

A scenic landscape photograph of a mountain valley. In the foreground, there are green bushes and a rocky path. The middle ground is dominated by a dense forest of evergreen trees. In the background, there are several mountain peaks, some with patches of snow or light-colored rock. A lake is visible on the left side of the valley. The sky is blue with many white, fluffy clouds.

Bone health in cancer patients

Susan Ott
August 2022



No conflicts of interest

Lifestyle



Is calcium a sacred cow?



Too much calcium might deposit in blood vessels



EAT YOUR CALCIUM: 1000 mg/day



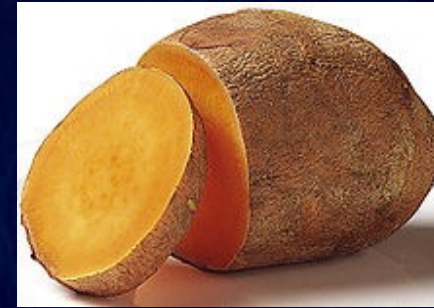
Cheese 200



Bok Choy: 100



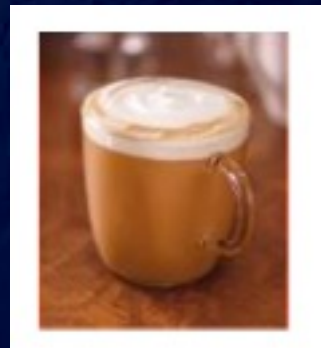
Tofu: 250



Sweet potato: 90



Yogurt: 300



Latte: 300



Kale: 200

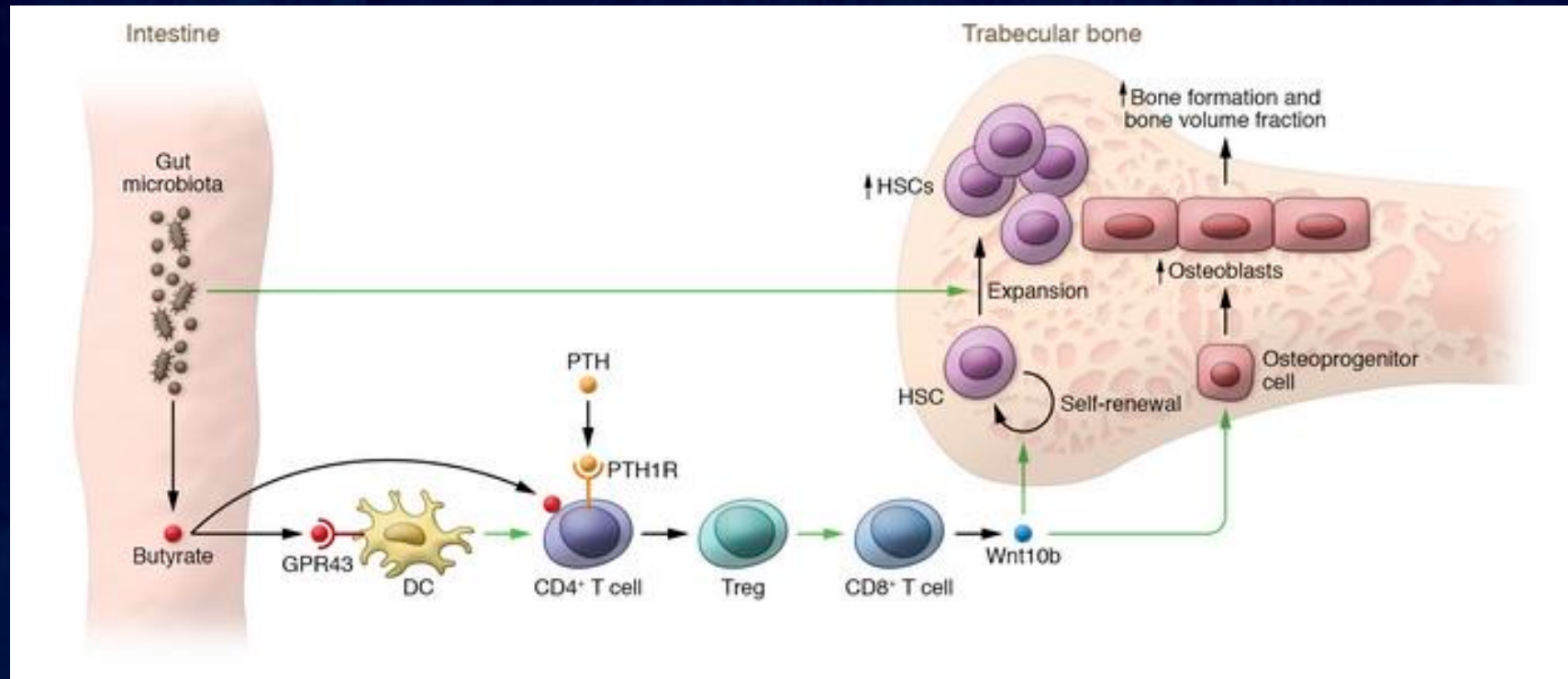


Almonds: 100

Spinach: zero

Butyrate from bacteria in yogurt increases bone formation.

