

News in osteoporosis

Rozkydal, Z.

I. ortopedická klinika MU

FN u sv. Anny v Brně

1. Diagnostic tools

DXA

FRAX

Laboratory tests

Imaging methods

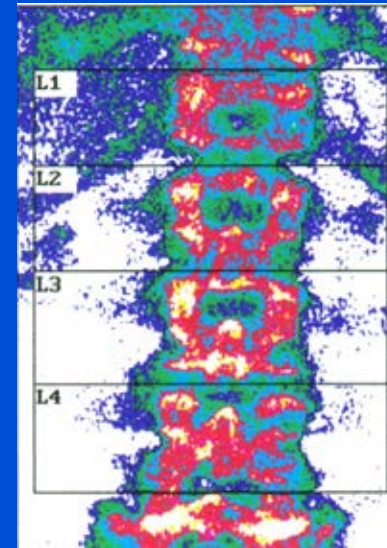
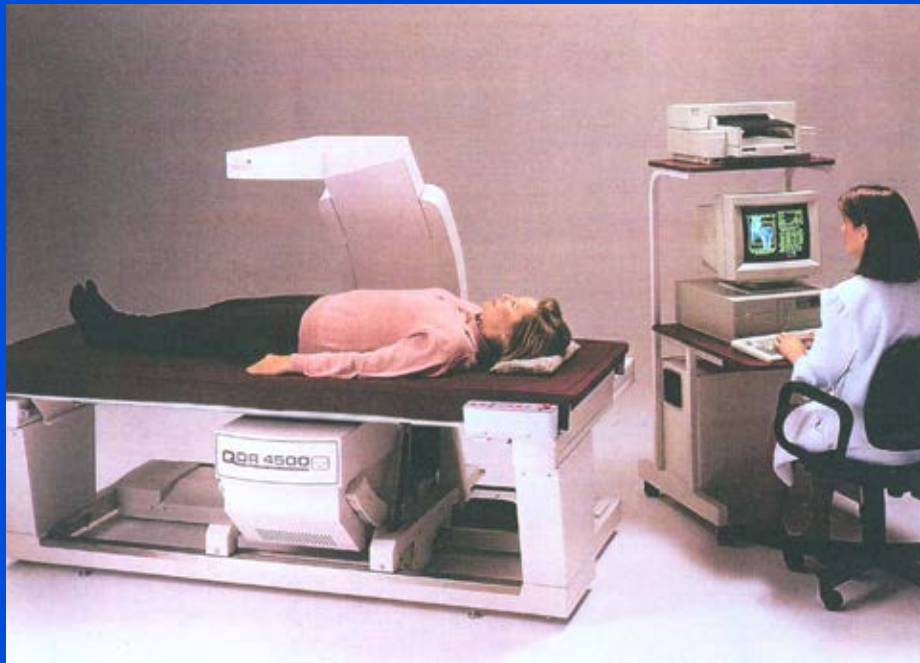
DXA – Dual Energy Absorptiometry

BMD v g/cm^2

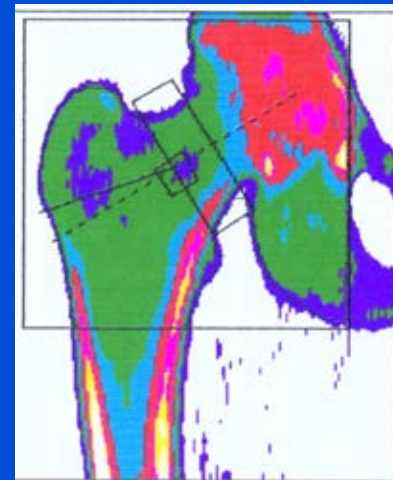
T score

Z score

Change



L1-L4



Hip Total

Hip neck

Wrist

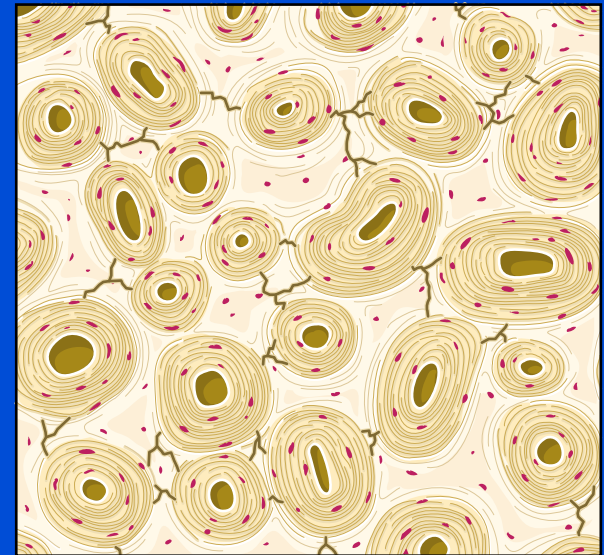
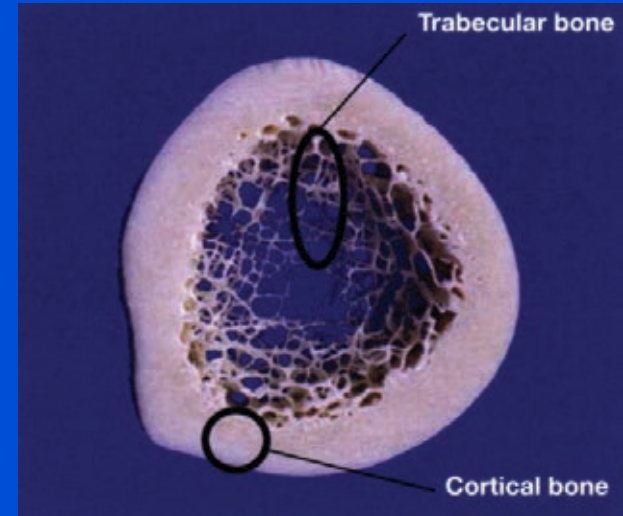
Strength of bone

