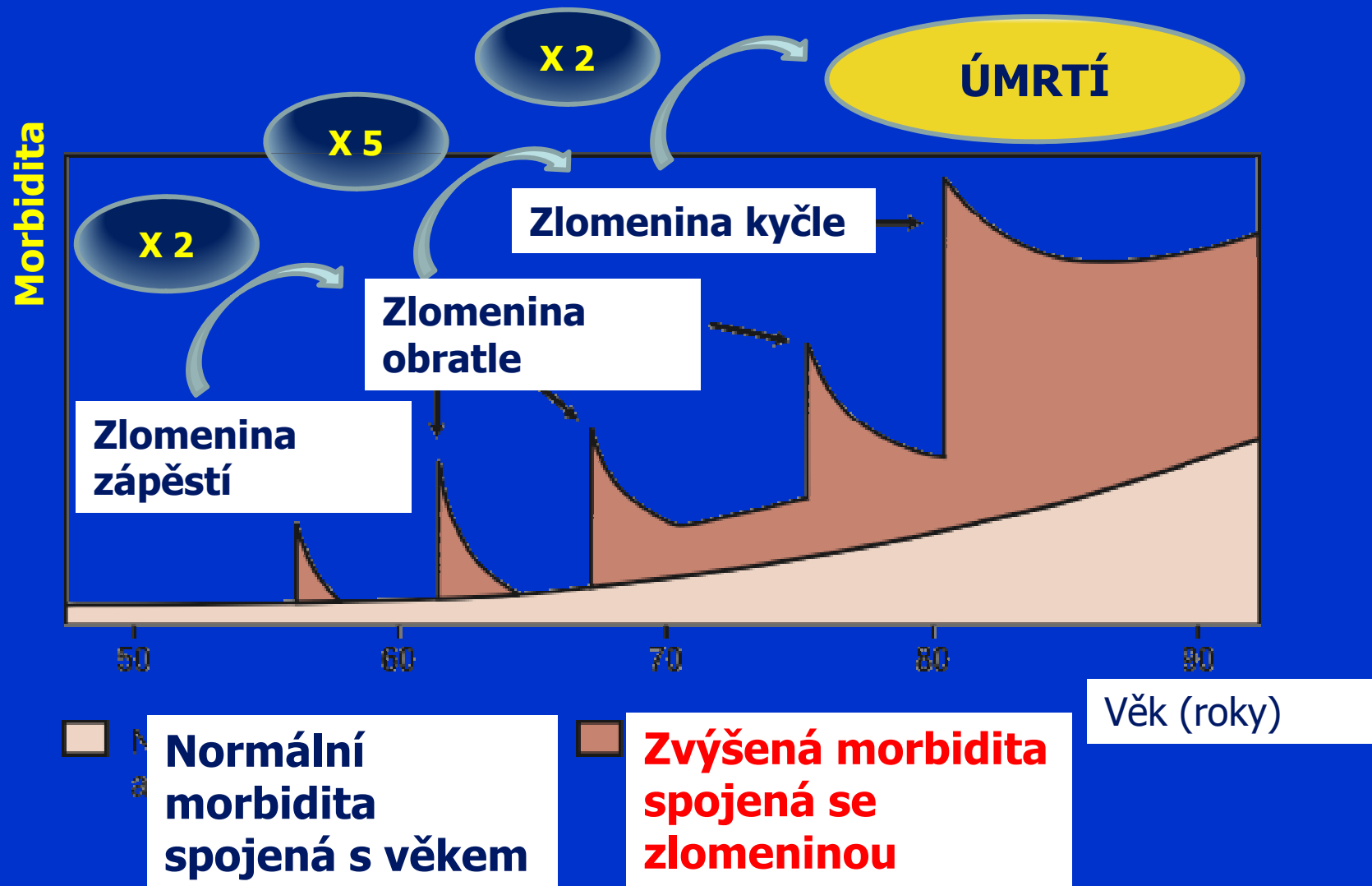
Projected Osteoporotic Hip Fractures Worldwide

Total number of hip fractures:
 1990 = **1.66 million**
 2050 = **6.26 million**

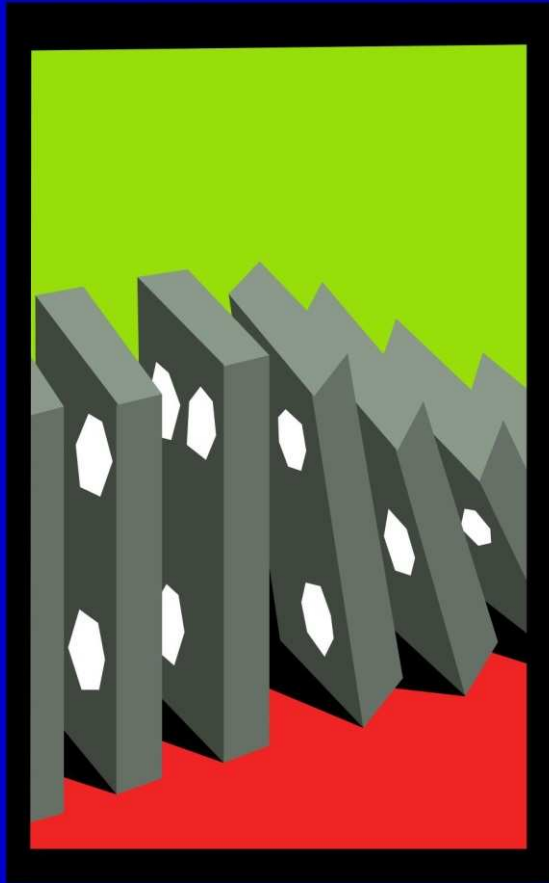


Adapted from Cooper C et al,
 Osteoporosis Int, 1992; 2:285-9

Osteoporosis- risk of further fx



A prevalent fracture is a major risk for another fracture



Incident Vertebral Fracture

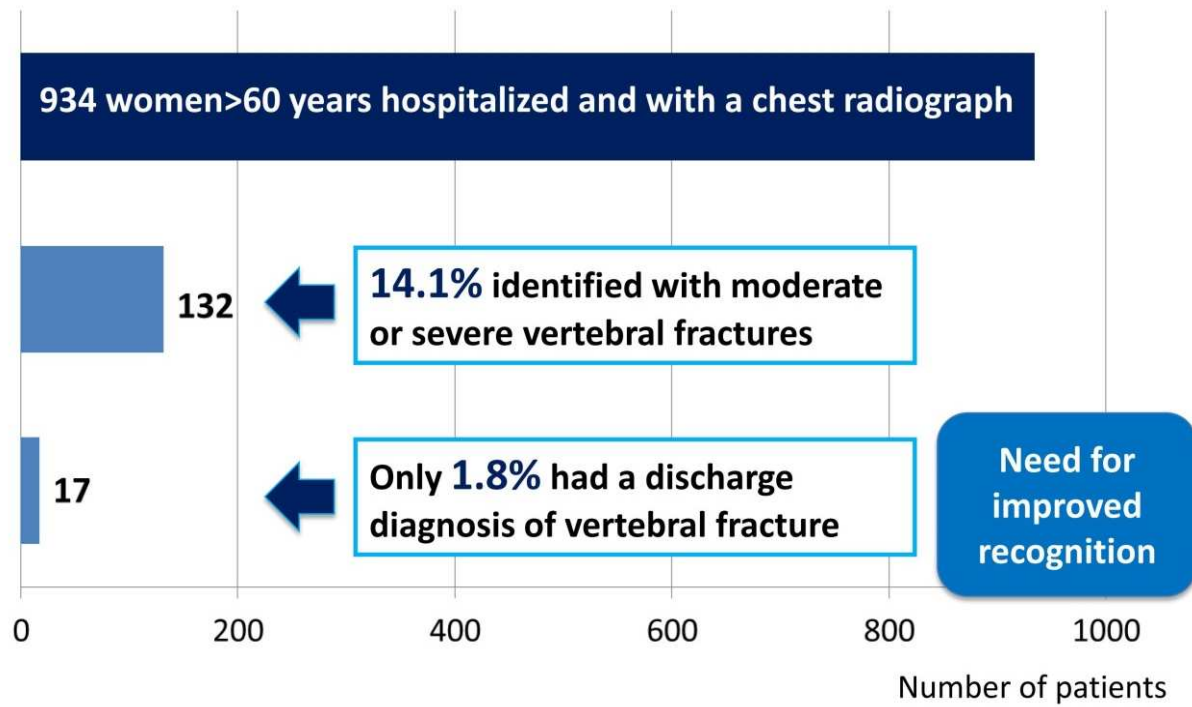
-> 20% Risk of another Fracture within One Year

Lindsay et al 2001

A Fracture:
An Opportunity to Identify
Patients at Increased Risk ?

Vertebral fracture are under-recognized

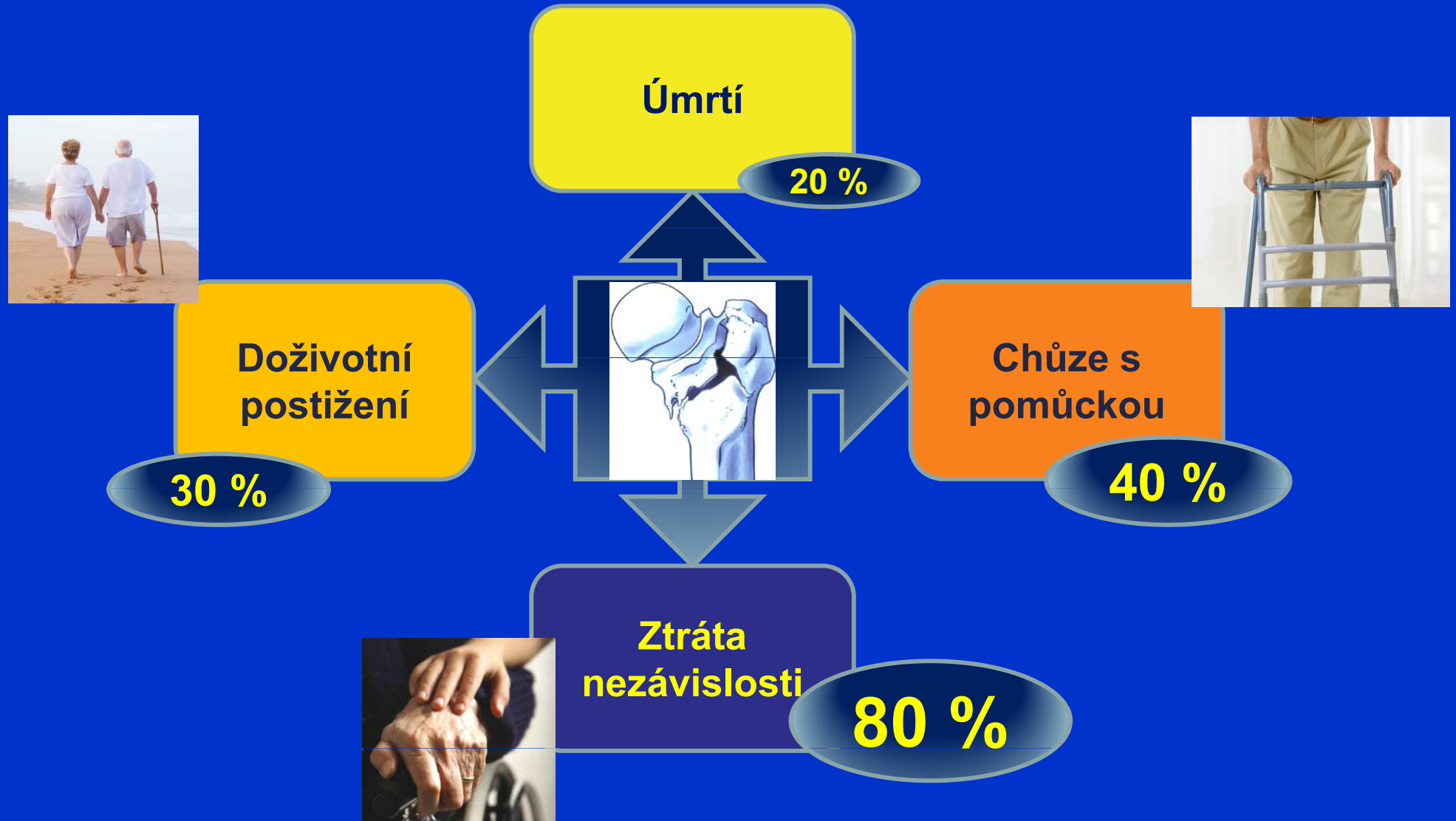
Cross-sectional survey in a large regional hospital in New England