Lactobacillus rhamnosus digest carbohydrates to generate butyrate

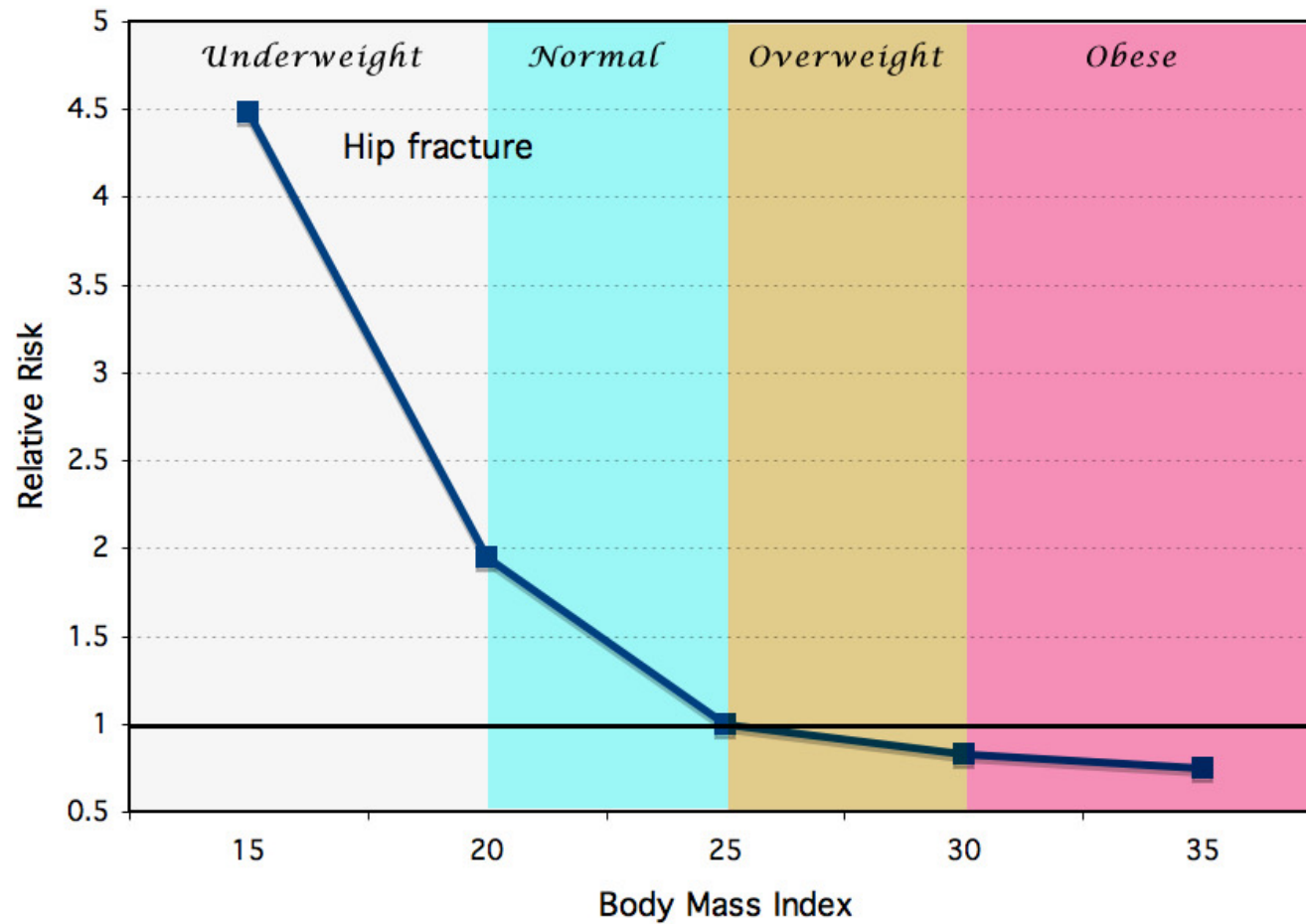


Parathyroid hormone-dependent bone formation requires butyrate production by intestinal microbiota

Jau-Yi Li,^{1,2} Mingcan Yu,^{1,2} Subhashis Pal,^{1,2} Abdul Malik Tyagi,^{1,2} Hamid Dar,^{1,2} Jonathan Adams,^{1,2} M. Neale Weitzmann,^{1,2,3} Rhianallt M. Jones,^{2,4,5} and Roberto Pacifici^{1,2,5}

Weight loss causes bone loss.

n = 60,000 men
and women



Dietary Protein

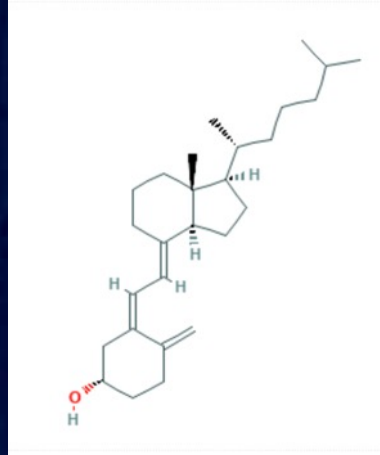
The European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO) recommends

- ❖ optimal dietary protein intake of 1.0–1.2 g/kg body weight/d
- ❖ vitamin D intake at 800 IU/d
- ❖ calcium intake of 1000 mg/d
- ❖ regular physical activity/exercise 3–5 times/week

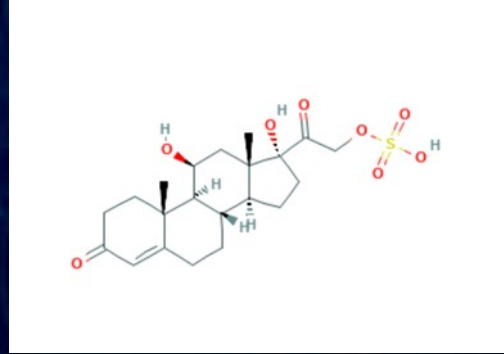
However, in the Women's Health Initiative, only 56% of participants met the RDA of 0.8mg/day