Density from BMD predicts only
60-75 % of mechanical power 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 links: HOME, CALCULATION TOOL, PAPER CHARTS, FAQ, and REFERENCES. The main heading is 'Calculation Tool'. Below this, it says 'Please answer the questions below to calculate the ten year probability of fracture with'. The form includes a UK flag and a 'Country: UK' dropdown. There are input fields for 'Name / ID' and a link 'About the risk factors'. The 'Questionnaire' section contains 12 questions: 1. Age (65), 2. Sex (Female), 3. Weight (55 kg), 4. Height (165 cm), 5. Previous fracture (No), 6. Parent fractured hip (No), 7. Current smoking (No), 8. Glucocorticoids (No), 9. Rheumatoid arthritis (No), 10. Secondary osteoporosis (No), 11. Alcohol (No), 12. Femoral neck BMD (T-Score: -2.3). On the left, there are 'Weight Conversion' and 'Height Conversion' sections with 'Convert' buttons. On the right, a red box displays '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 NICO Outcome' link is at the bottom of the red box.

Fracture Type	Probability (%)
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 isoenzyme 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 i woman.

- indicator of osteoblasts function. Marker of bone formation.

High levels in osteomalatia !!

Bone isoenzyme ALP- marker of bone formation.

Osteocalcin 3,4- 11,7 ng/ml u mužů, a 2,4- 10,0 ng/ml u žen.

C terminal propeptid of collagen I (PICP)