Gehlbach SH, et al. *Osteoporos Int.* 2000



Consequenses



4. Secondary prevention of fx

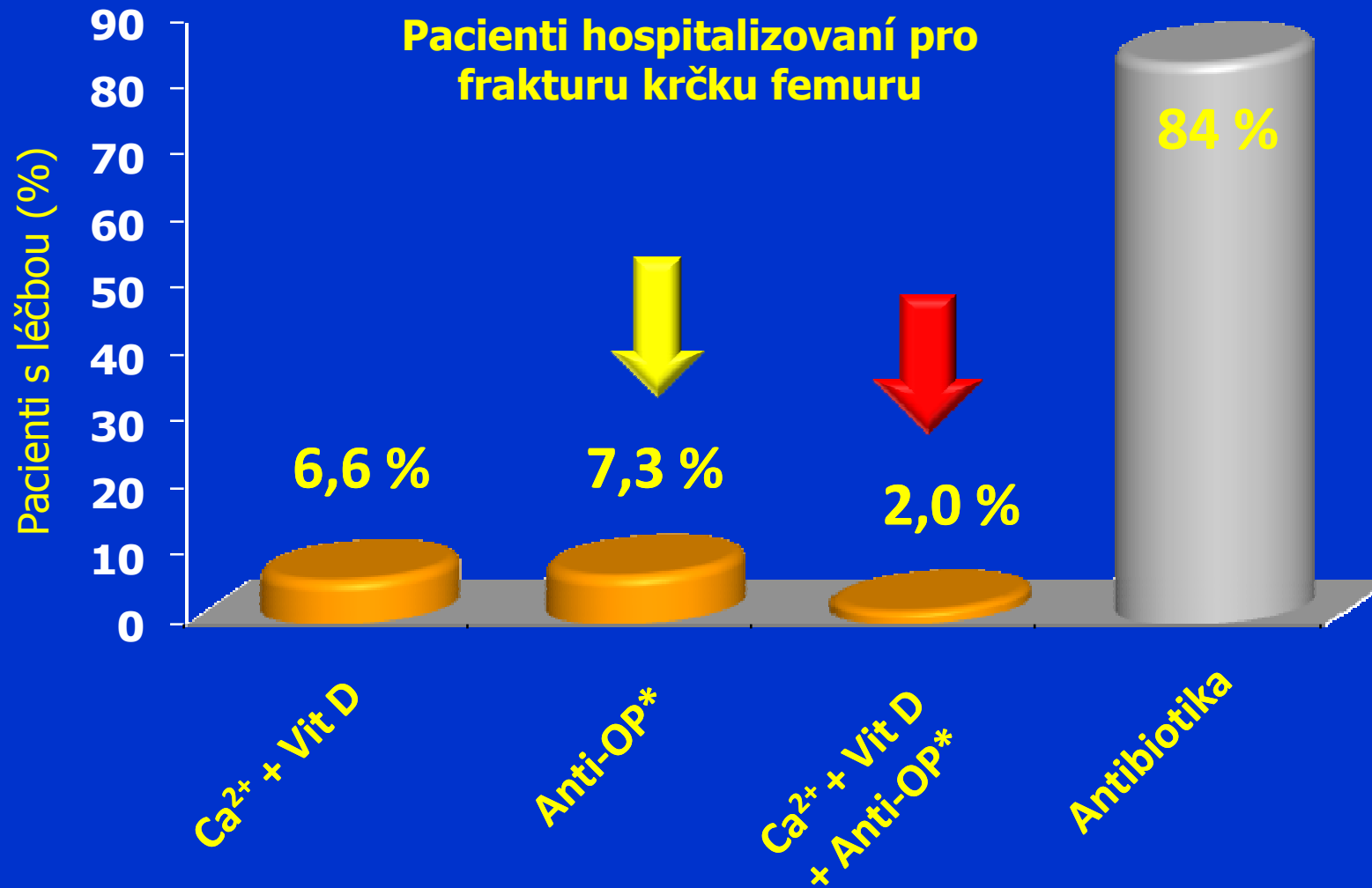
Low treatment prevalence after hip fracture

Treatment prevalence (%)

▪ Andrade & al	2003	24
▪ Bellantonio & al	2001	47
▪ Bahl & al	2003	15
▪ Formiga & al	2005	6
▪ Gardner & al	2002	19
▪ Harrington & al	2002	16
▪ Hooven & al	2005	42
▪ Juby & al	2002	10
▪ Kamel & al	2000	5
▪ Kiebzak & al	2002	27
▪ Panneman & al	2004	15
▪ Port & al	2003	0
▪ Rabenda & al	2008	6
▪ Simonelli & al	2003	17
▪ Solomon & al	2003	<u>22</u>

16%

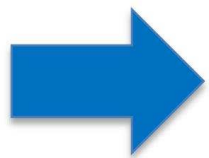
Secondary prevention



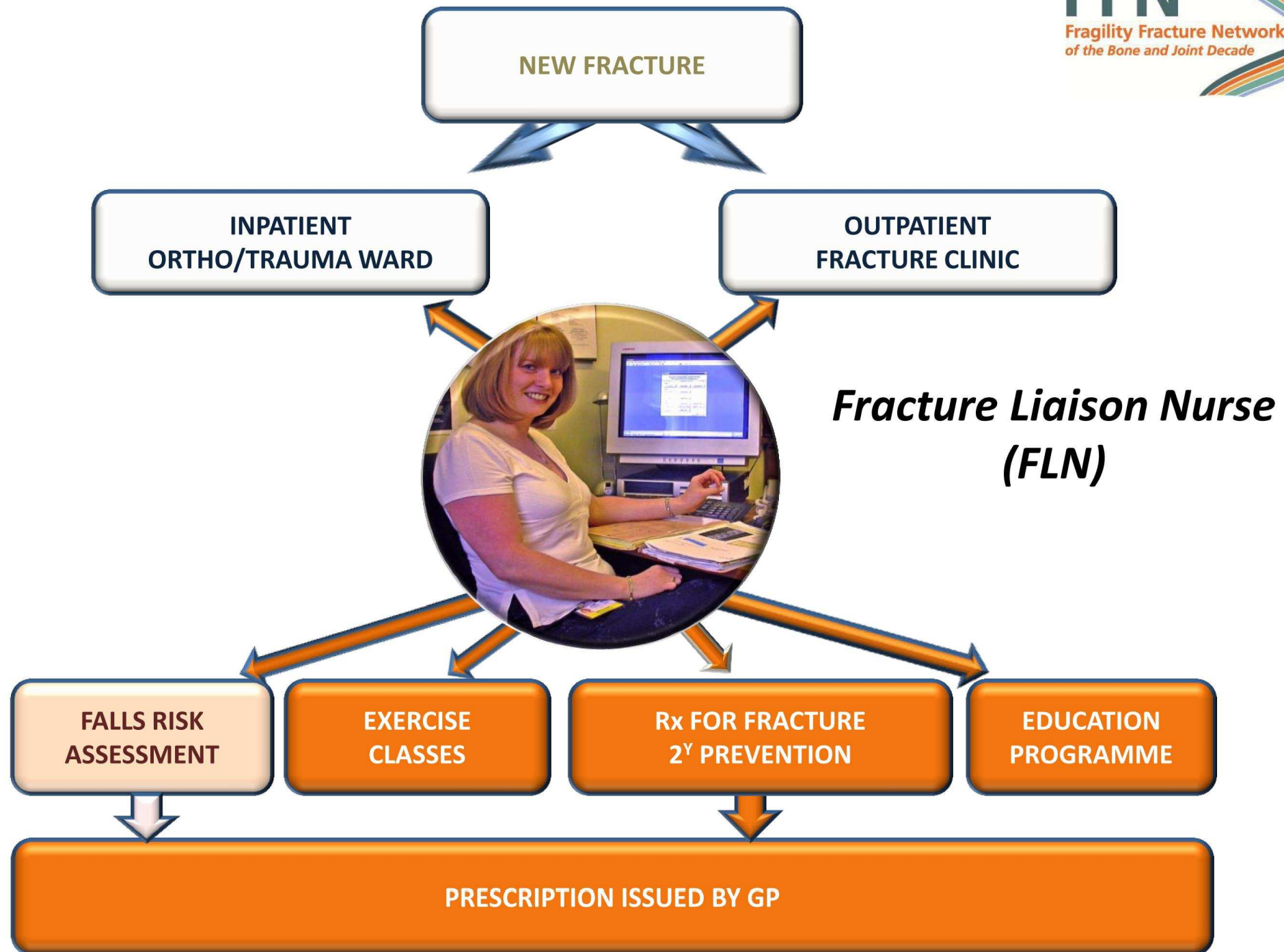
Colles' fracture: are physicians missing an opportunity?

1162 women with a distal radial fracture, >55 yrs (60% < 74 yrs)

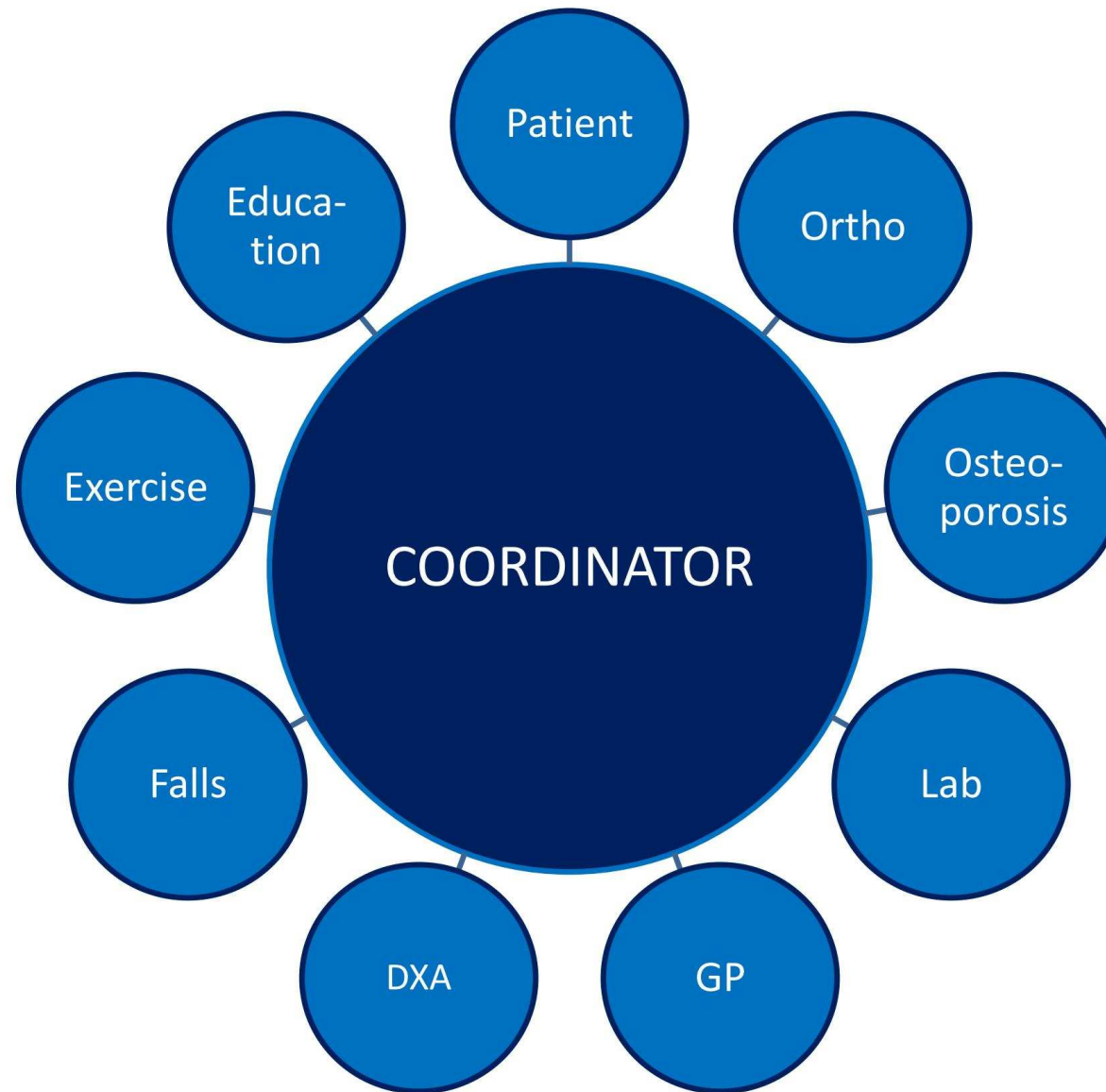
- 23% received medical treatment for osteoporosis
- 2.8% had a bone density scan



76% received neither a bone density scan nor medical treatment of osteoporosis



The coordinator at the center of the system



Recommendation

Pravidelná tělesná aktivita

Udržovat bezpečnou chůzi a pohybovou nezávislost

Dostatečný přívod kalcia a vit. D

1000- 1500 mg Ca

400-800 IU vit. D

Dostatečná výživa

Odstranit rizikové faktory

Alkohol a cigarety- ne !

Léčba osteoporózy

Results - FLS

Maastricht: po 5 letech nižší výskyt opakovaných zlomenin
o 35 % a pokles mortality o 33 %

South California: po 7 letech snížení výskytu zlomenin
krčku femuru o 37 %

Sydney: po 4 letech snížena incidence opakované zlomeniny
o 80 % nižší než v kontrolní skupině

Results - FLS

Glasgow: během 18 měsíců vyšetřeno koordinátorem
4600 pacientů se zlomeninou
82 % zjištěno jako zl. při osteoporóze
nebo osteopenii

50 000 pacientů /10 let zhodnoceno
Snížení počtu zlomenin kyčle o 5,3 %

Mc Lelan: na 1000 pacientů 18 OP zlomenin preventováno
(z toho 11 zl. kyčle)
Úspora 21 000 £

Cost-benefit analysis

FLS cohort of 686 patients, compared with “usual care” cohort of 193 patients:

- 18 fewer fractures
- 3 life years gained
- 22 QALYs gained (Quality-adjusted life-years= a unit of measurement of both the quality and the quantity of life lived)
- 266 hospital bed-days saved
- Cost saving of 312 000 £ from fractures avoided

	FLS cohort	Usual care cohort
Cost of assessments	98,000 £	14,000 £
Cost of drugs	292,000 £	85,000 £
Overall saving:	21,000 £ / 1000 patients	

Post–Hip Fracture Use of Prescribed Calcium Plus Vitamin D or Vitamin D Supplements and Antiosteoporotic Drugs Is Associated With Lower Mortality: A Nationwide Study in Finland

Medication Purchase-Specific Hazard Ratios for 1-Year Mortality Among Patients Discharged Home After Hip Fracture,

	Men		Women	
Medication purchases after discharge home				
No purchases of antiosteoporotic drugs or calcium plus vitamin D or vitamin D supplements	1	ref	1	ref
Only purchases of antiosteoporotic drugs	0.79	0.56–1.11	0.79	0.67–0.93
Only purchases of calcium plus vitamin D or vitamin D supplements	0.74	0.56–0.97	0.91	0.75–1.12
Purchases of antiosteoporotic drugs and calcium plus vitamin D or vitamin D supplements	0.72	0.50–1.03	0.62	0.50–0.76
	Men + Women: 0.74 0.67–0.81			

Nurmi- Luthje, C. et al., 2011

Comparison with other priorities

Issues:	Strokes & TIAs	Heart attacks	Fragility fractures
Incidence/year	110,000	275,000	310,000
Current trend	Falling	Falling	Rising
NHS bed days*	1.85m	1.15m	1.2m (hips)
Annual costs	£2.8bn	£1.7bn	£2bn

5. Influence of medication on fractures

Nurishment

Podvýživa je determinantem fraktury krčku
Zvyšuje sklon k pádům pro horší koordinaci pohybu a
pokles svalové síly.

