

# News in osteoporosis

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# 1. Diagnostic tools

DXA

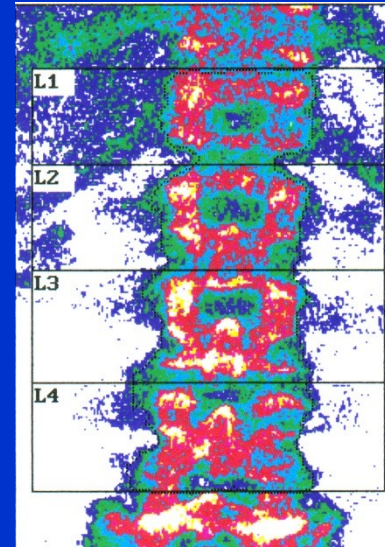
FRAX

Laboratory tests

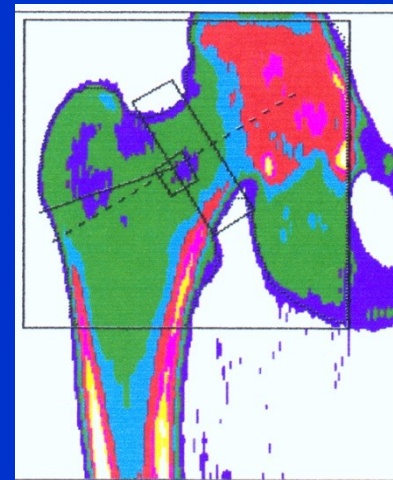
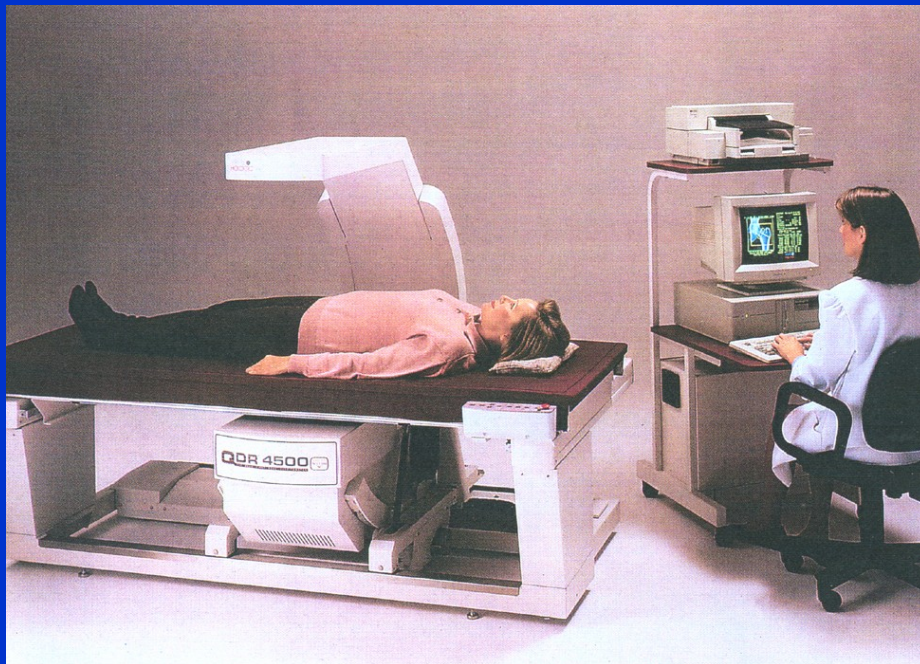
Imaging methods

# DXA – Dual Energy Absorptiometry

BMD v  $\text{g}/\text{cm}^2$   
T score  
Z score  
Change



L1-L4



Hip Total

Hip neck

Wrist

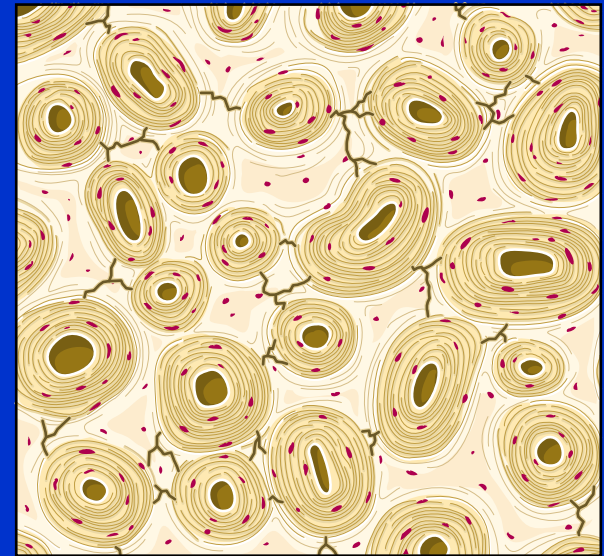
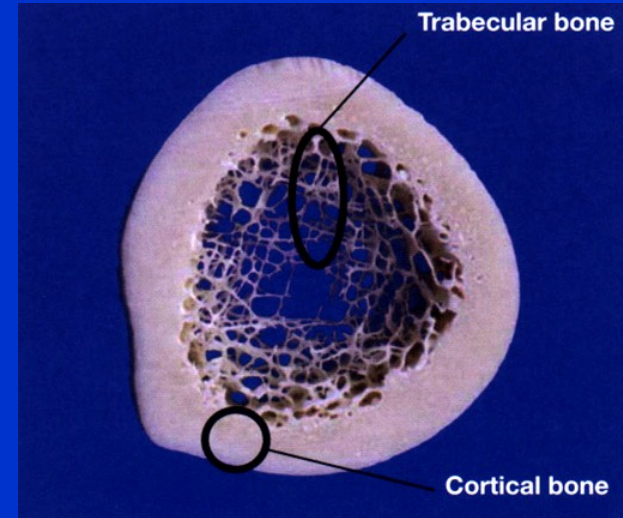
# Strength of bone