N terminal propeptid 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

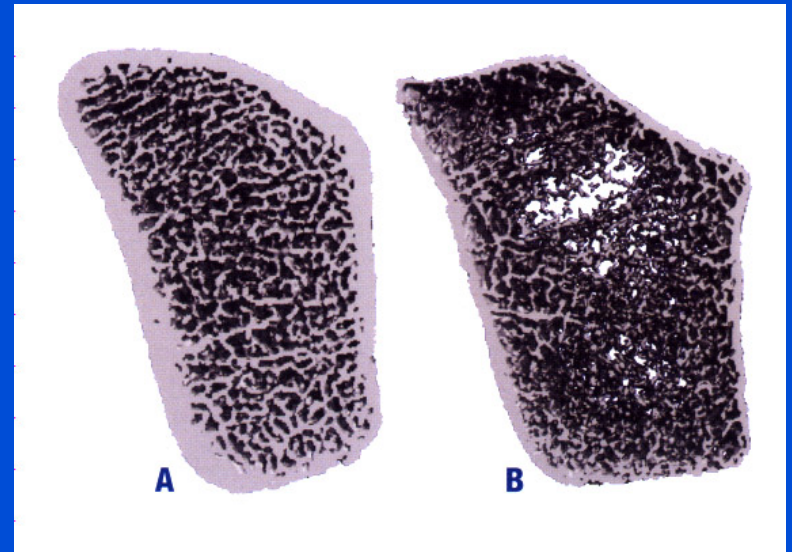
HR- pQCT

High resolution, peripheral,
quantitative CT

Noninvasive measurement
of bone morphology

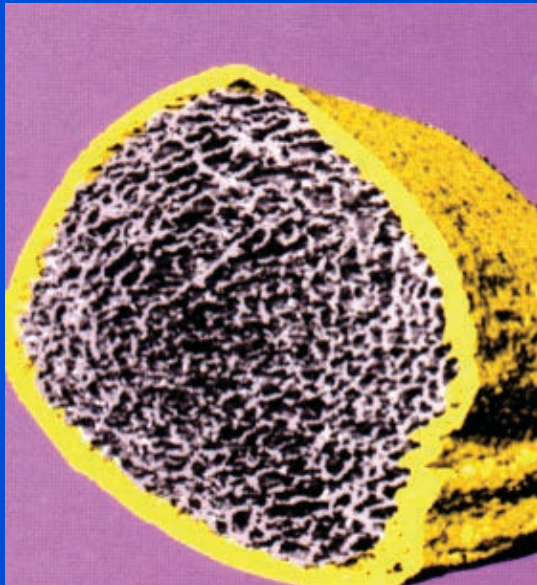
Virtual biopsy

Assess microarchitecture
up to 82 μm



Xtreme CT

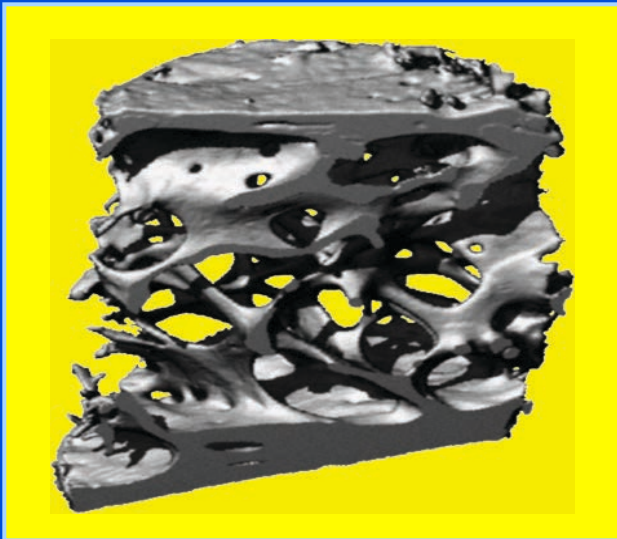
Assess thickness
of cortical bone



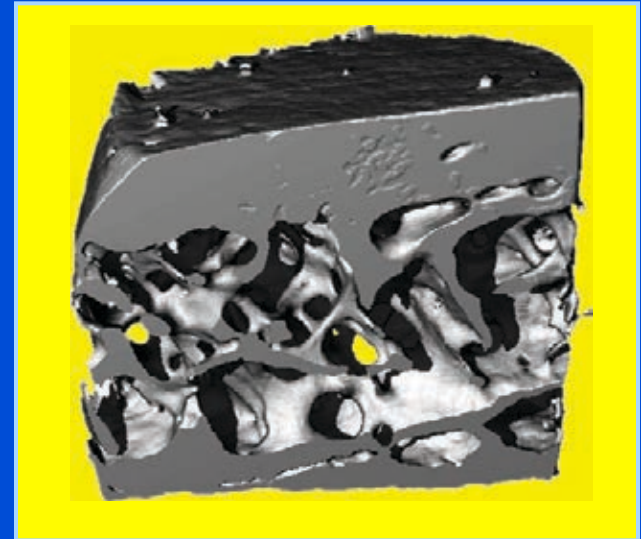
SCANCO
Xtreme CT
HR qCT

Pair biopsies- before and after treatment

Placebo 36 months



PROTELOS 36 months



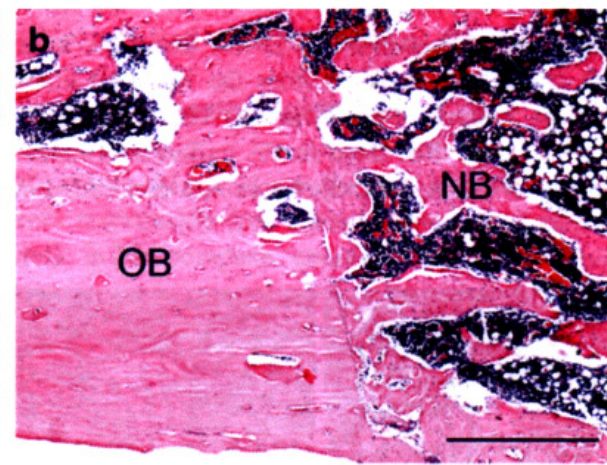
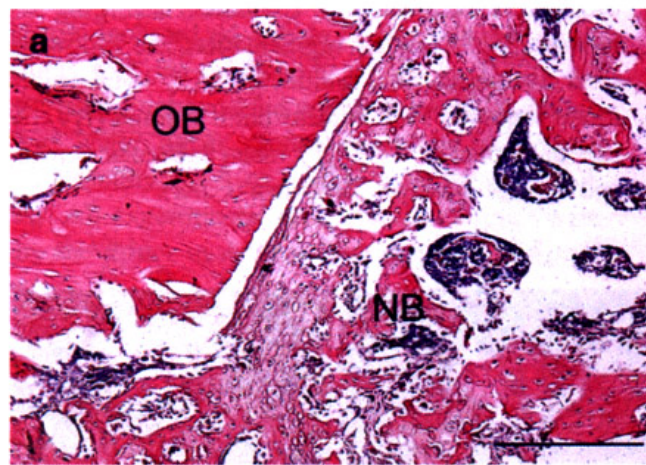
Thickness of cortical bone	+ 18 %	$p=0,008$
Number of trabeculae	+ 14 %	$p=0,05$