U nemocných s fr. krčku byla zjištěna
nižší albuminémie.

Vysokoproteinový přídavek 30g/den-
Albuminémie se zvýšila po 28 dnech o 7g/l.

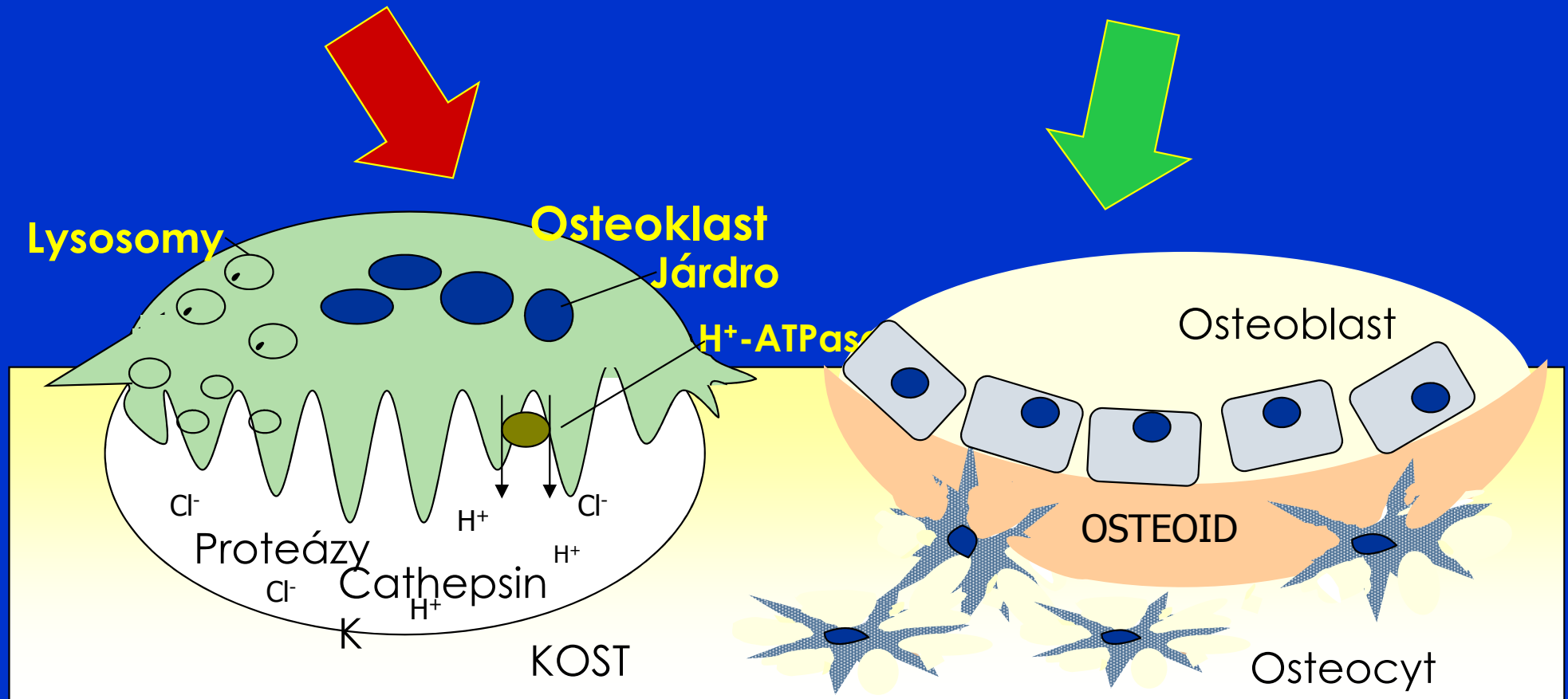
Riziko – alkoholici, vdovci neznalí vaření

Medication

Cíle

Inhibice osteoklastů

Stimulace osteoblastů



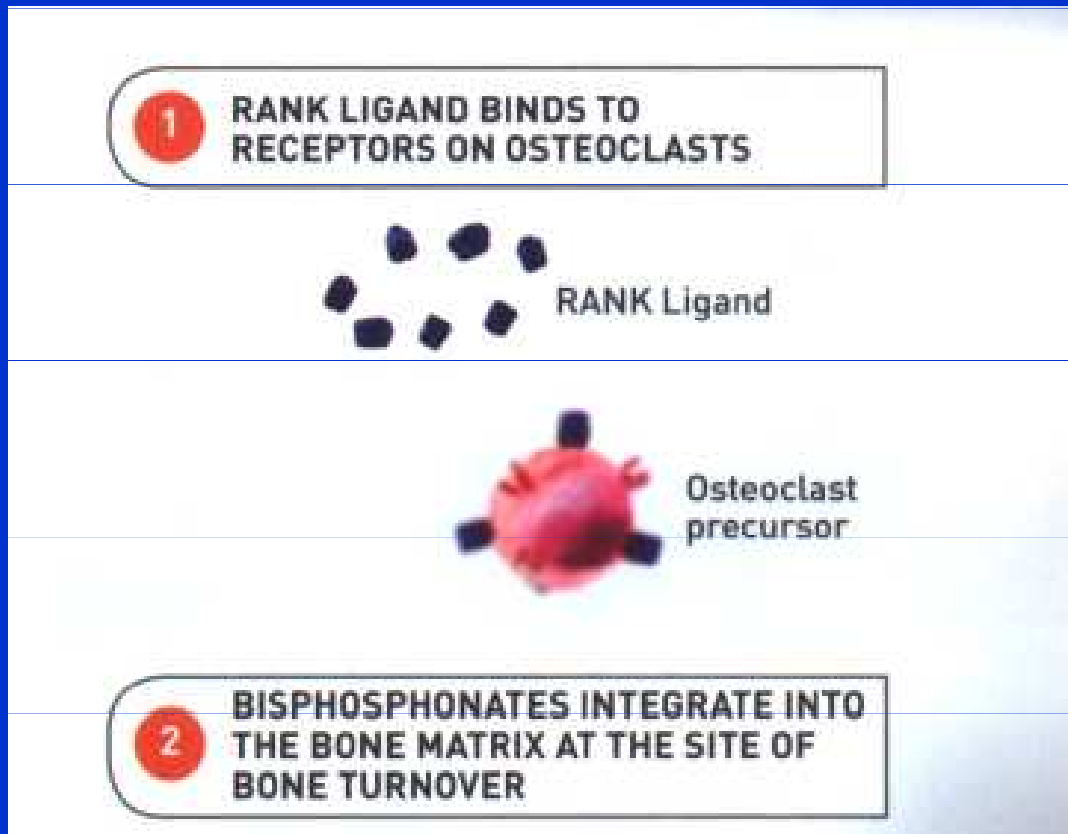
Medication

- Antiresorptiva
 - Bisfosfonáty
 - Denosumab
 - Estrogeny a SERMs
- Osteoformační léky
 - PTH peptidy
 - Stroncium ranelát
 - *protilátky - DKK1 a sklerostin*
 - *Antagonisté calcium sensing receptorů*



Bisphosphonates

- Zvyšují velikost a mineralizaci kostního svalku
- Zvyšují mechanickou pevnost svalku
- Snižují remodelaci svalku
- Riziko atypických zlomenin

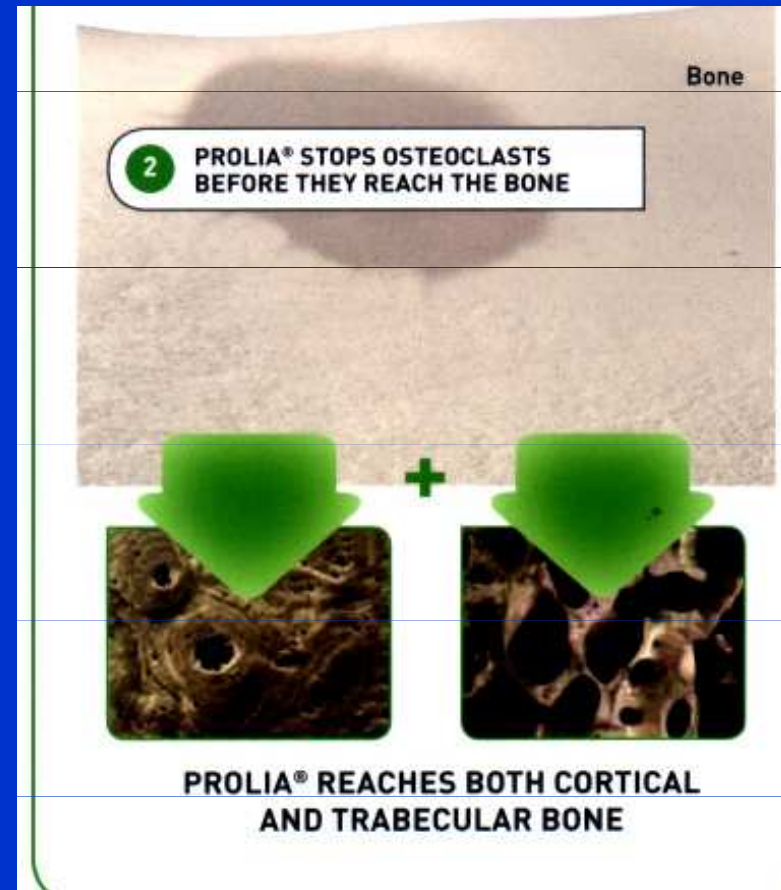
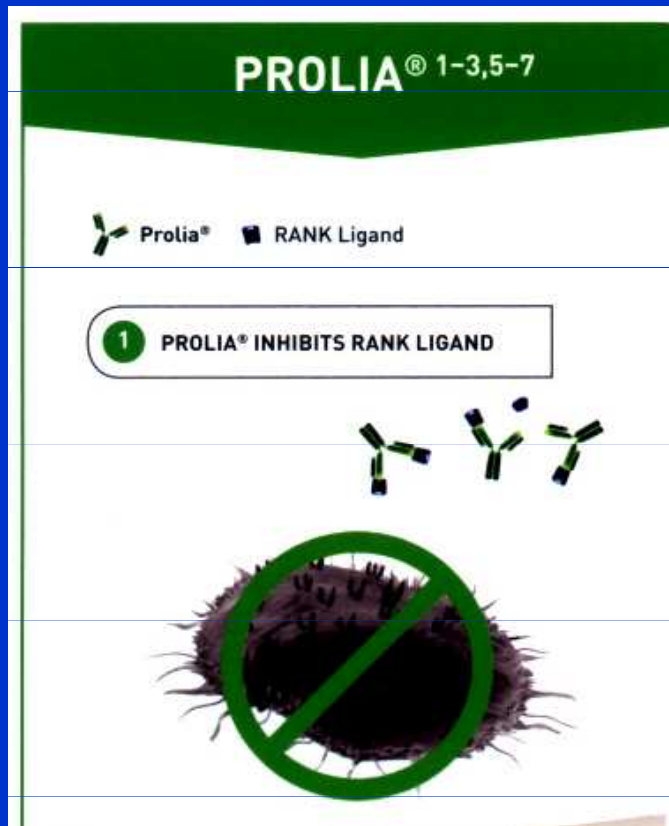