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

Quality of cortical and trabecular bone,  
collagen and bone mineral

Cumulation of microdamage  
and microfractures

Remodelation of bone:  
-permanent removal of old  
and damaged bone



Microcracks

# FRAX

## FRAX

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

The screenshot shows the FRAX WHO Fracture Risk Assessment Tool interface. The header includes the FRAX logo and navigation tabs: HOME, CALCULATION TOOL, PAPER CHARTS, FAQ, and REFERENCES. The main heading is "Calculation Tool". Below this, there is a prompt: "Please answer the questions below to calculate the ten year probability of fracture with".

On the left side, there are two conversion tools: "Weight Conversion" (pound to kg) and "Height Conversion" (inch to cm), both with "convert" buttons. A UK flag is displayed above the questionnaire.

The questionnaire consists of 12 questions:

- Age (between 40-90 years) or Date of birth: Age: 65, Date of birth: Y: M: D:
- Sex:  Male  Female
- Weight (kg): 55
- Height (cm): 165
- Previous fracture:  No  Yes
- Parent fractured hip:  No  Yes
- Current smoking:  No  Yes
- Glucocorticoids:  No  Yes
- Rheumatoid arthritis:  No  Yes
- Secondary osteoporosis:  No  Yes
- Alcohol 3 or more units per day:  No  Yes
- Femoral neck BMD (g/cm<sup>2</sup>): T-Score: -2.3

At the bottom right, a red box displays the results: "BMI: 20.2", "The ten year probability of fracture (%):", and a table showing "Major osteoporotic" at 23% and "Hip fracture" at 5.5%. A "View NÖGG Guidance" button is also present.