Histology

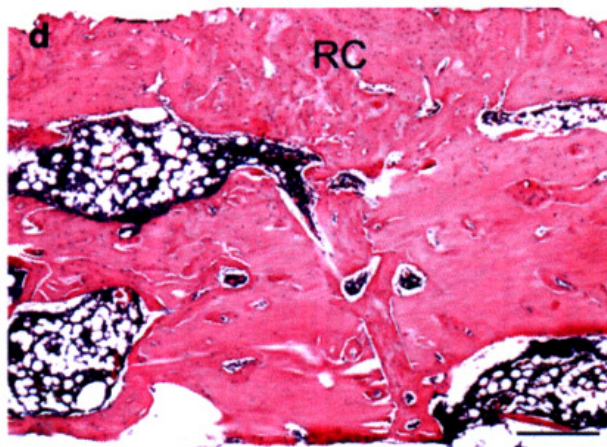
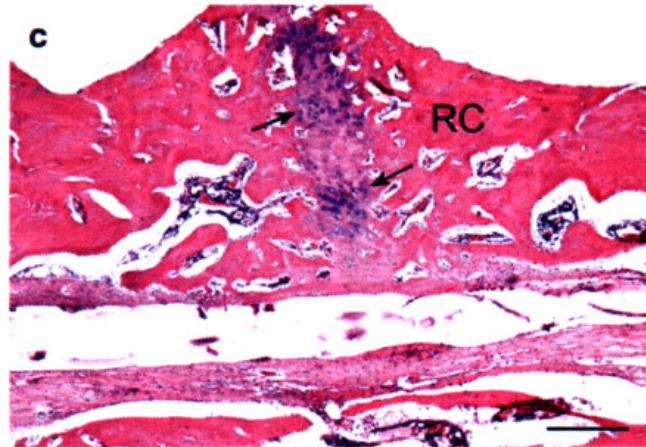
Kontrola

OVX a SR

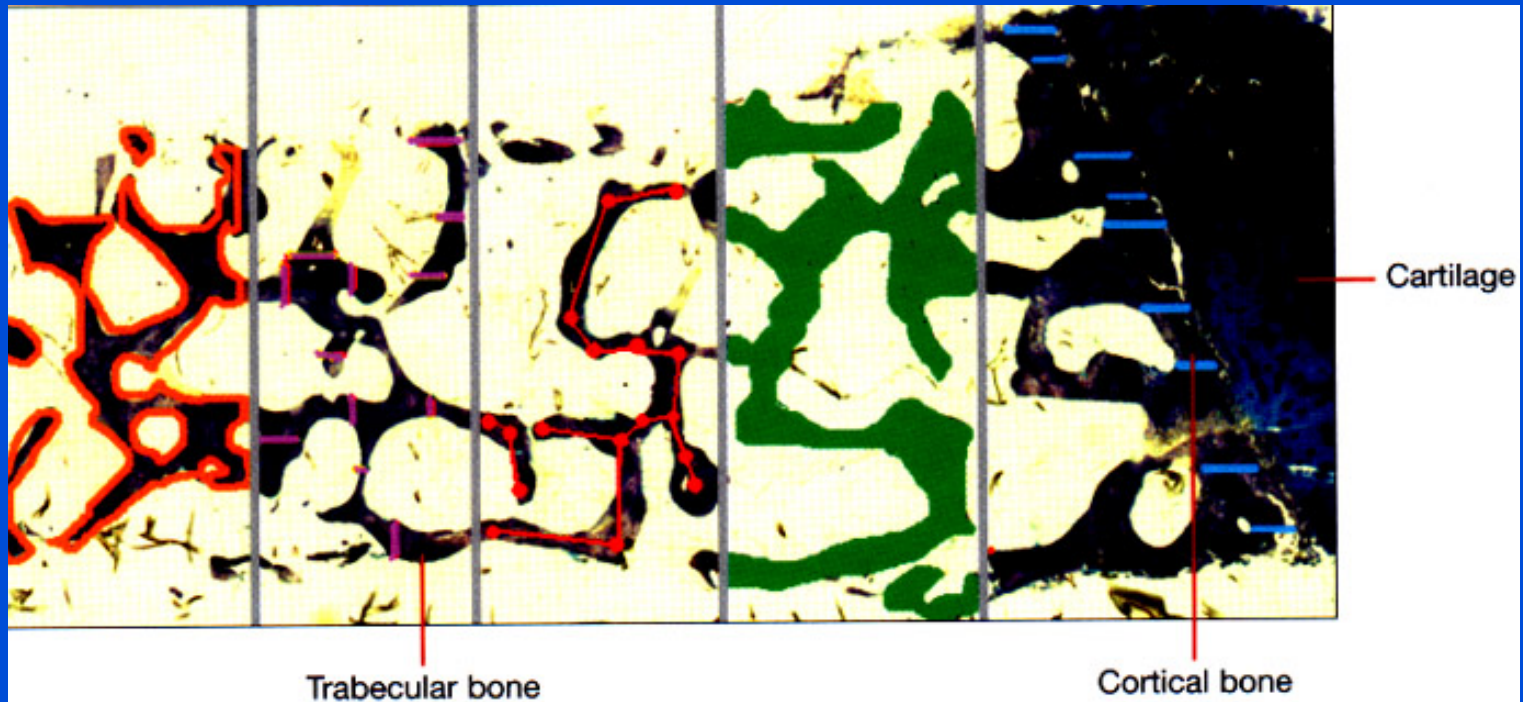
4 t.



8 t.