Denosumab

Zvyšuje pevnost svalku

Opožděná remodelace

Denosumab *není* asociován se zpomaleným hojením nonvertebrálních zlomenin



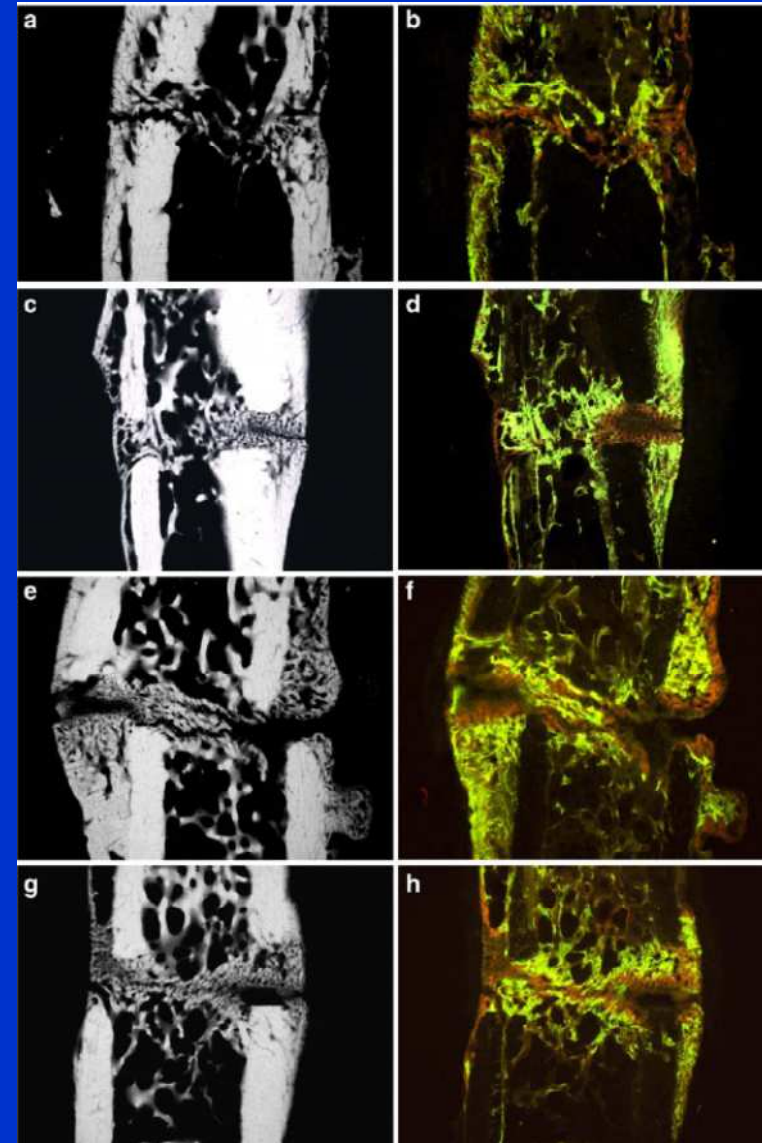
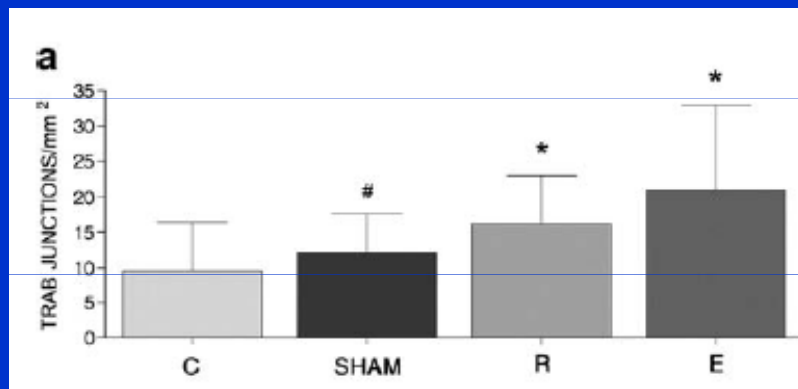
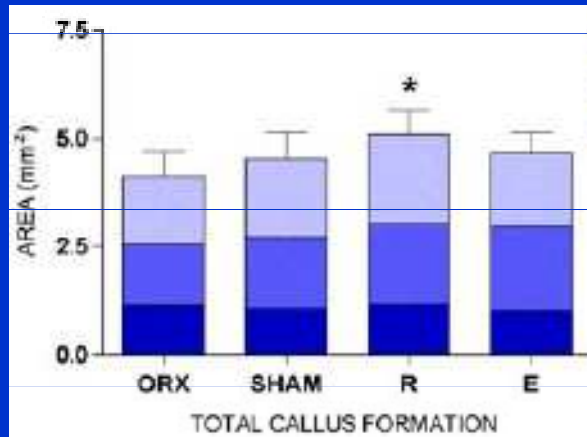
Estrogens, SERM

Langenbecks Arch Surg (2010) 395:163–172
 DOI 10.1007/s00423-008-0436-x

ORIGINAL ARTICLE

Estrogen and raloxifene improve metaphyseal fracture healing in the early phase of osteoporosis. A new fracture-healing model at the tibia in rat

E. K. Stuermer · S. Schmisch · T. Rack · E. Wenda ·
 D. Seidlova-Wuttke · M. Tezval · W. Wuttke ·
 K. H. Frosch · K. M. Stuermer



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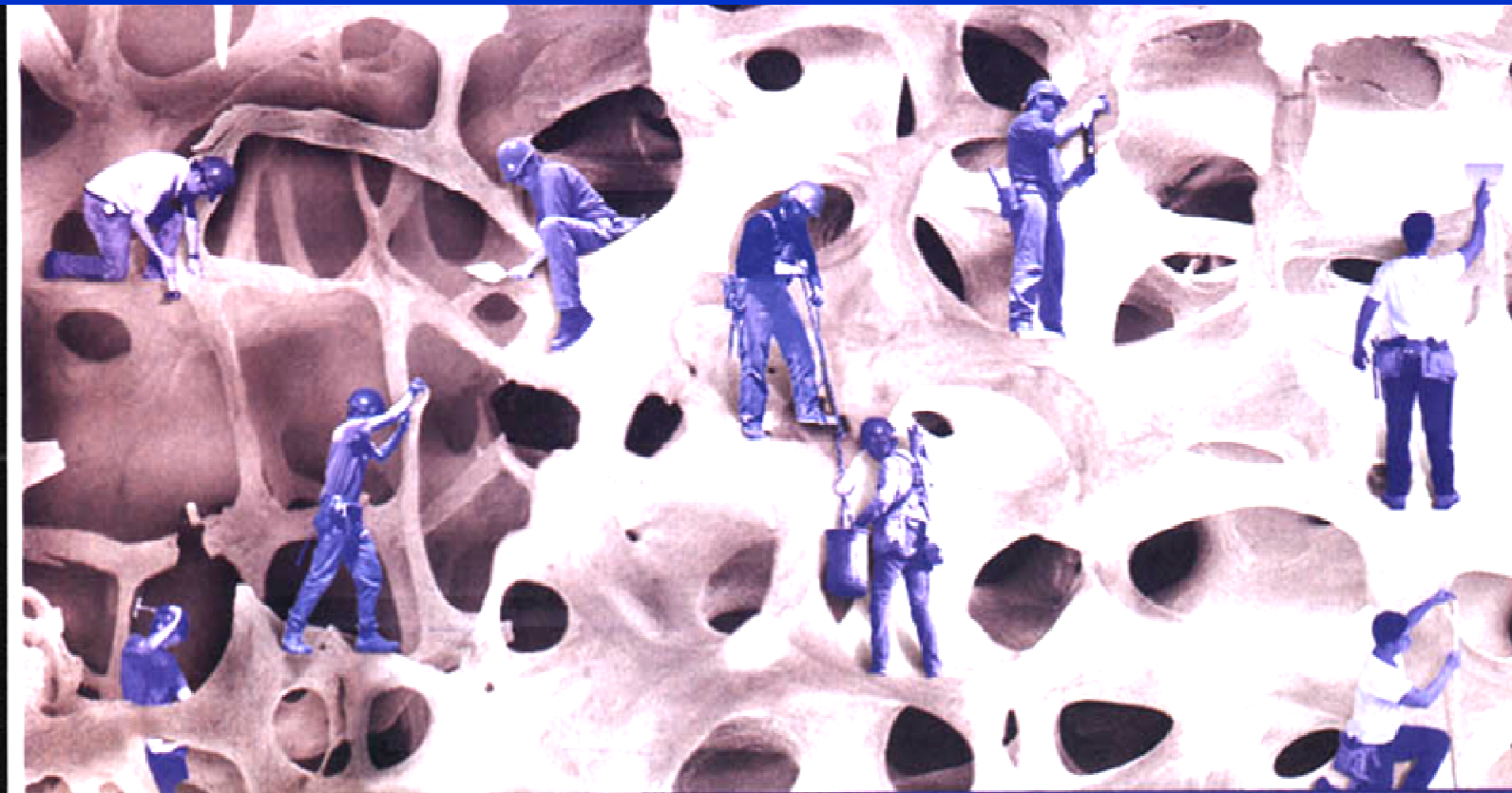
Teriparatide

Zvyšuje tvorbu svalku

Zvyšuje objem, mineralizaci a obsah buněk
ve svalku

Zvyšuje pevnost svalku

vč. pevnosti a tuhosti v torzi



Parathyroid Hormone 1-84 Accelerates Fracture-Healing in Pubic Bones of Elderly Osteoporotic Women

Peter Peichl, MD, Lukas A. Holzer, MD, Richard Maier, MD, and Gerold Holzer, MD

TABLE II Fracture-Healing, VAS Score, and Timed "Up and Go" Test

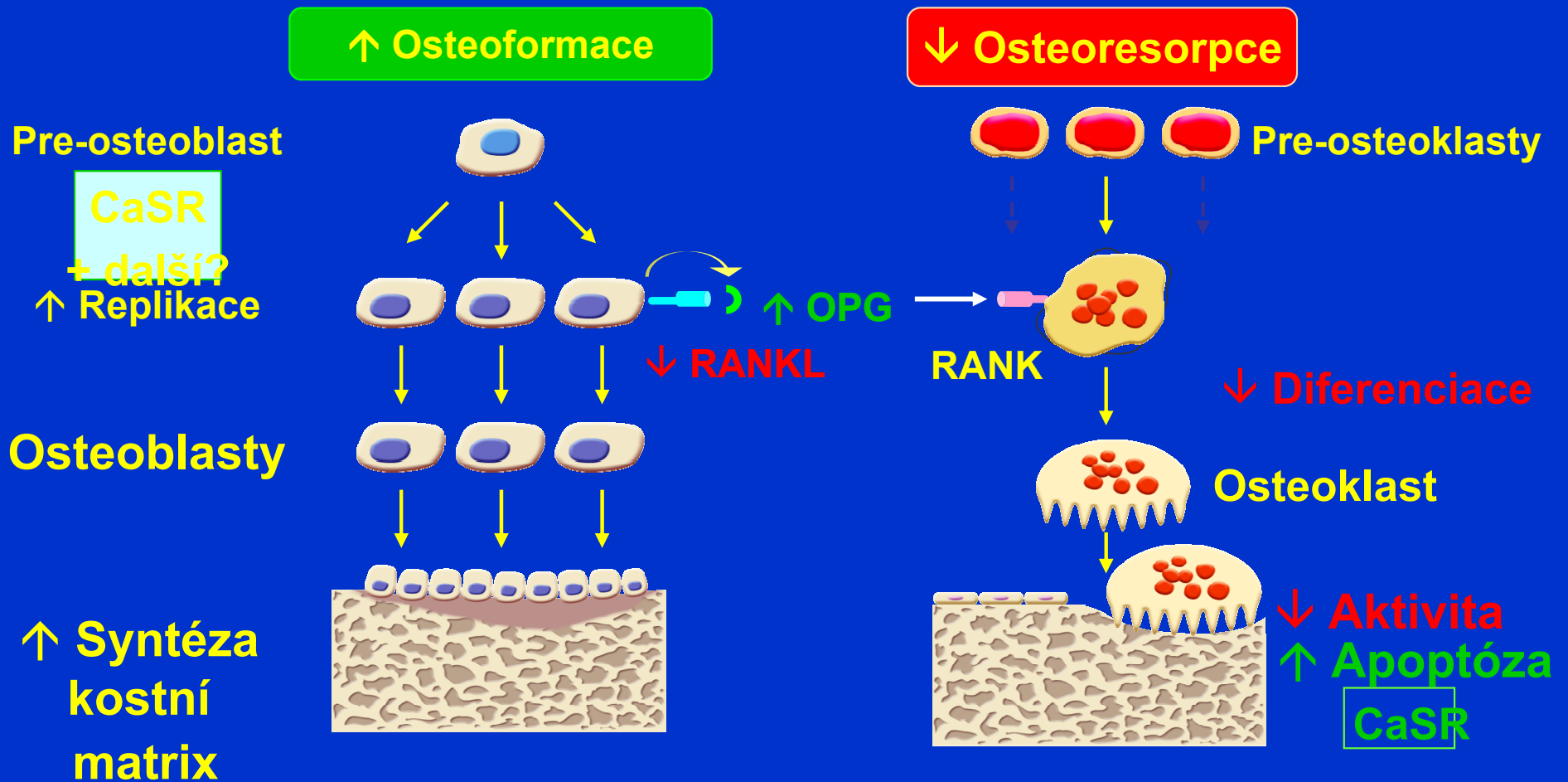
	PTH 1-84 Treatment Group (n = 21)	Control Group (n = 44)	P Value
Fracture-healing			
Week 4*	1 (4.8%)	0 (0%)	0.145†
Week 8*	21 (100%)	4 (9.1%)	<0.001†
Week 12*	21 (100%)	30 (68.2%)	0.004†
VAS score‡			
Week 0	7.6 ± 1.1	7.7 ± 1.1	0.743§
Week 8	3.2 ± 1.0	6.5 ± 0.9	<0.001§
Timed "Up and Go" at Week 12‡ (s)	22.9 ± 7.7	54.3 ± 19.9	<0.001§

*The values are given as the number of fractures, with the percentage in parentheses. †Chi-square test. ‡The values are given as the mean and the standard deviation. §Mann-Whitney U test.

Conclusions: In elderly patients with osteoporosis, PTH 1-84 accelerates fracture-healing in pelvic fractures and improves functional outcome.

Stroncium ranelate

Mechanismus účinku



Stroncium ranelate

Pozitivní efekt v prevenci vzniku další zlomeniny

Vyšší kvalita kostního svalku

Lepší vhojování implantátu

Rychlejší hojení zlomenin

Vyšší kvalita nově tvořené kosti

PROTELOS[®] 2g
Stroncium-ranelát

Unikátní duální mechanismus účinku^{1,2}
zvysuje kostní formaci a současně redukuje kostní resorpci

Snižuje riziko vzniku osteoporotické zlomeniny^{3,4}
obratlů i kyčle

NOVINKA
V LÉČBĚ
POSTMENOPAUZÁLNÍ
OSTEOPOROZY

PROTELOS[®] 2g
28 sáčků

Zkrácená informace o přípravku:
PROTELOS[®] 2g je kombinací stroncia a ranelátu.

Case report

Ž, 57 r.