## 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

**Vitamin D** 40-80 ng/ml, under 20 ng/ml – advances hypovitaminosis

**Parathormon** normal level 10-65 ng/ml.



# Diagnostic tools

HR- pQCT

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

Finite element analysis

Raman microspectroscopy

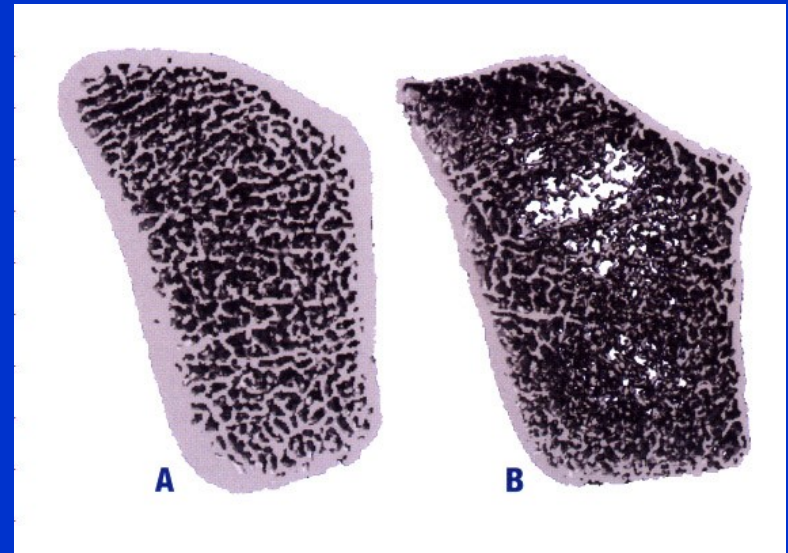
# HR- pQCT

High resolution, peripheral, quantitative CT

Noninvasive measurement of bone morphology

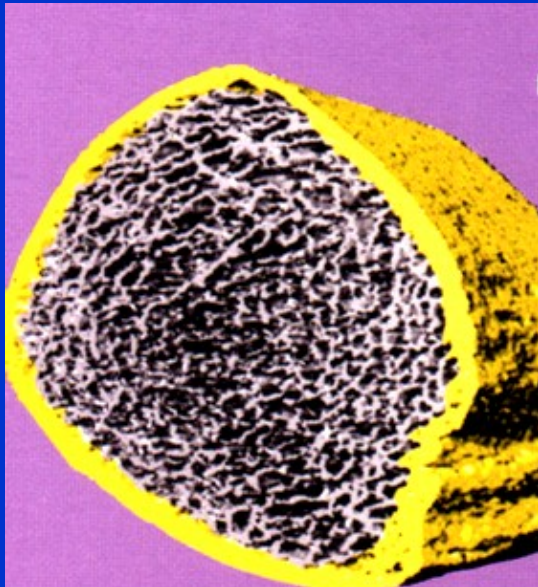
Virtual biopsy

Assess microarchitecture up to  $82\ \mu\text{m}$



# Xtreme CT

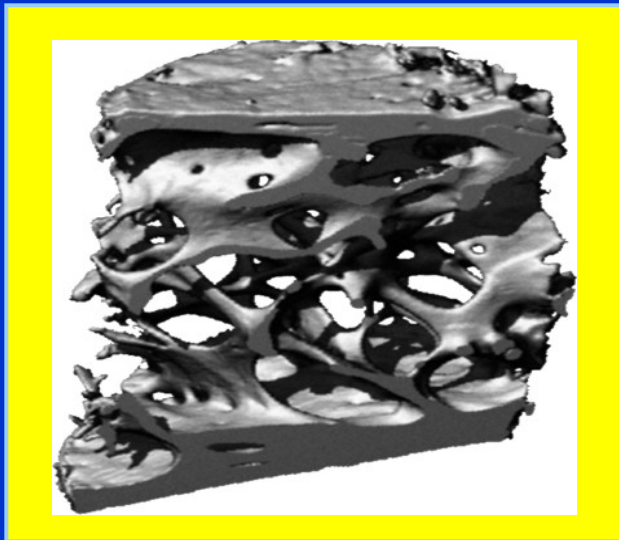
Assess thickness  
of cortical bone



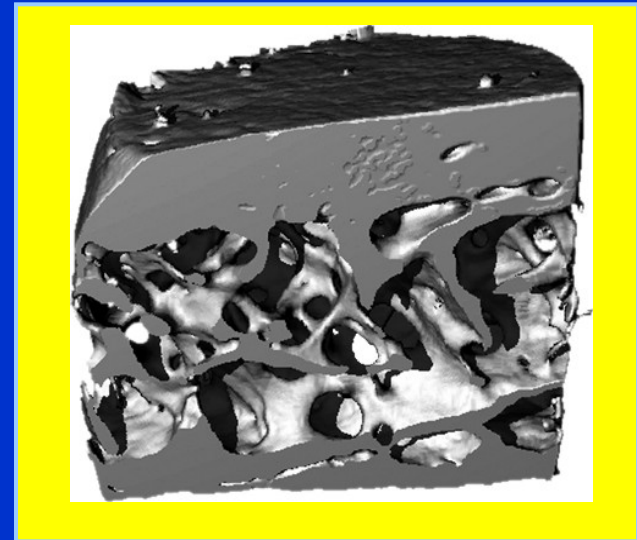
SCANCO  
Xtreme CT  
HR qCT

# Pair biopsies- before and after treatment

Placebo 36 months



PROTELOS 36 months



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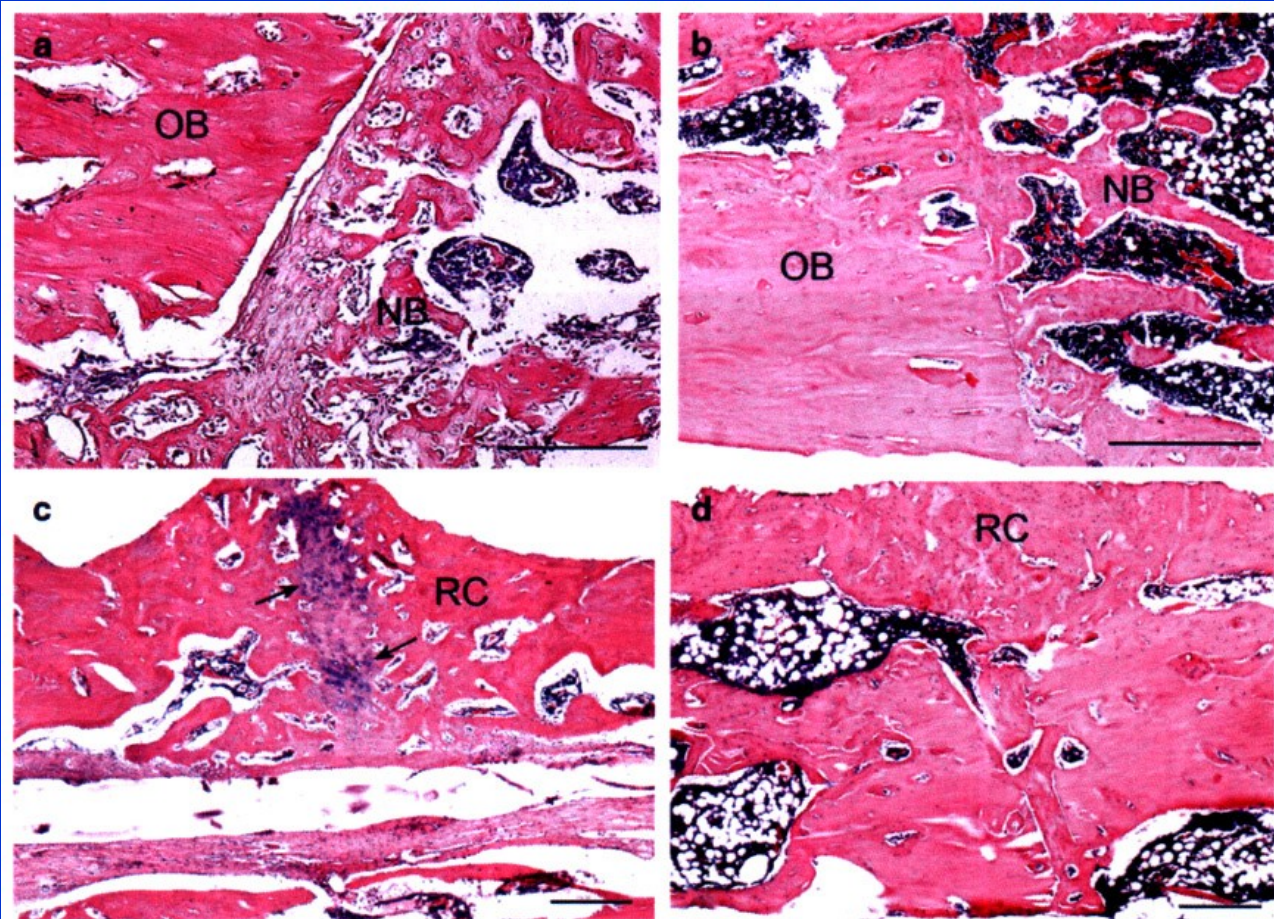
Number of trabeculae	+ 14 %	$p=0,05$
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# Histology