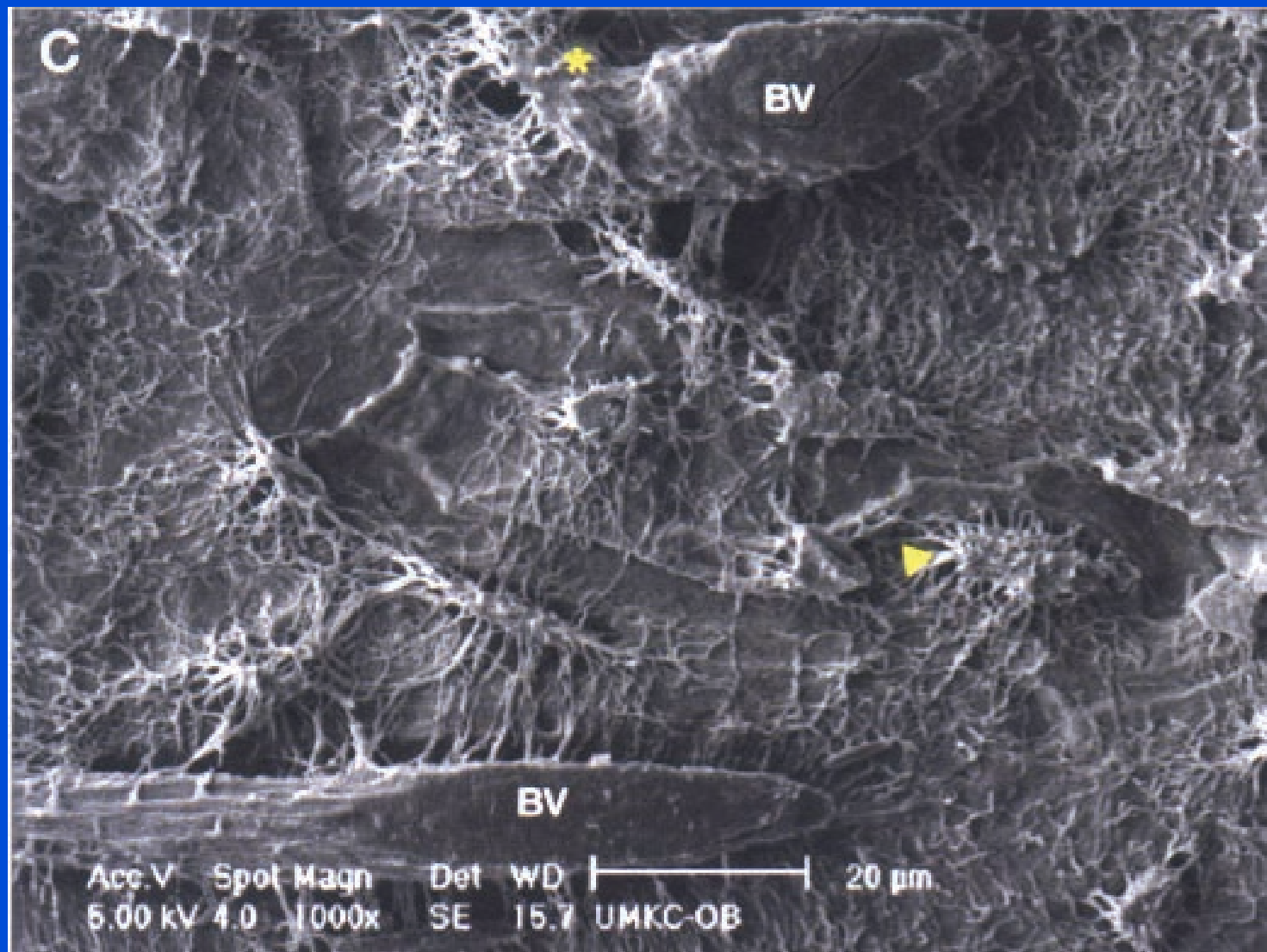


Histomorfometry



Povrch kosti
Mineralizovaný povrch
Erodovaný povrch
Tloušťka trabekul

Konektivita trámců
Trabekulární objem
Kortikální tloušťka



SEM: canaliculi between osteocytes

FEA- finite element analysis

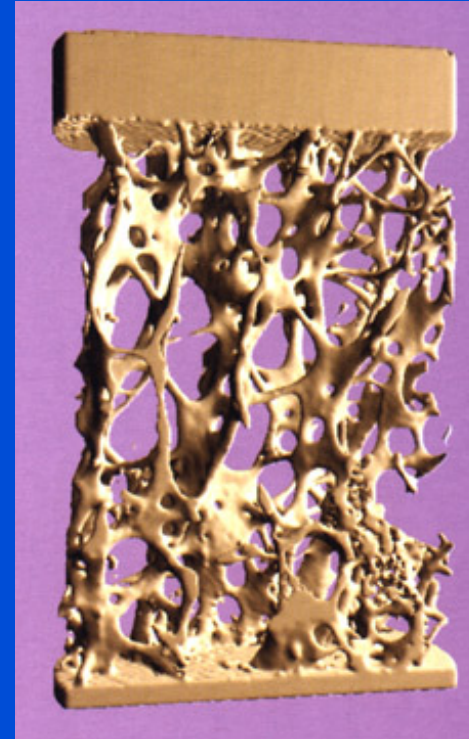
Trabecular bone (upto 82 μm)