Repozice, sádr. fixace

30 dnů po úraze

- nedostatečná tvorba svalku

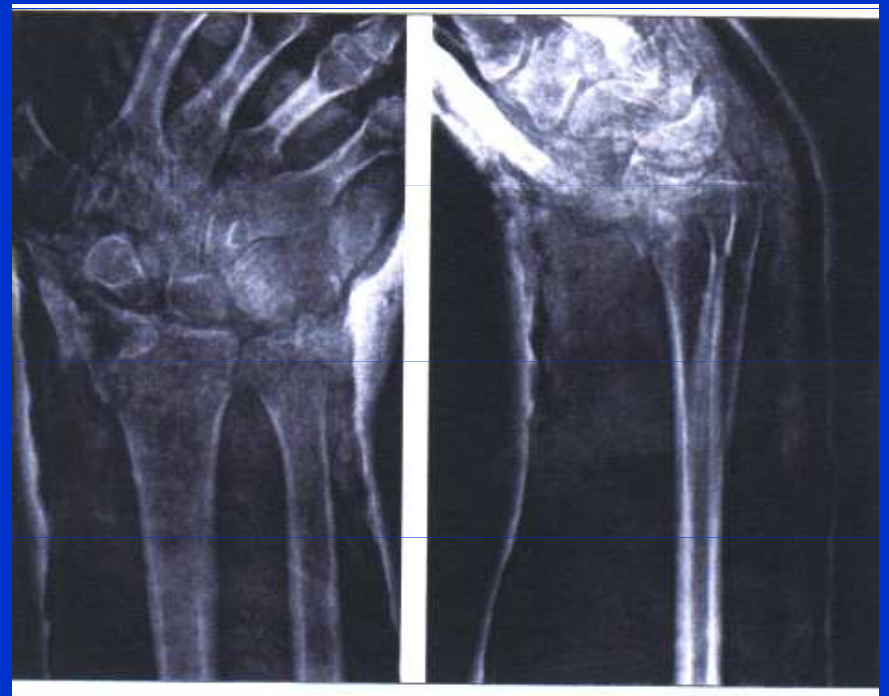
- DXA osteopenie

Plastová sádra

Calcium 1200 mg/den

Vit D. 800 IU

SR 2 g/ den



Case report

Po 30 dnech léčby



Case report

Po 60 dnech léčby



News in osteoporosis

Rozkydal, Z.

I. ortopedická klinika MU

FN u sv. Anny v Brně

1. Diagnostic tools

DXA

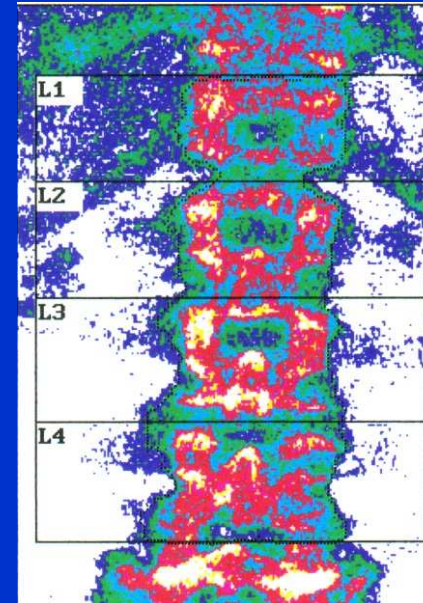
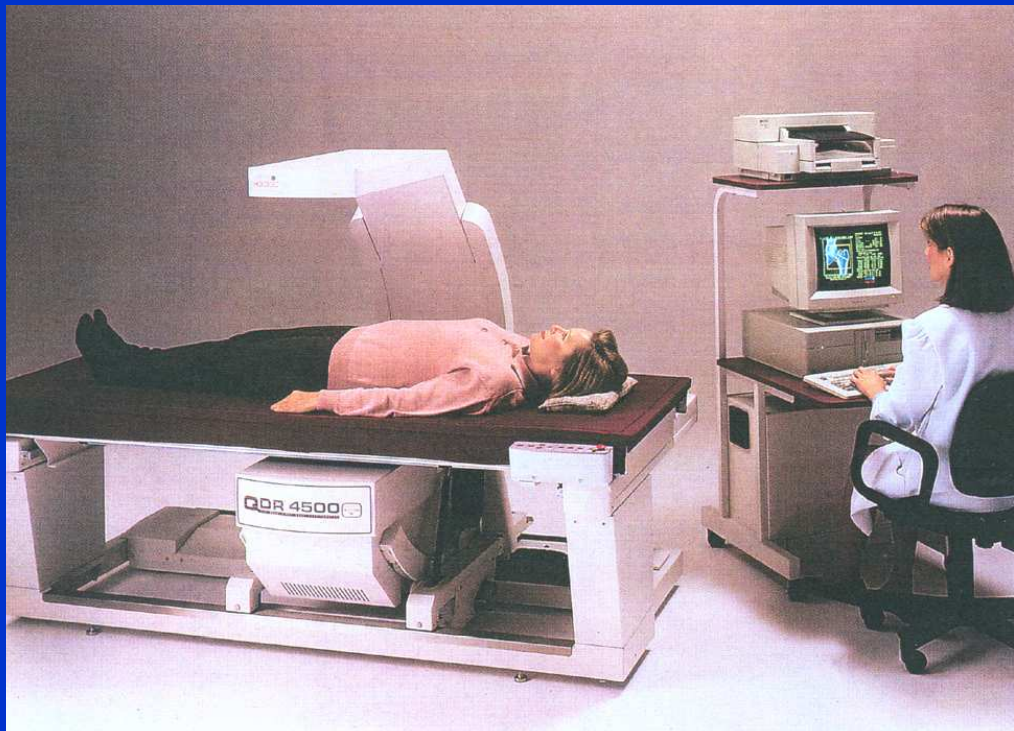
FRAX

Laboratory tests

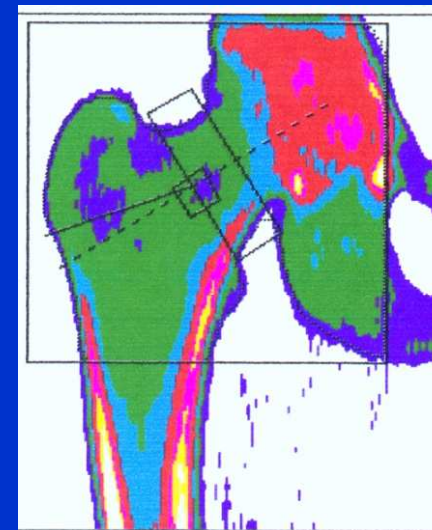
Imaging methods

DXA – Dual Energy Absorptiometry

BMD v g/cm^2
T score
Z score
Change



L1-L4



Hip Total

Hip neck

Wrist

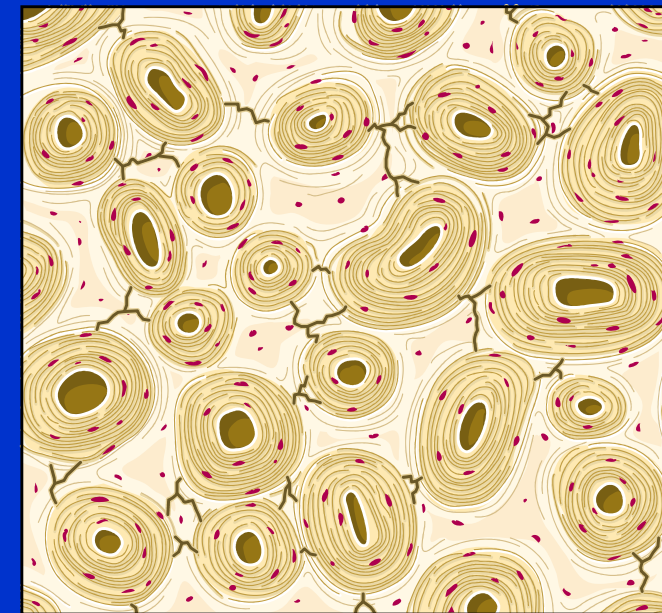
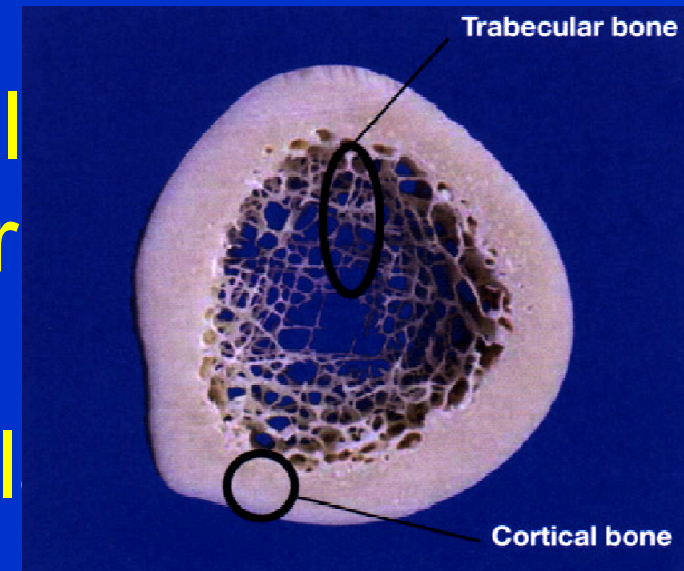
Strength of bone

Density from BMD predicts only 60-75 % of mechanical power

Quality of cortical and trabecular collagen and bone mineral

Cumulation of microdamage and microfractures

Remodelation of bone:
-permanent removal of old



Microcracks

FRAX

FRAX

- fracture risk assessment tool
- 10 year risk of a major fracture

FRAX[®] WHO Fracture Risk Assessment Tool

HOME CALCULATION TOOL PAPER CHARTS FAQ REFERENCES

Calculation Tool

Please answer the questions below to calculate the ten year probability of fracture with

Country: **UK** Name / ID : [About the risk factors](#)

Questionnaire:

1. Age (between 40-90 years) or Date of birth
Age: Date of birth: Y: M: D:

2. Sex Male Female

3. Weight (kg)

4. Height (cm)

5. Previous fracture No Yes

6. Parent fractured hip No Yes

7. Current smoking No Yes

8. Glucocorticoids No Yes

9. Rheumatoid arthritis No Yes

10. Secondary osteoporosis No Yes

11. Alcohol 3 or more units per day No Yes

12. Femoral neck BMD (g/cm²)
T-Score

BMI 20.2
The ten year probability of fracture (%)

with BMD

Major osteoporotic	23
Hip fracture	5.5

Clinical data

Age

Sex

Weight

Height

Sustained fractures

Fracture in parents

Smoking

Alcohol 3 or more units/day

Corticosteroids

Reumathoid arthritis

Secondary osteoporosis

Combination DXA + FRAX

Laboratory tests

Calcium

Phosphorus

ALP, bone isoemzyme of ALP

Vitamin D normal level: 20-80 ng/ml

Parathormon

Osteocalcin

CTX- C terminální peptid kolagenu

NTX- N terminální telopeptid kolagenu

Pyridinolin, deoxypyridinolin

Acid phosphatase

Normal calcium 2,0 – 2,75 mmol/l

Normal phosphorus 0,7- 1,5 mmol/l.

Bone formation

ALP normal level 2,7 ukat/l in man and 2,3 ukat/l in woman.

- indicator of osteoblasts function. Marker of bone formation.

High levels in osteomalacia !!

Bone isoenzyme ALP- marker of bone formation.

Osteocalcin 3,4- 11,7 ng/ml in men, and 2,4- 10,0 ng/ml in women.

C terminal propeptide of collagen I (PICP)

N terminal propeptide of collagen I (PINP) - products of collagen synthesis

Bone resorption

Tartrate resistant acid phosphatase – marker of bone resorption

Pyridinolin and deoxypyridinolin (crosslinks)
- marker of collagen degradation

CTx- (C terminal peptid of collagen I)

NTx (N-terminal peptid of collagen I)