Kontrola

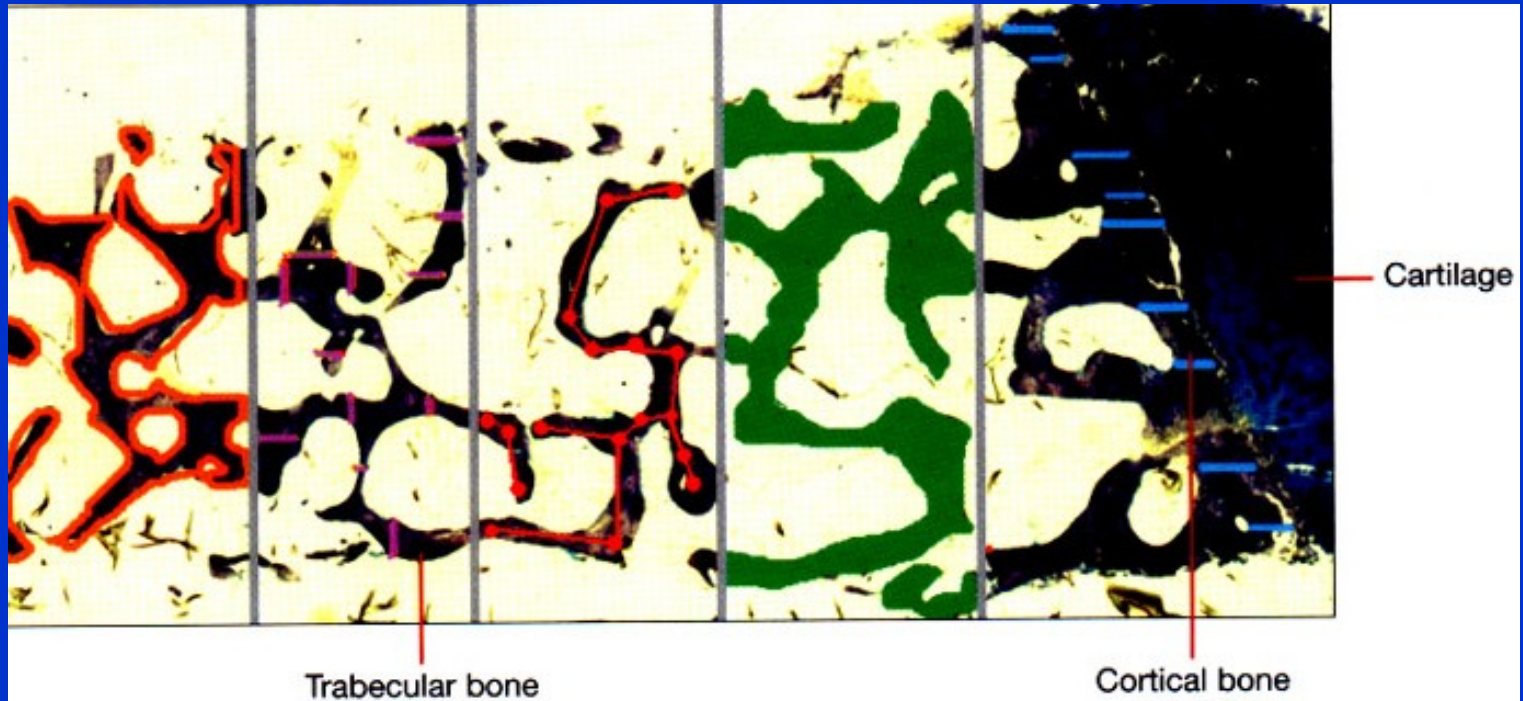
OVX a SR

4 t.



8 t.