Healthy bone



Plates

Osteoporotic bone

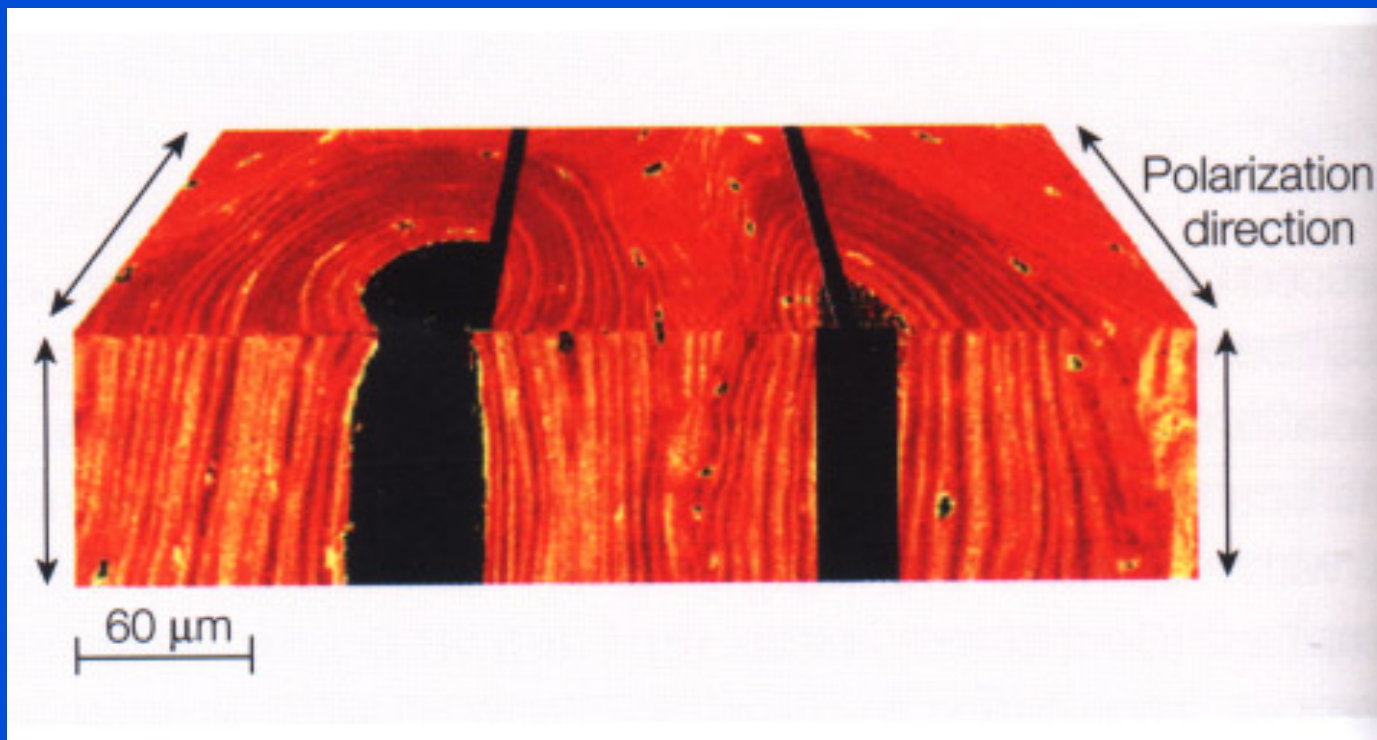


Rods

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

Subclinical

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 µg

Strengthening of muscles, exercise, walking

Strengthening of stability, prevention of falls

Prevention of atherosclerosis

Management of other comorbidities

Alleviating 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

Consequences of sarcopenia

Lower physical activity (myosteatosis, 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 μ 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)

Zolendronate (Aclasta)

Denosumab (Prolia)