- products of proteolytic resorption of collagen in bone

Diagnostic tools

HR- pQCT

Pair biopsies- histology, histomorfometry
2 D micro CT, microindentation
SEM

Finite element analysis

Raman microspectroscopy

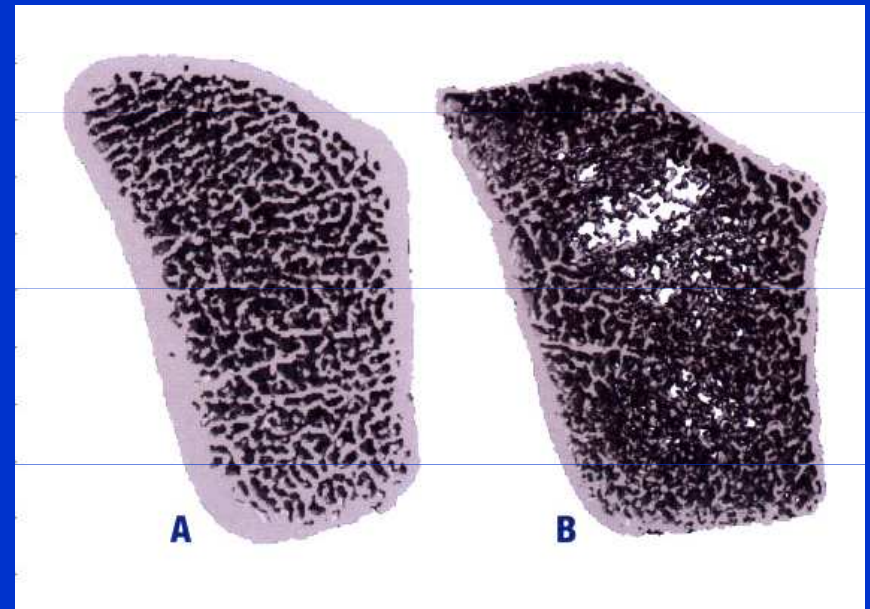
HR- pQCT

High resolution, peripheral,
quantitative CT

Noninvasive measurement
of bone morphology

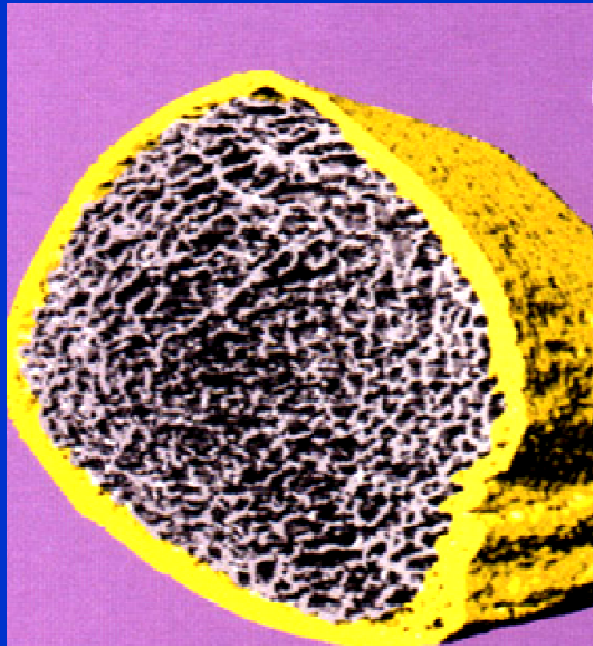
Virtual biopsy

Assess microarchitecture
up to 82 μm



Xtreme CT

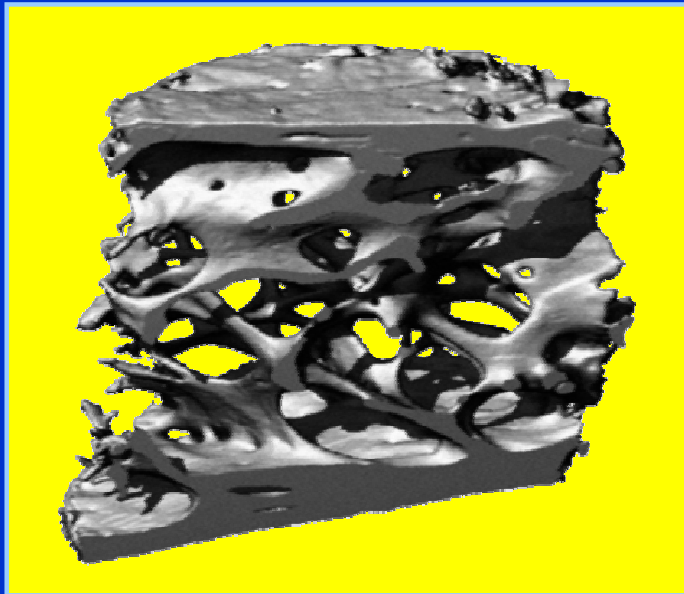
Assess thickness
of cortical bone



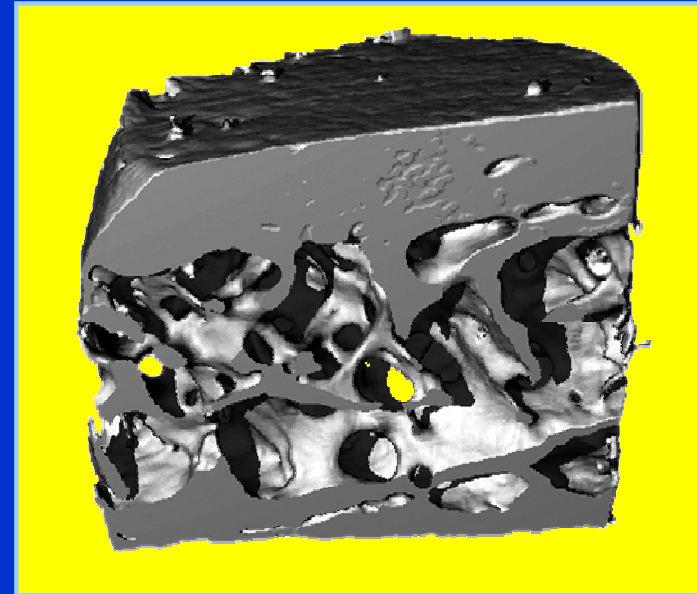
SCANCO
Xtreme CT
HR qCT

Pair biopsies- before and after treatment

Placebo 36 months



PROTELOS 36 months



Thickness of cortical bone	+ 18 %	$p=0,008$
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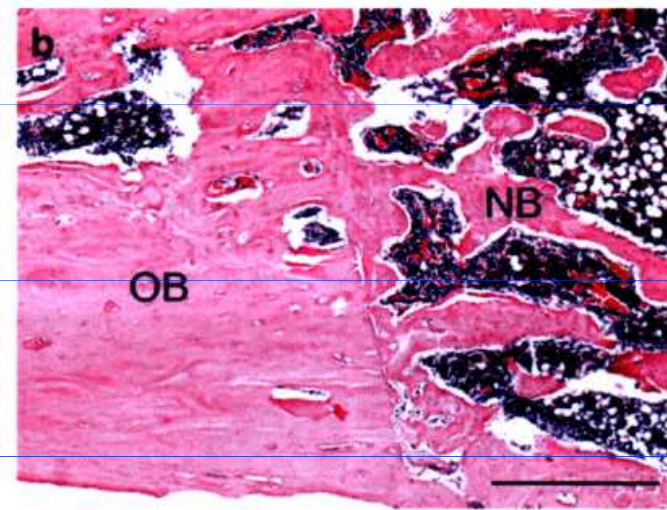
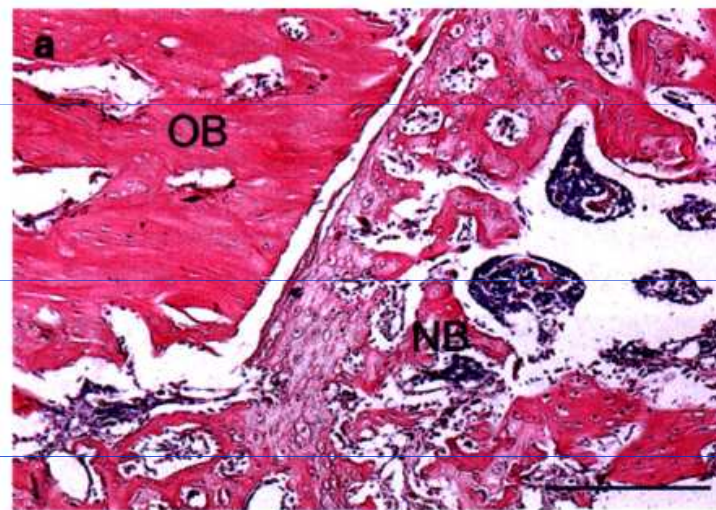
Number of trabeculae	+ 14 %	$p=0,05$
----------------------	--------	----------

Histology

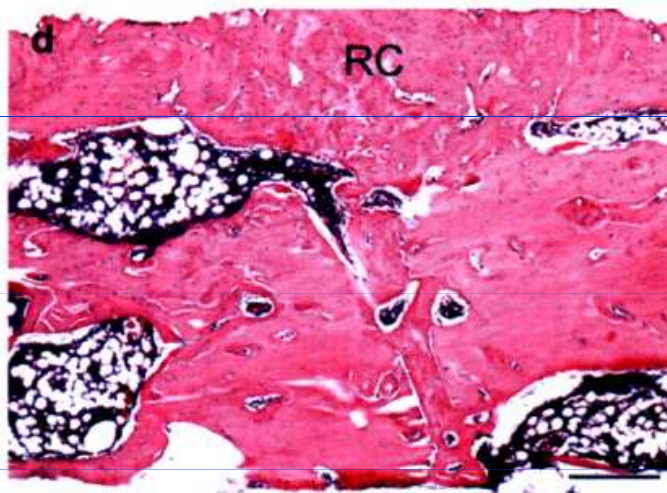
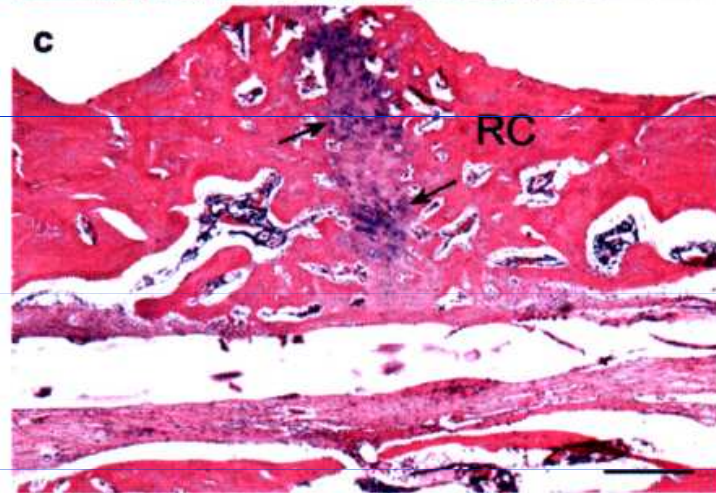
Kontrola

OVX a SR

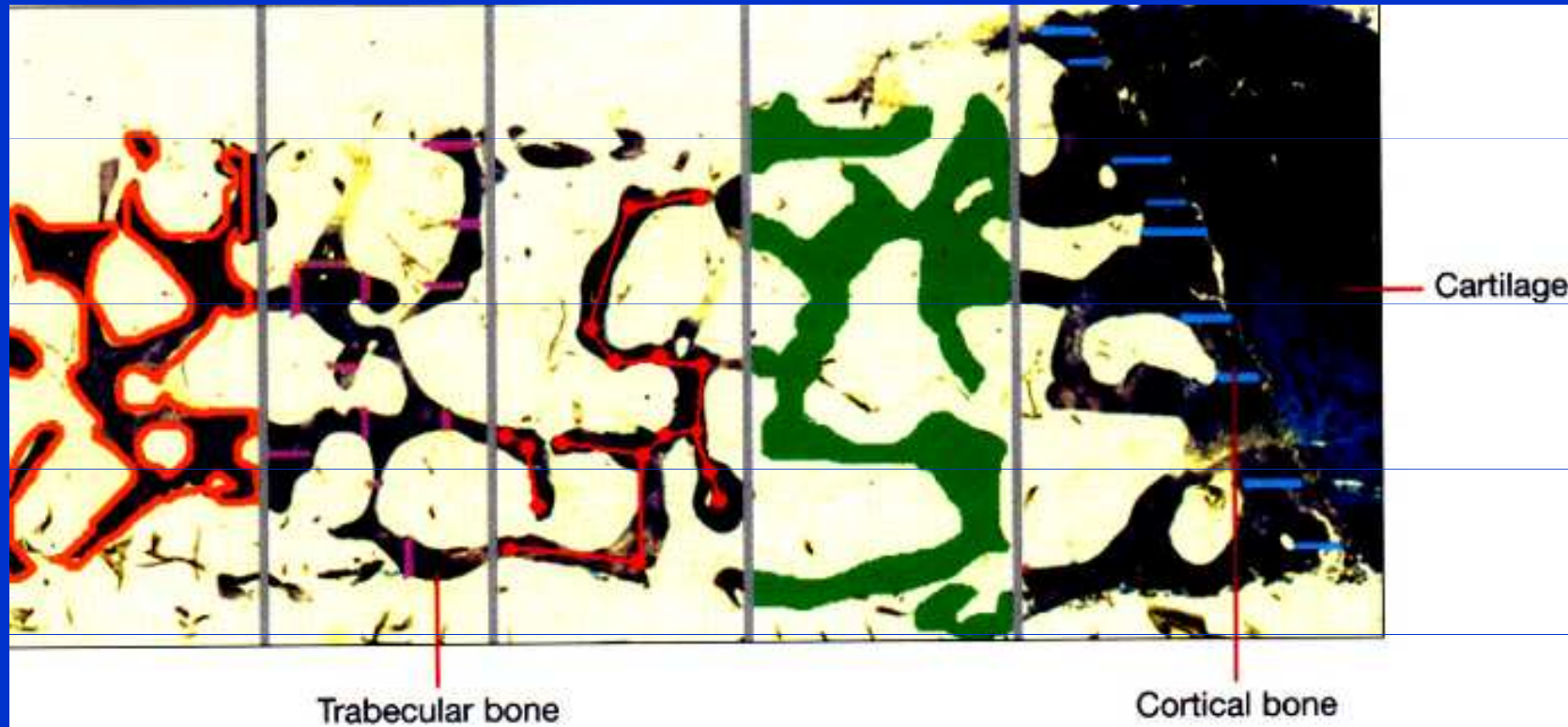
4 t.



8 t.