# Histomorfometry



Povrch kosti

Mineralizovaný povrch

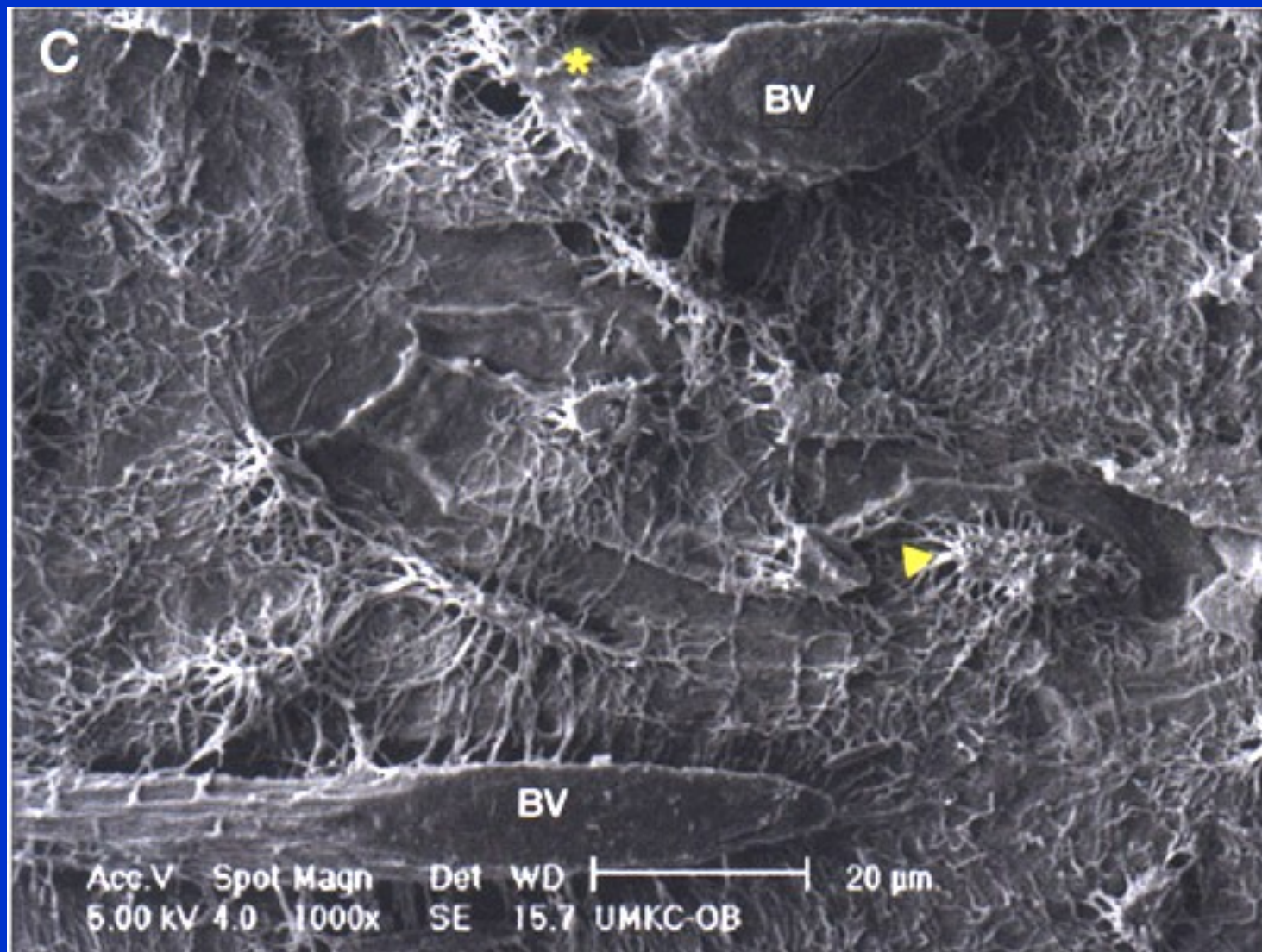
Erodovaný povrch

Tloušťka trabekul

Konektivita trámců

Trabekulární objem

Kortikální tloušťka



SEM: canaliculi between osteocytes

# FEA- finite element analysis

Trabecular bone (upto 82  $\mu\text{m}$ )

Healthy bone



Plates

Osteoporotic bone



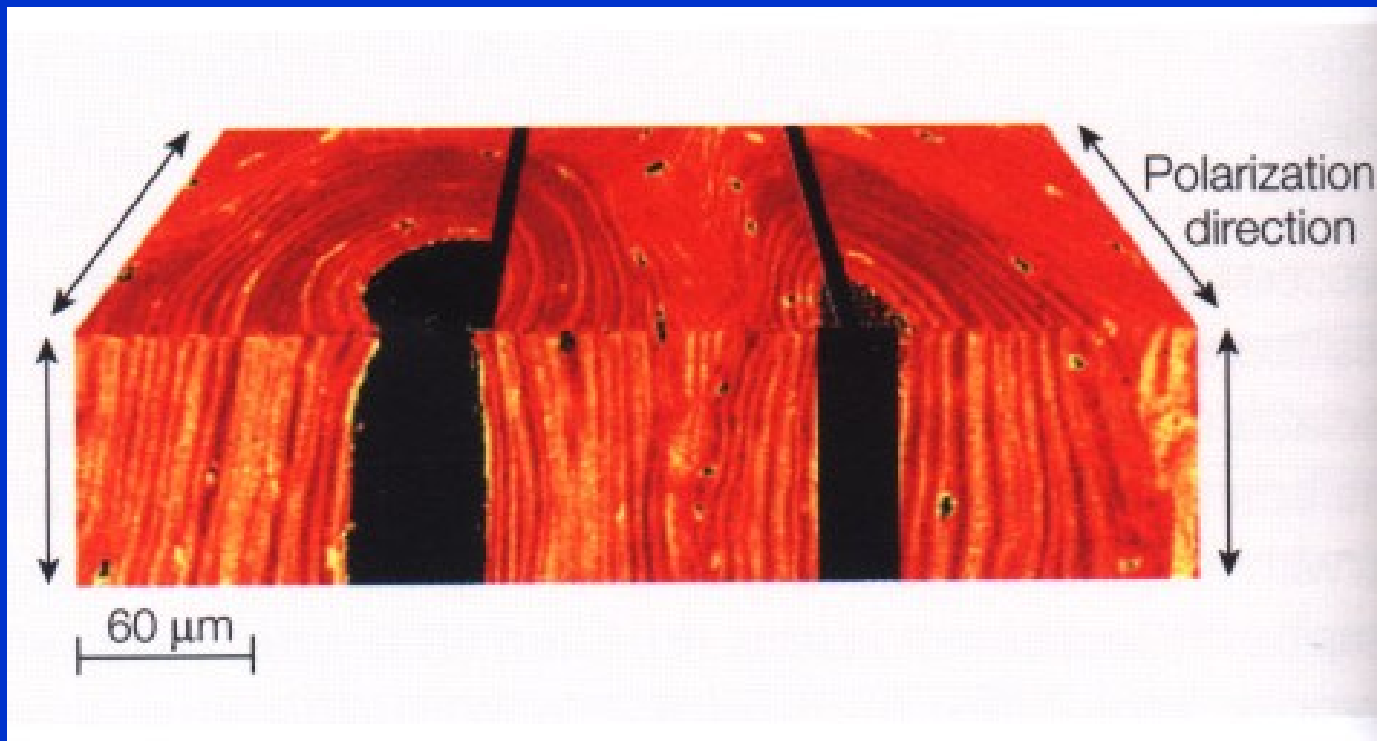
Rods



# 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  $\mu$ 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/m<sup>2</sup>  
- woman under 5,45 kg/m<sup>2</sup>