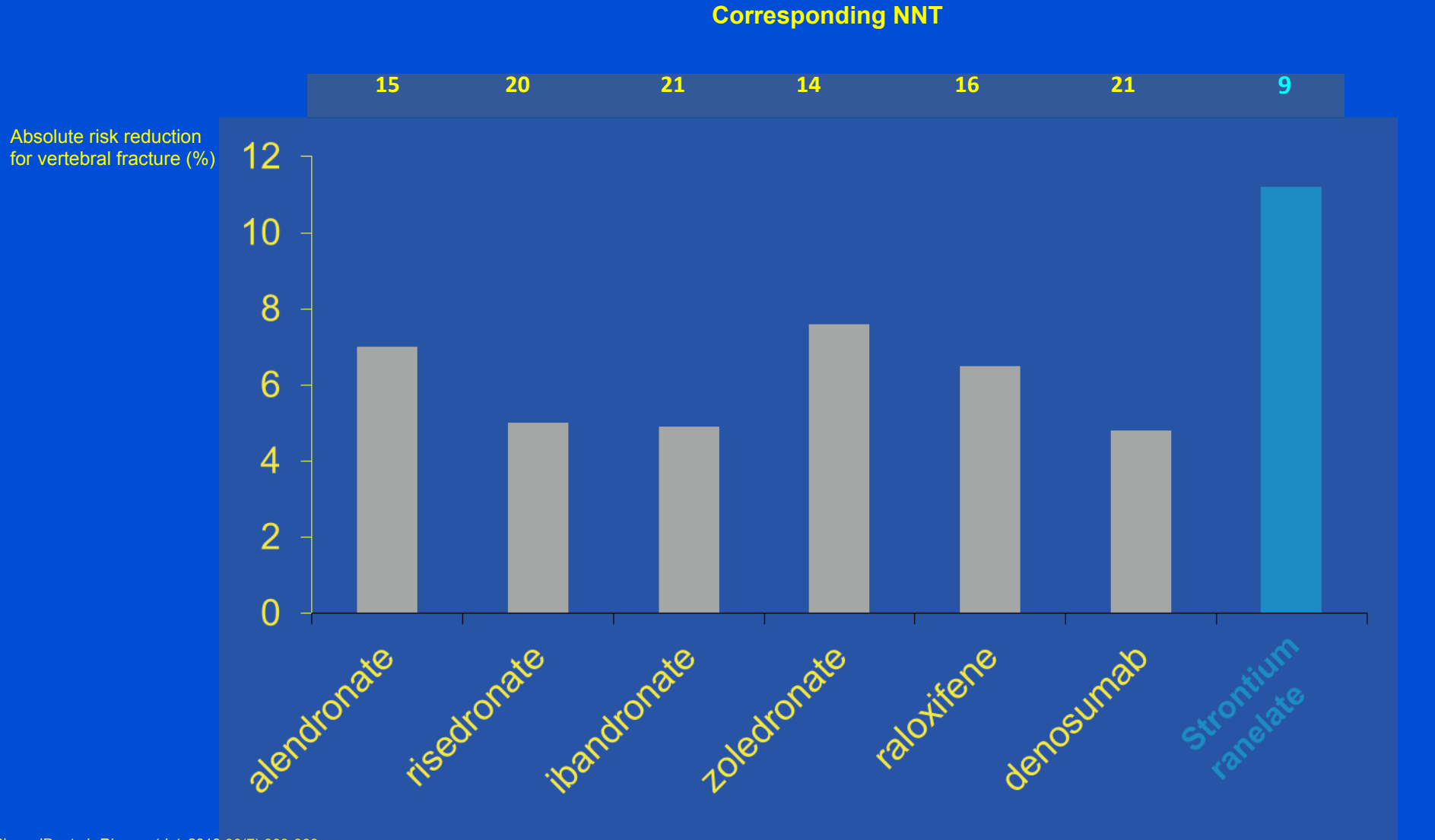
Stroncium ranelate (Protelos)

Parathormon, teriparatid
– (Forsteo)