Rizzoli, Maturitas 2014
Beasley, J A Nutr Diet 2020

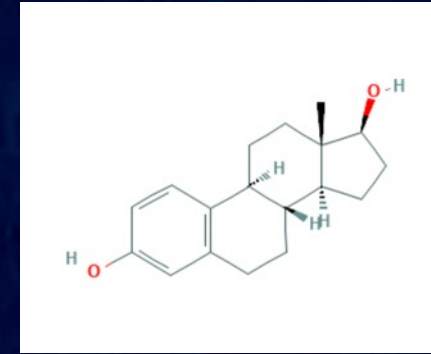
Vitamin D is really a hormone



Cholecalciferol



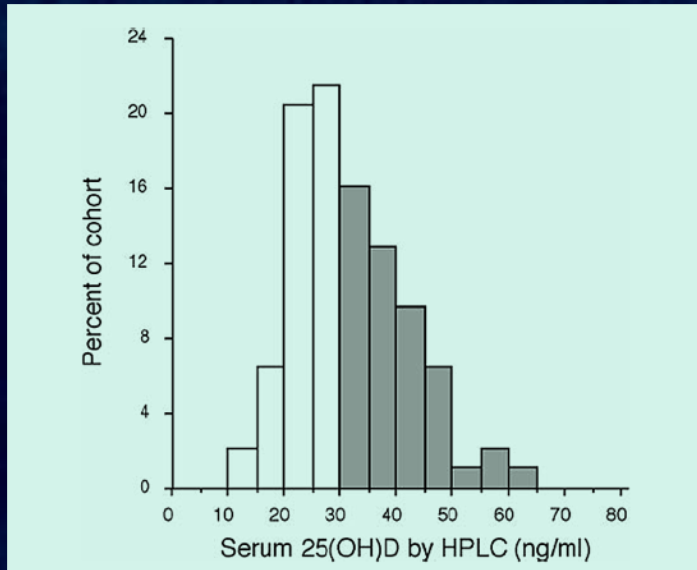
Cortisone



Estradiol

The body can make it, without any in the diet
The levels are regulated
There are receptors in different kinds of cells
It's harmful to be too low or too high.

Vitamin D levels in healthy young skateboarders from a beach in Hawaii



N = 93

Mean age = 24

51% had levels lower than 30 ng/ml

Binkley, J Clin Endocrin Metab 2007


But Qwest and LabCorps still say normal levels are 30 - 100

Vitamin D and cancer prevention

VITAL study of 2,000 iu/day vs placebo
Randomized clinical trial
26,000 subjects x 7 years:

Vitamin D supplementation did not prevent cancer or cardiovascular disease, prevent falls, improve cognitive function, reduce atrial fibrillation, change body composition, reduce migraine frequency, improve stroke outcomes, decrease age-related macular degeneration, or reduce knee pain, or reduce fracture rate.

Too much vitamin D causes bone loss



DOSE:
800 iu/day

3 randomized trials in elderly women showed more hip fractures with high dose vitamin D than with placebo.

Canadian study showed more bone loss with 4000 iu/day compared to 400 iu/day after 3 years.

Vitamin D activates osteoclasts which resorb bone.