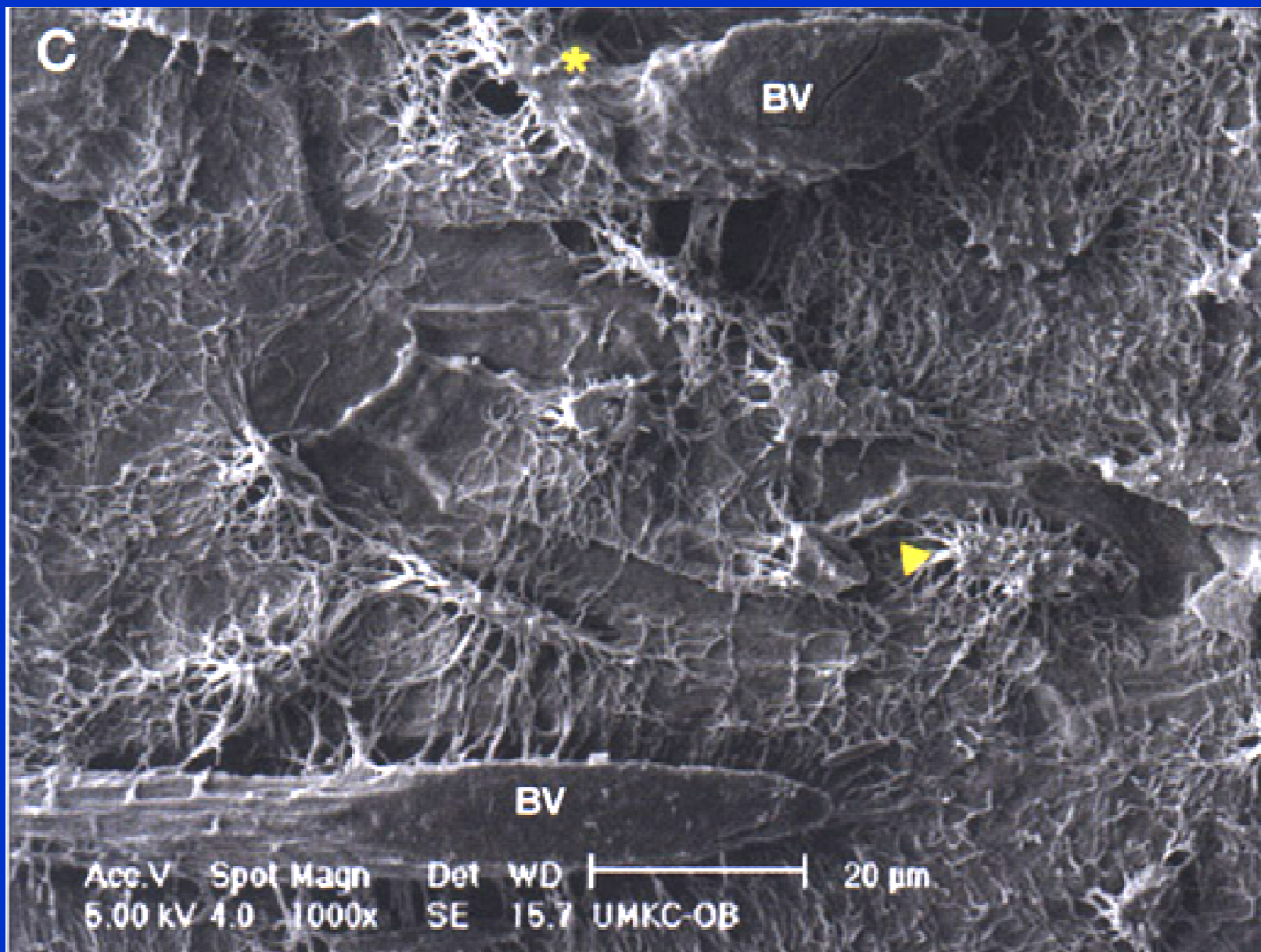


Histomorfometry



Povrch kosti
Mineralizovaný povrch
Erodovaný povrch
Tloušťka trabekul

Konektivita trámců
Trabekulární objem
Kortikální tloušťka



SEM: canaliculi between osteocytes

FEA- finite element analysis

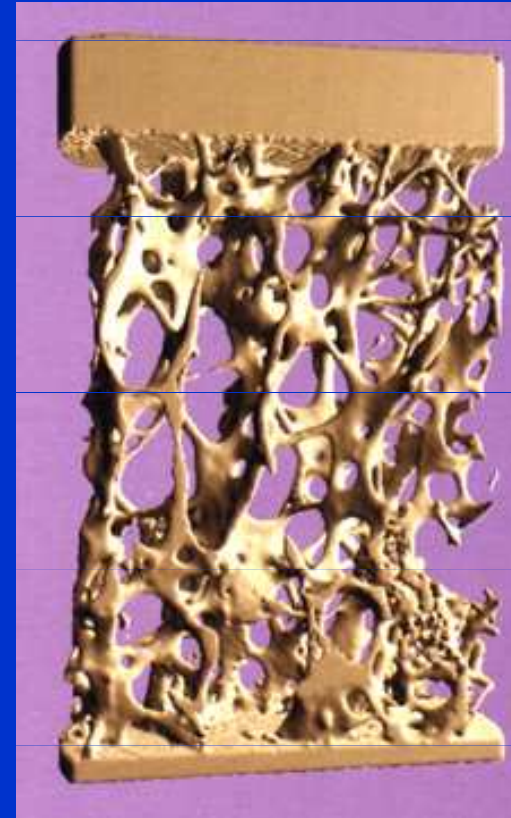
Trabecular bone (upto 82 μm)

Healthy bone



Plates

Osteoporotic bone

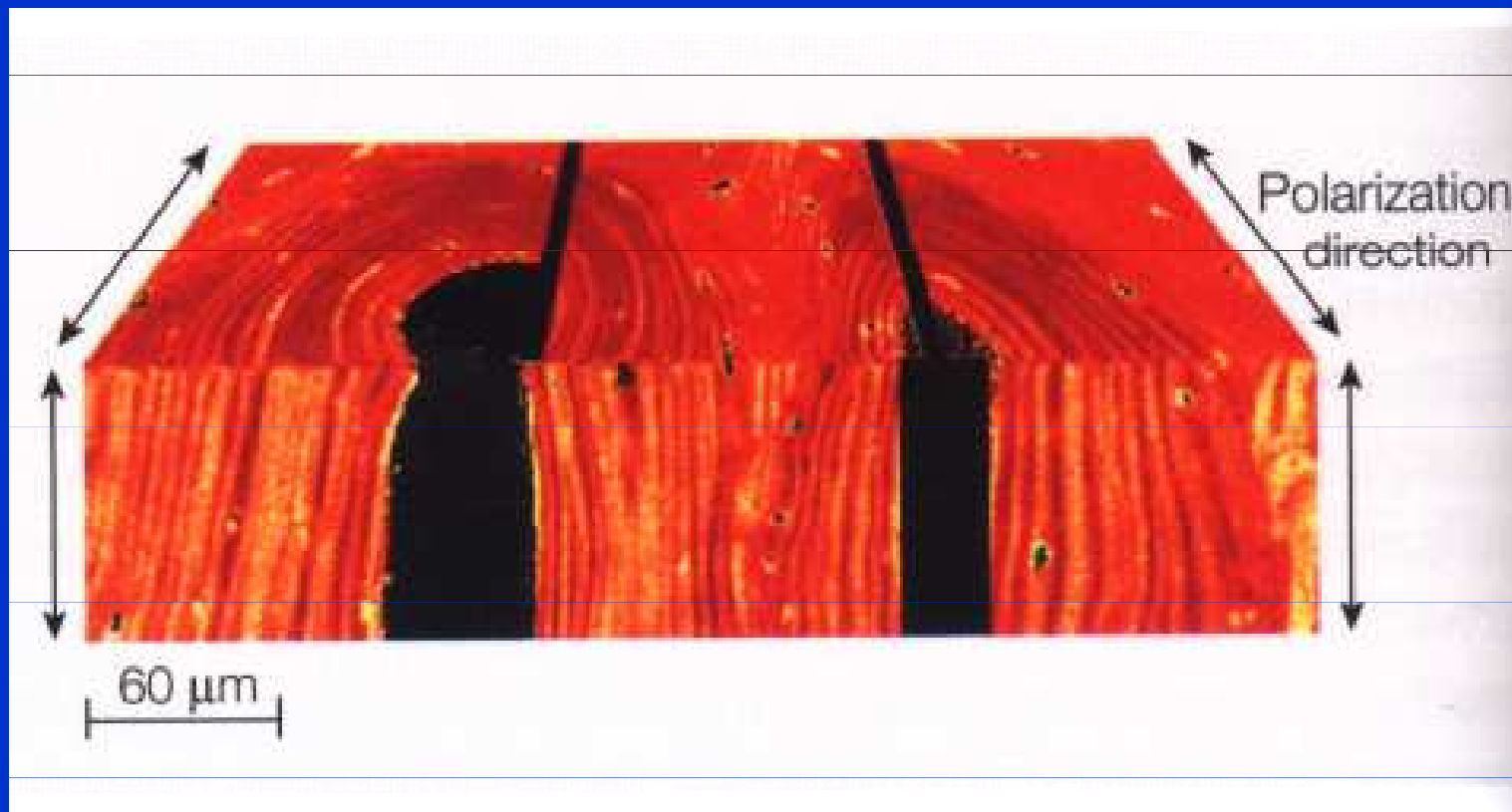


Rods

Raman microspectroscopy - cortical porosity

Increases after 40 years of age

- begins with resorption around Havers canal



Raman microspectroscopy

2. Frailty syndrom

1. Loss of weight 4-5 kg/year
2. Exhaustion
3. Muscle weakness / handgrip more than 20 %
4. Lower velocity of gait less than 20 %
5. Lower physical activity less than 20 %

Frailty syndrom

Subclinicaly

Early frail

Late frail

Endstage frailty syndrom: terminal geriatric deterioration

Frailty syndrom

Disposition to falls

Disposition to organ decompensation

Worsening of cognitive functions

Need for help in daily activities

Sarcopenia

Osteoporosis

Low level of vitamin D

Occurrence

Advanced age

7 % persons over 65 years

25 % persons over 75 years

Loss of muscle power 20 % in 65-70 years

Loss of muscle power 60 % in 80 years

Cause: longlasting deficiency of vitamin D

Risk factors of frailty syndrom

Cardiovascular disease

Diabetes mellitus

Atherosclerosis

Renal failure

Neurologic disorders

Obesity

Hormonal dysfunction

Hypovitaminosis D

Prevention and treatment of frailty syndrom

Frailty syndrom is reversible

Nutrition and proteins 1,3 g/kg/day

Vit D 800 IU/day till 2000 IU/day

Vigantol 1 drop = 500 IU, alpha kalcidol 1 μ g

Strengthening of muscles, exercise, walking

Strengthening of stability, prevention of falls

Prevention of atherosclerosis

Management of other comorbidities

Aleviating of pain

Stop walking when talking

3. Sarcopenia

Loss of muscle substance more than 20-30 %

Dysbalance between synthesis and degradation of muscles
(myostatin, glucocorticoids, sexual hormones, insulin, IGF-I)

Osteopenia

Sedentary way of life

Sarcopenia

Muscle densitometry: below 2 SD – man under 7,26 kg/m²
- woman under 5,45 kg/m²

MRI

Hand grip- dynamometr

Flexion- extension of the knee

Maximal forced breathing out

Velocity of gait

Test of balance

Get up and go test

Walking on stairs

Consequenses of sarcopenia

Lower physical activity (myosteatorosis, sarcopenic obesity)

Sarcoporosis

Higher risk of falls

Risk factors for developing of sarcopenia:

Parkinson sy, multiple sclerosis, CVA, catarracta

Medication

Vit D 800 IU/day till 2000 IU/day

Vigantol 1 drop= 500 IU

Alpha kalcidol 1 μg

Testosteron

Ghrelin

GH secretogoga

Estrogens

Leptin

4. Management

Farmacotherapy of osteoporosis
diminishes risk of fragility fractures
only 20-50 %

- + frailty syndrom
- + sarcopenia
- + osteoarthritis
- + other comorbidities
- + prevention of falls



Medication

Bisphosphonates:

Alendronate (Fosava)

Risedronate (Actonel)

Ibandronate (Bonvivon)

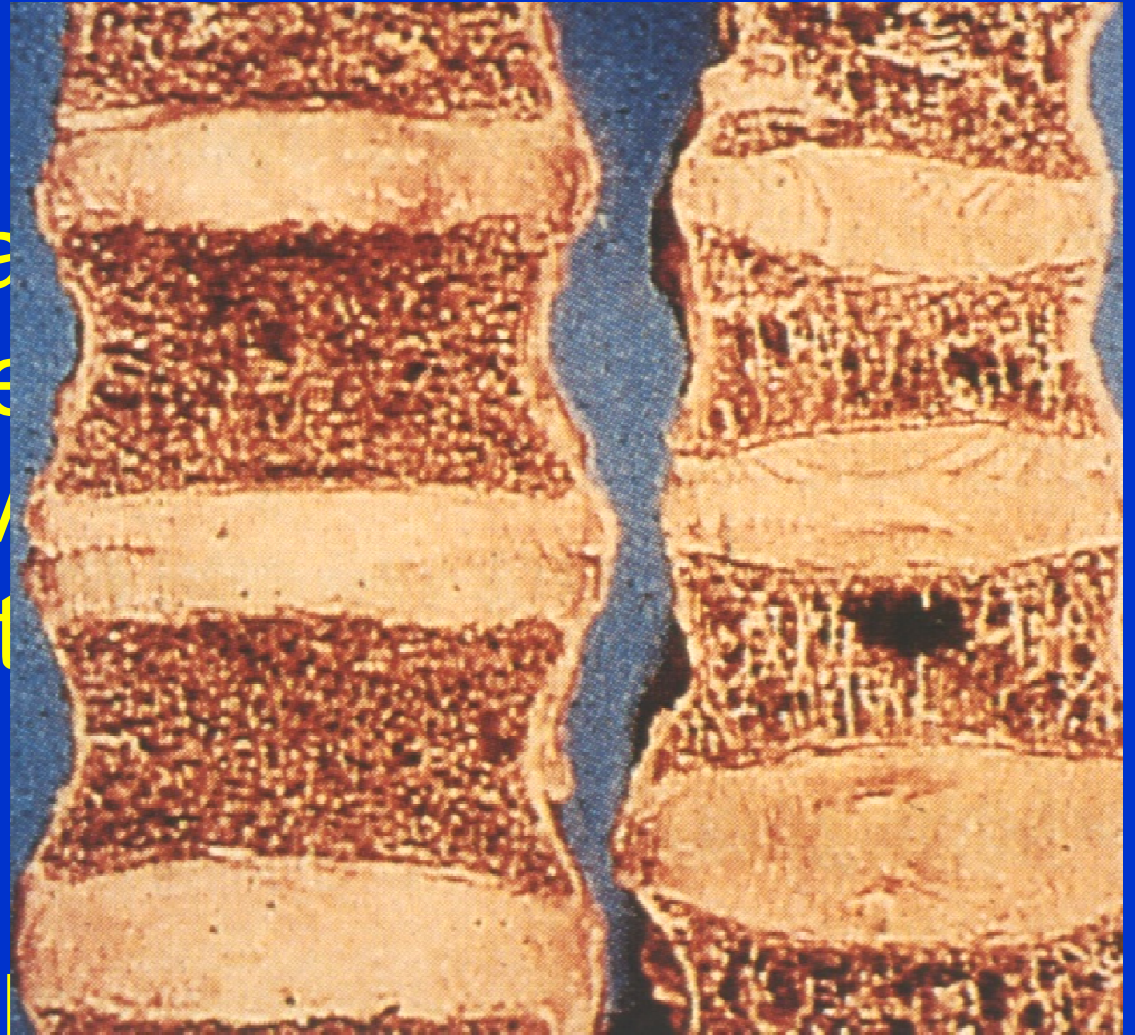
Zoledronate (Aclasta)