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  $\mu$ g

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 (Fosavance)

Risedronate (Actonel)

Ibandronate (Bonviva)

Zoledronate (Aclasta)

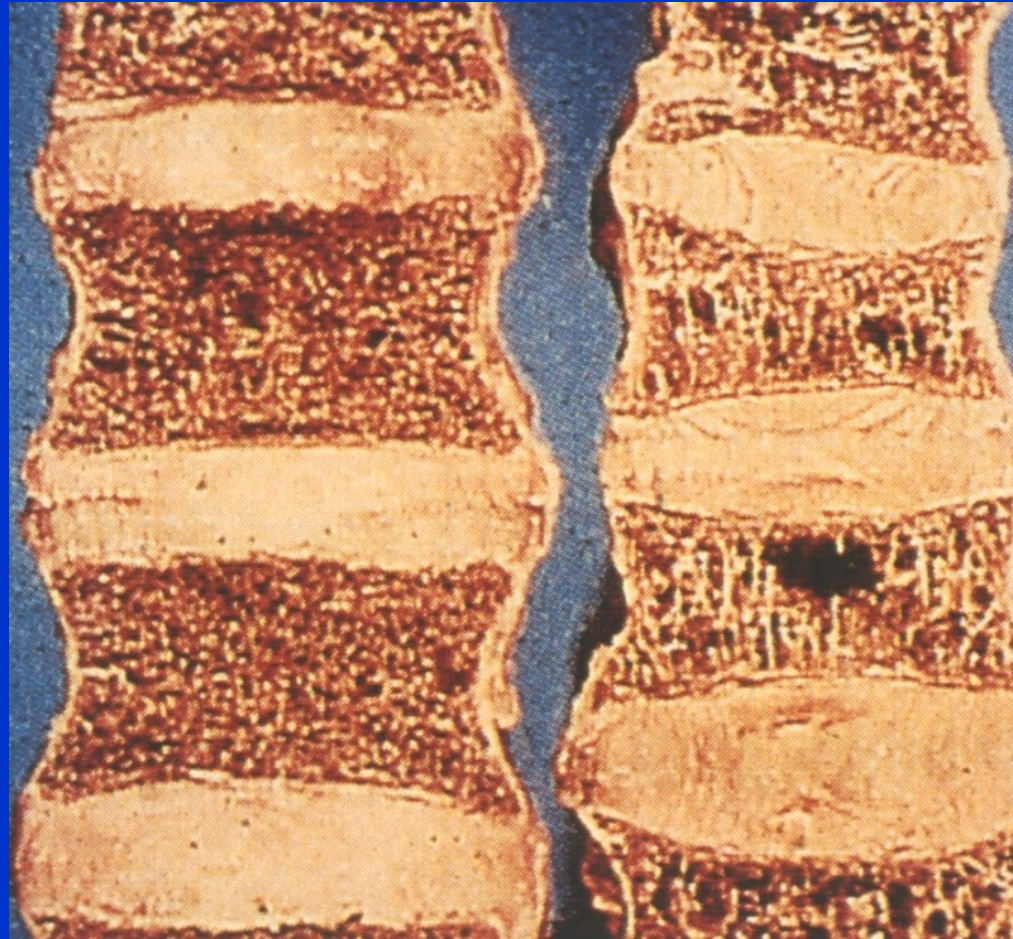
Denosumab (Prolia)

Stroncium ranelate (Protelos)

Parathormon, teriparatid

– (Forsteo)