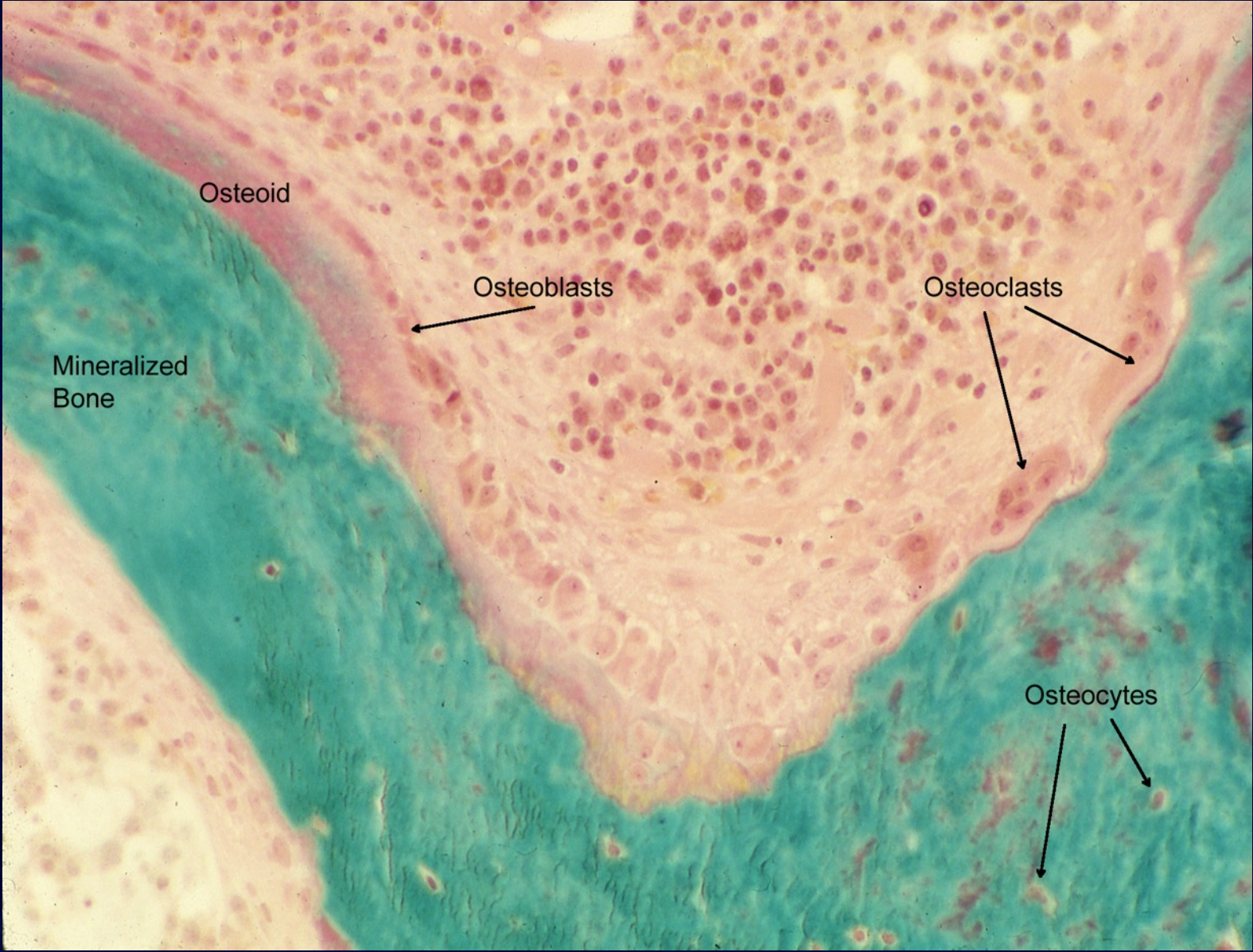
Is the Sun Setting on Vitamin D?