SERM- bazedoxifen



Protection to prevent vertebral fractures



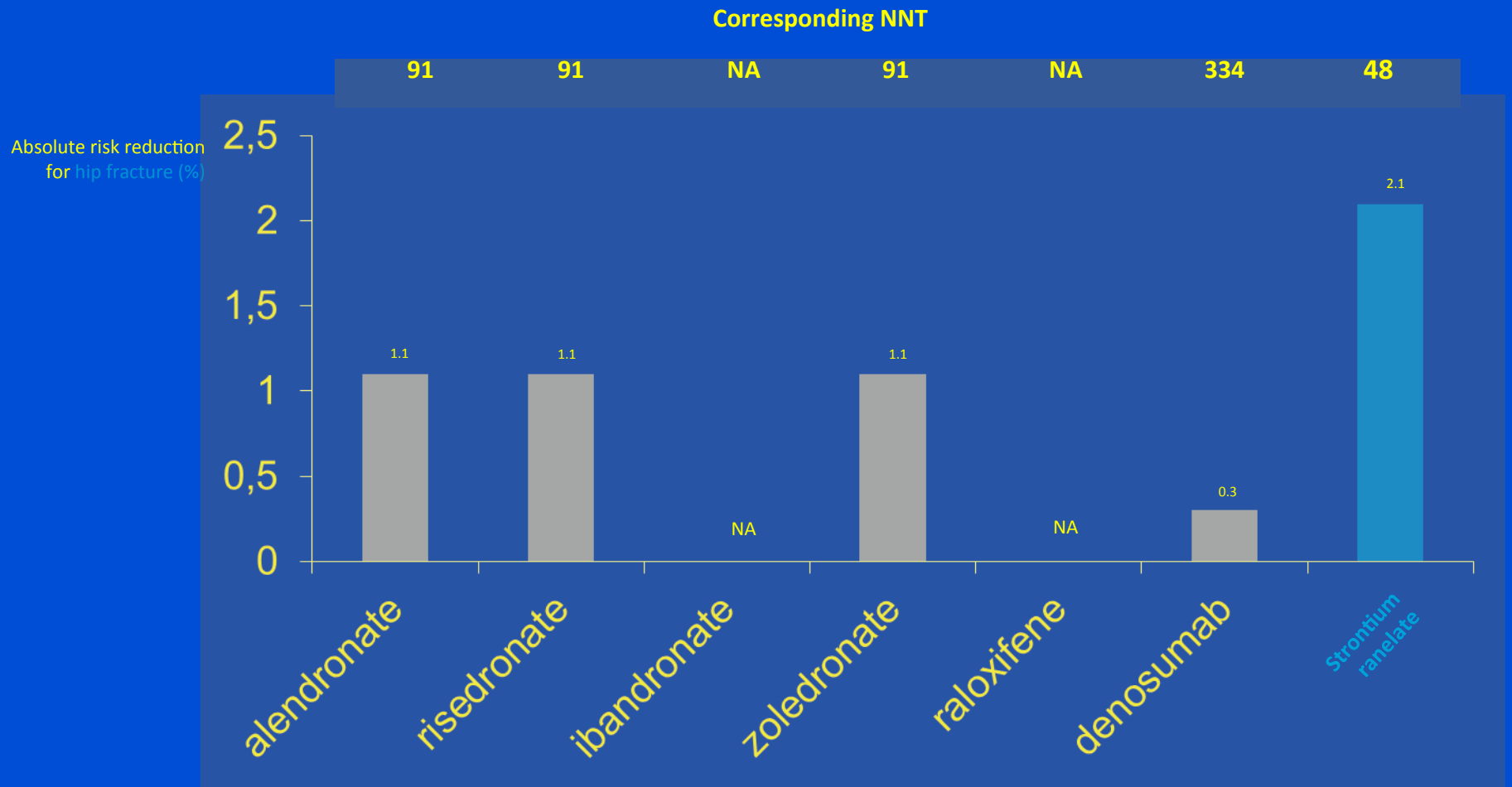
Comparison of antifracture efficacy

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
Lasofoxifene ^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.

New agents

Monoclonal sclerostin antibodies

Romosozumab

Blosozumab

Osteoformative effect

Sclerostin – inhibitor of osteoblasts

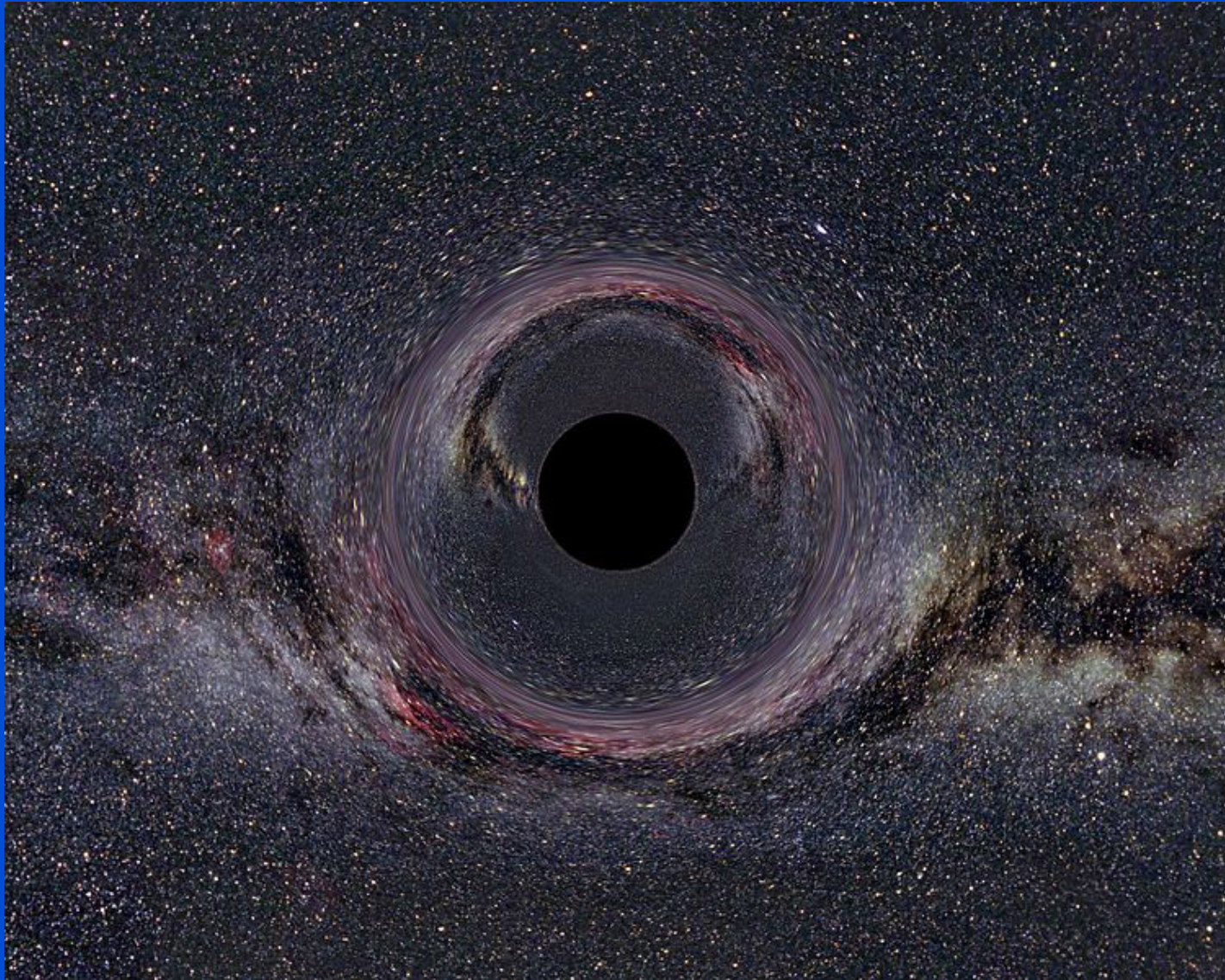
production from osteocytes

stimulates bone resorption via RANKL

Inhibitors of cathepsin K- inhibition of bone resorption

Odanacetic acid

Thank You for Your attention



Black Hole of the Milky Way