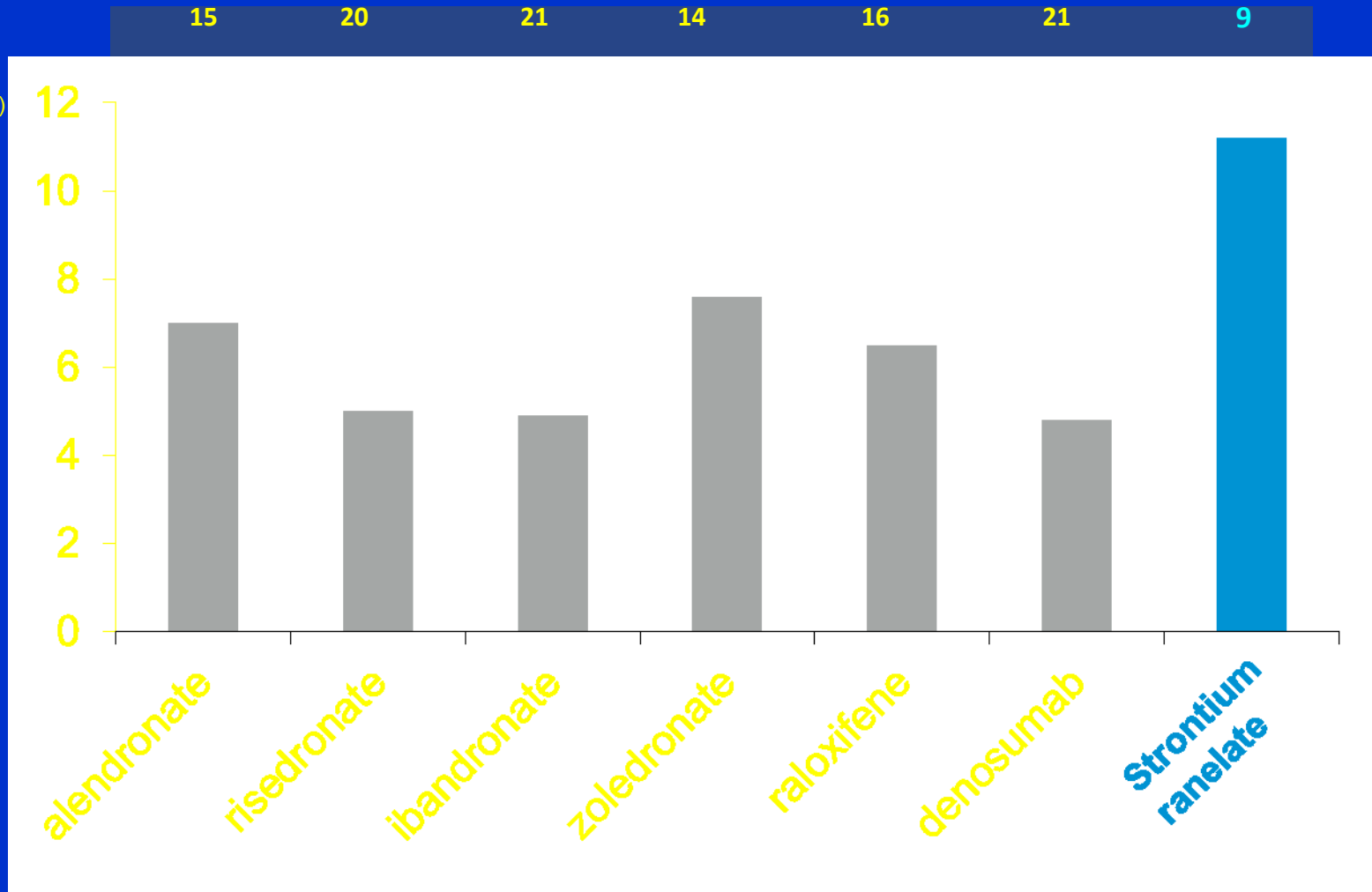
SERM- bazedoxifen



# Protection to prevent vertebral fractures

Corresponding NNT

Absolute risk reduction  
for vertebral fracture (%)