Sharon H. Chou,^{a,b} Meryl S. LeBoff,^{a,b} and JoAnn E. Manson^{b,c,d,*}

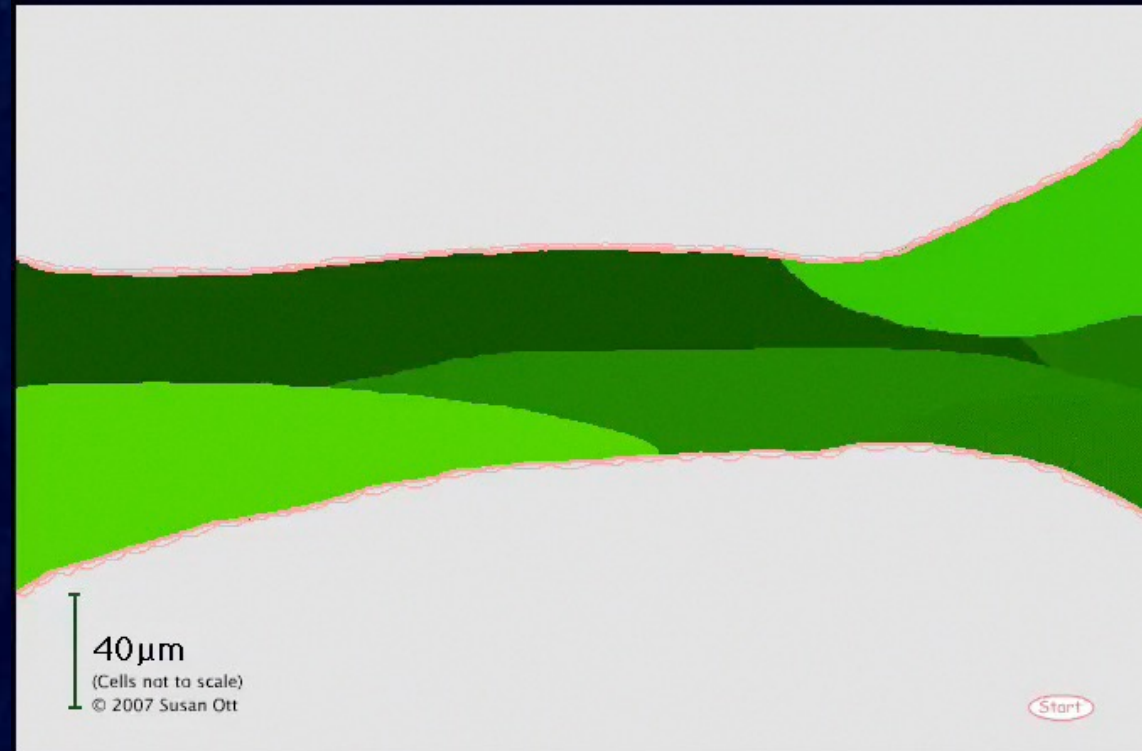


Prevent Falls!