Denosumab (Prolia)

Strontium ranelate (Protelos)

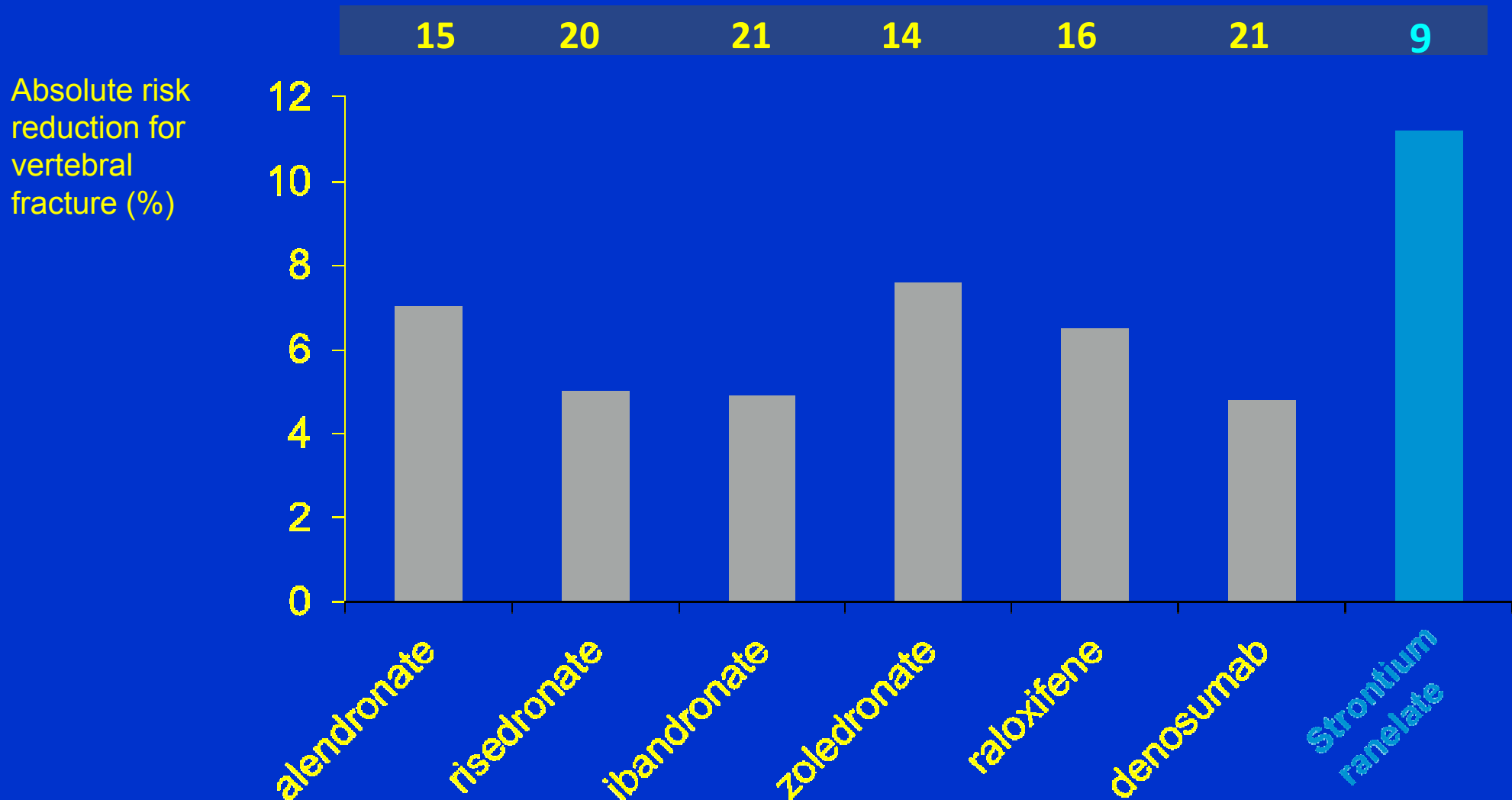
Parathormon, teriparatid

(Forteo)



Protection to prevent vertebral fractures

Corresponding NNT



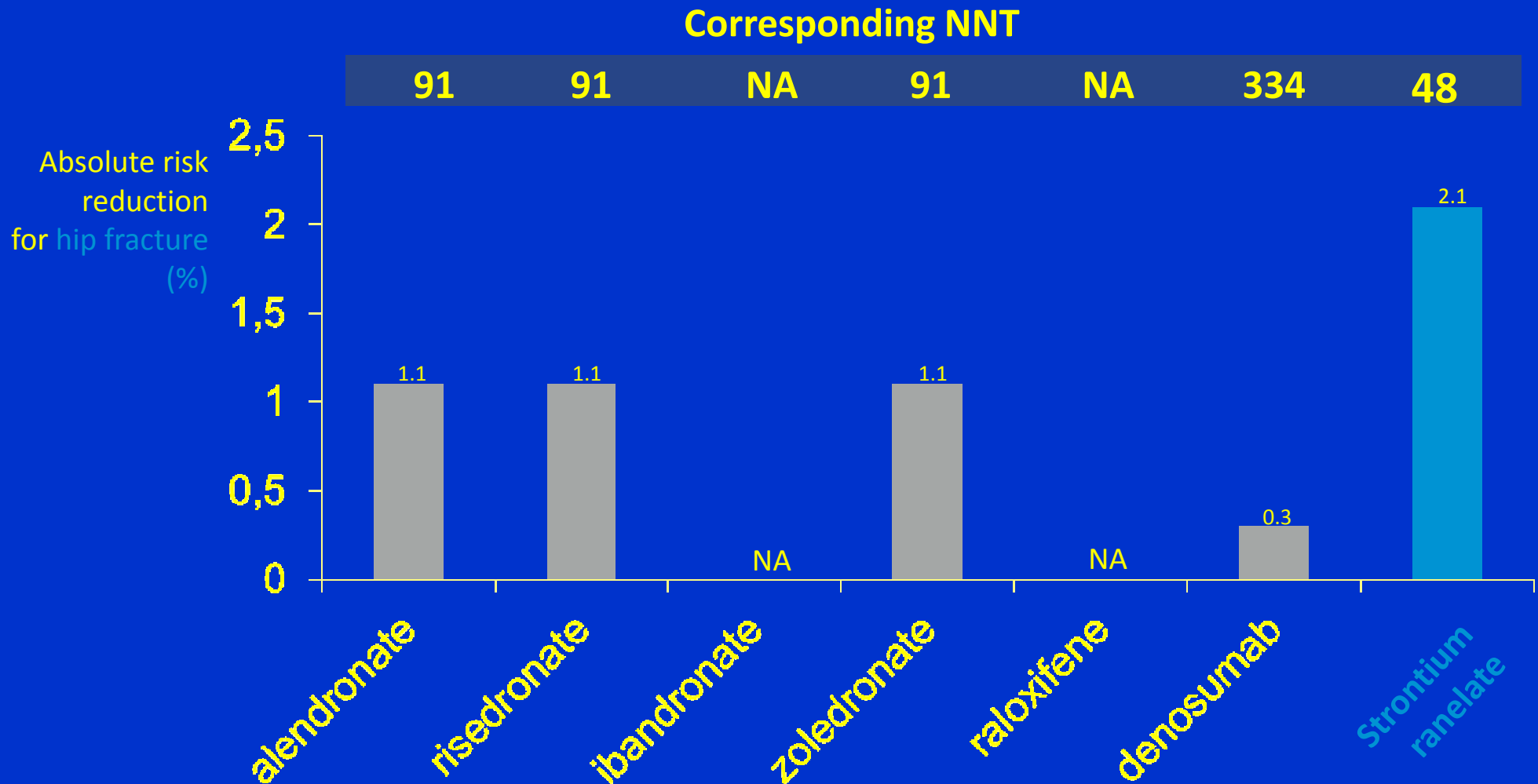
Comparison of antifracture efficacy

Vertebral fracture

Treatment	Study	Fracture incidence (%)		RRR (%)	ARR (%)	NNT
		placebo	treatment			
Alendronate	FIT 1	15.0	8.0	47	7.0	15
Risedronate	VERT-NA	16.3	11.3	41	5.0	20
Risedronate	VERT-MN	29.0	18.1	49	10.9	10
Ibandronate	BONE	9.6	4.7	62	4.9	21
Zoledronic acid	HORIZON	10.9	3.3	70	7.6	14
Denosumab	FREEDOM	7.2	2.3	68	4.8	21
Raloxifene	MORE	21.2	14.7	30	6.5	16
Lasofloxifene ^b	PEARL	9.5	5.7	40	3.9	26
Bazedoxifene	No acronym	4.1	2.3	42	1.8	56
Teriparatide	FPT	14.0	5.0	65	9.0	12
Strontium ranelate	SOTI	32.8	20.9	41	11.9	9

ARR= absolute risk reduction; NNT= number needed to treat (to prevent one event over 3 years);
NS = not statistically significant; RRR= relative risk reduction.

Protection to prevent hip fractures



Comparison of antifracture efficacy

Hip fracture

Treatment	Study	Fracture incidence (%)		RRR (%)	ARR (%)	NNT
		placebo	treatment			
Alendronate	FIT 1	2.2	1.1	51	1.1	91
Risedronate	HIP	3.9	2.8	30	1.1	91
Zoledronic acid	HORIZON	2.5	1.4	41	1.1	91
Denosumab	FREEDOM	1.2	0.7	40	0.3	334
Lasofoxifene ^a	PEARL	1.2	0.9	N.S.		
Strontium ranelate	TROPOS	6.4	4.3	36	2.1	48

a Data over 5 years.

ARR= absolute risk reduction; NNT= number needed to treat (to prevent one event over 3 years);
NS = not statistically significant; RRR= relative risk reduction.

Reginster JY et al. *Drugs* 2011; 71(1):65-78

New agents

Monoclonal sclerostin antibodies

Romosozumab

Blosozumab

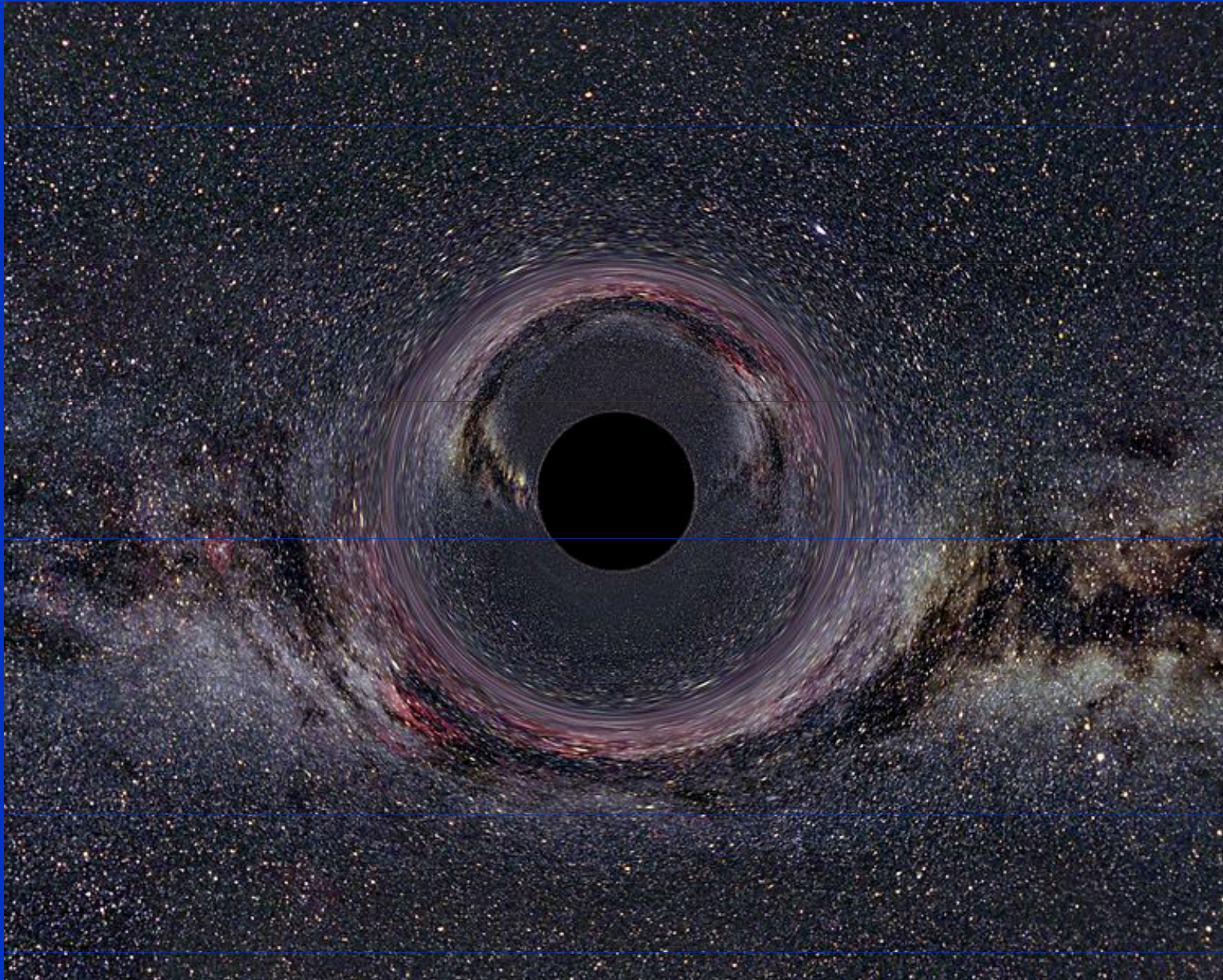
Osteoformative effect

Sclerostin – inhibitor of osteoblasts

production from osteocytes

stimulates bone resorption via

Thank You for Your attention



Black Hole of the Milky Way