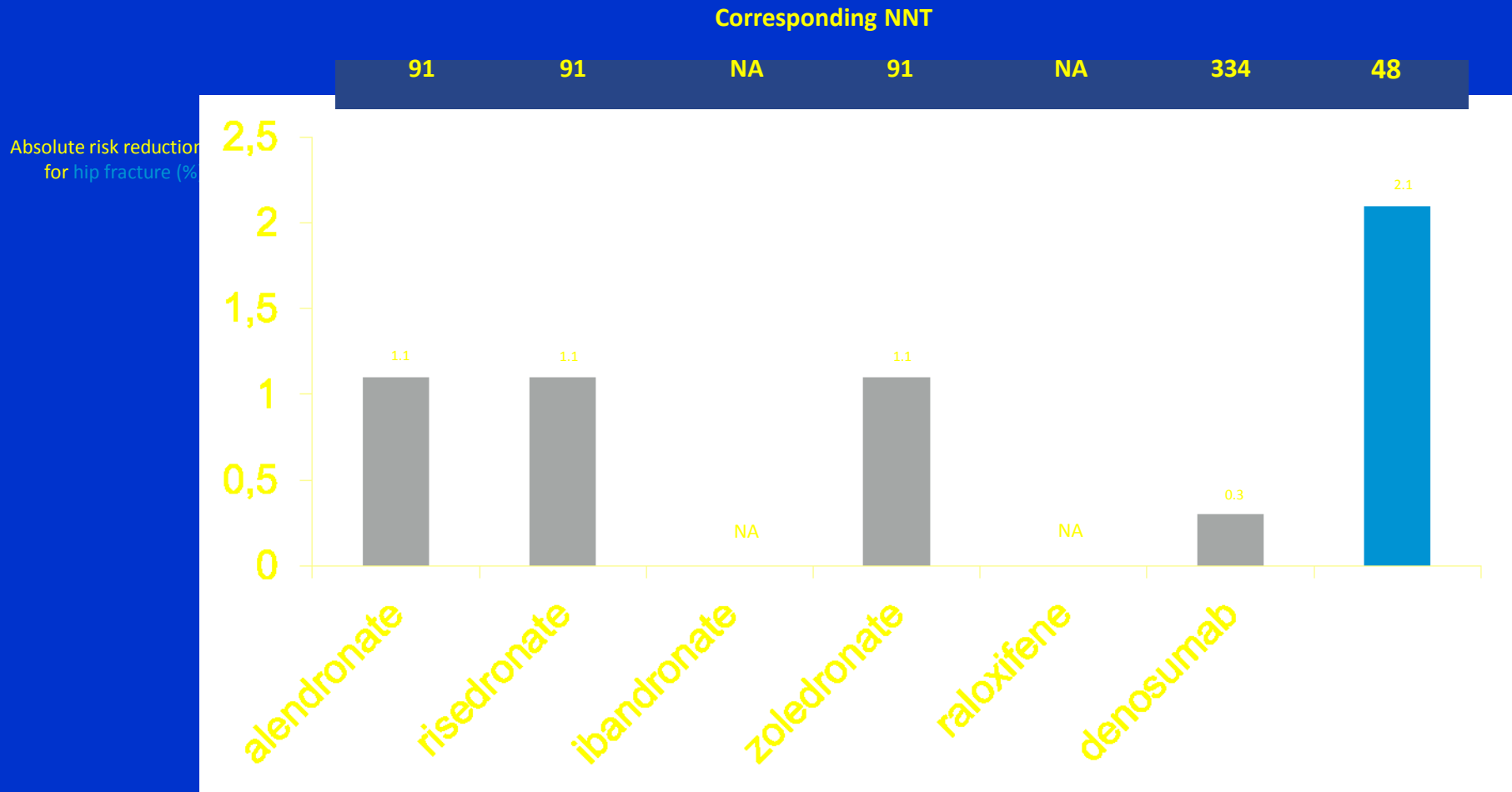
# Comparison of antifracture efficacy

## Vertebral fracture

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

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 <sup>a</sup>	PEARL	1.2	0.9	N.S.		
Strontium ranelate	TROPOS	6.4	4.3	36	2.1	48

<sup>a</sup> Data over 5 years.

# New agents

Monoclonal sclerostin antibodies

Romosozumab

Blosozumab

Osteoformative effect

Sclerostin – inhibitor of osteoblasts

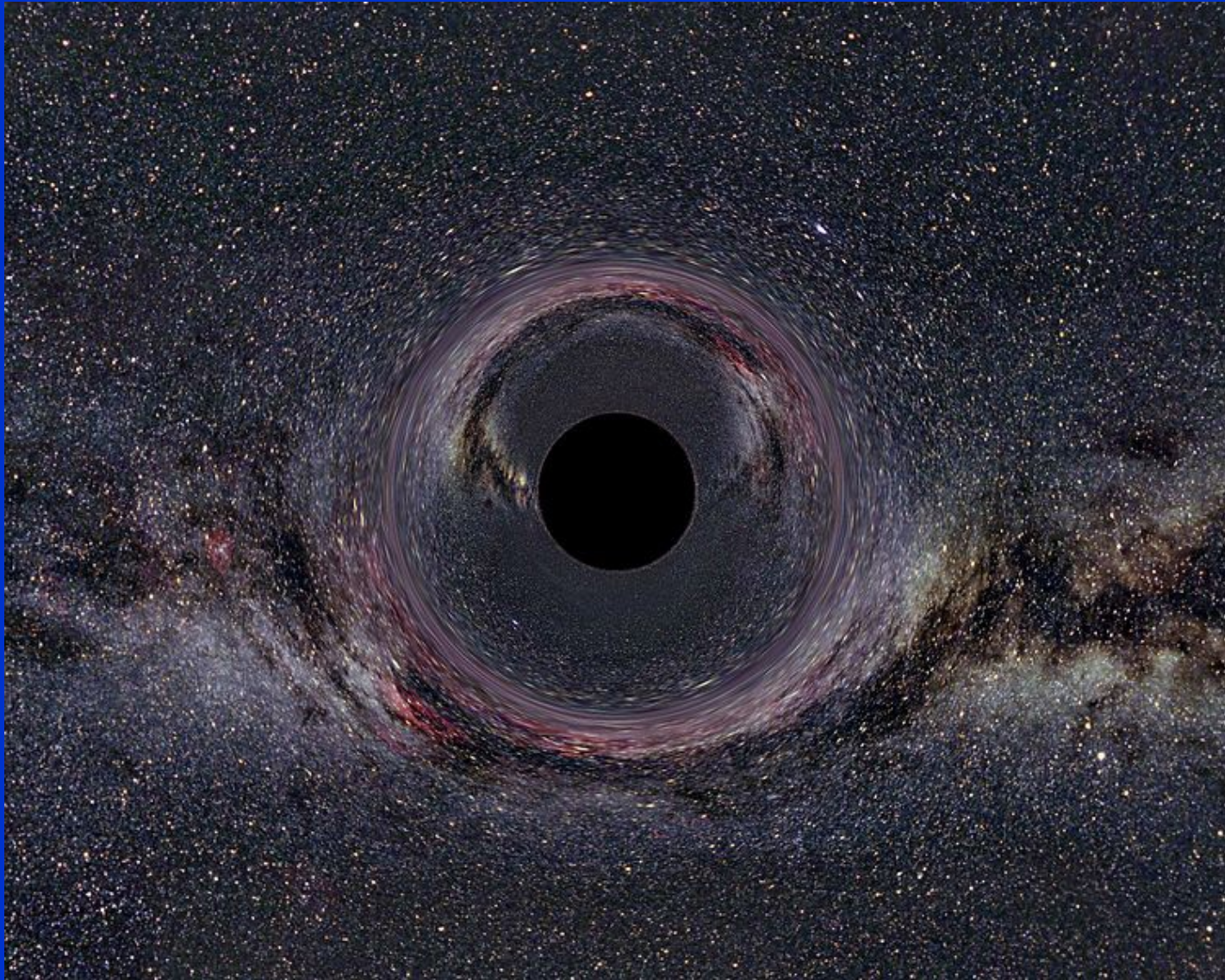
production from osteocytes

stimulates bone resorption via RANKL

Inhibitors of cathepsin K- inhibition of bone resorption

Odanatocic

Thank You for Your attention



Black Hole of the Milky Way