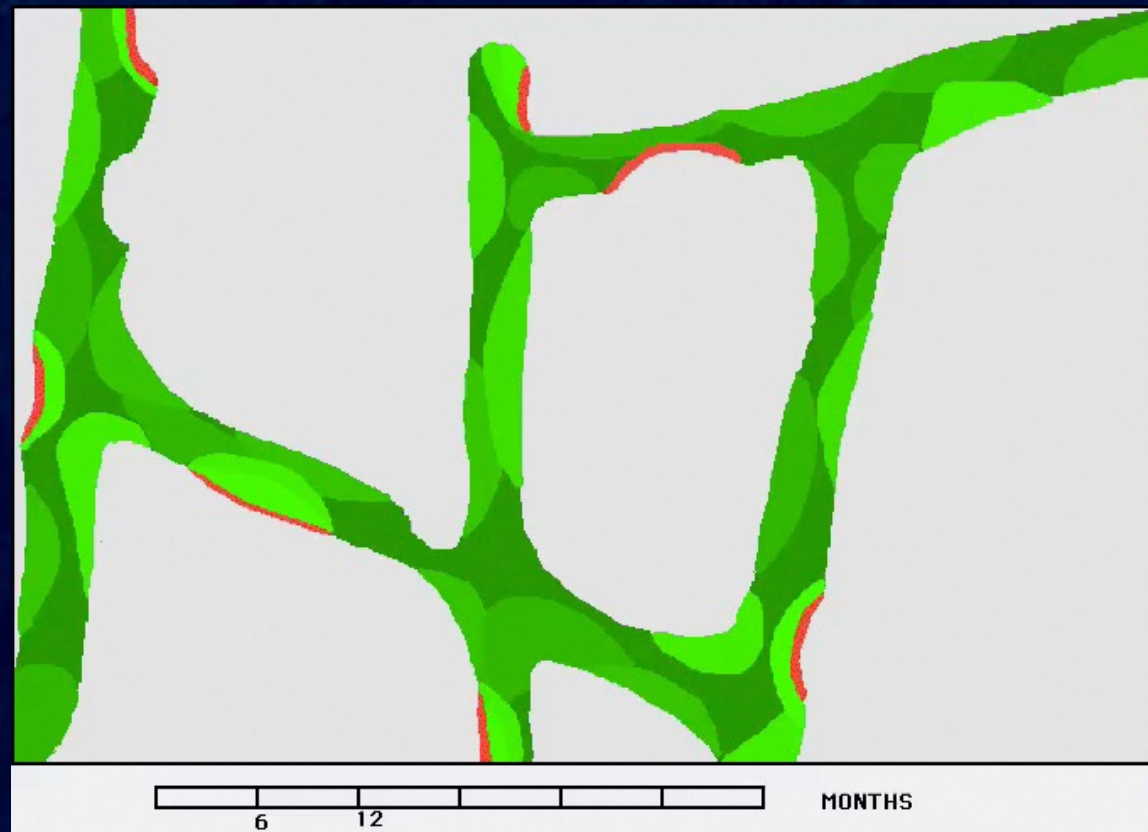




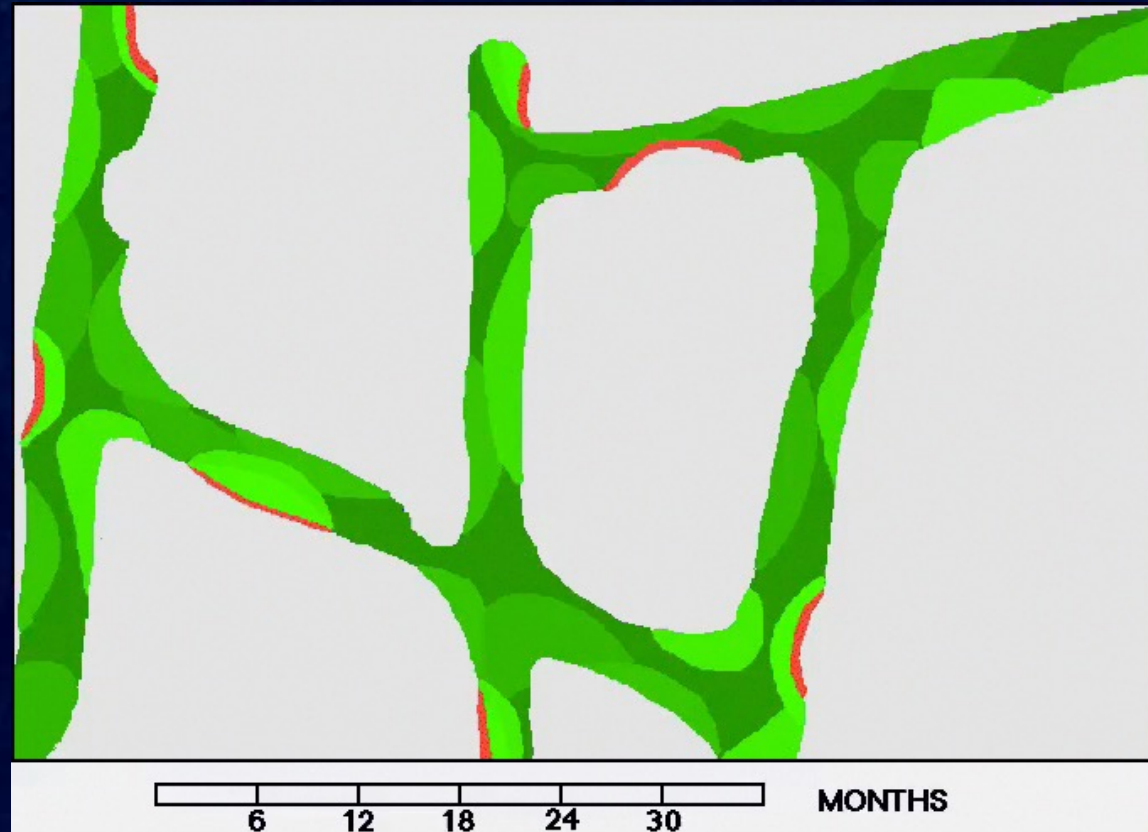
One BMU



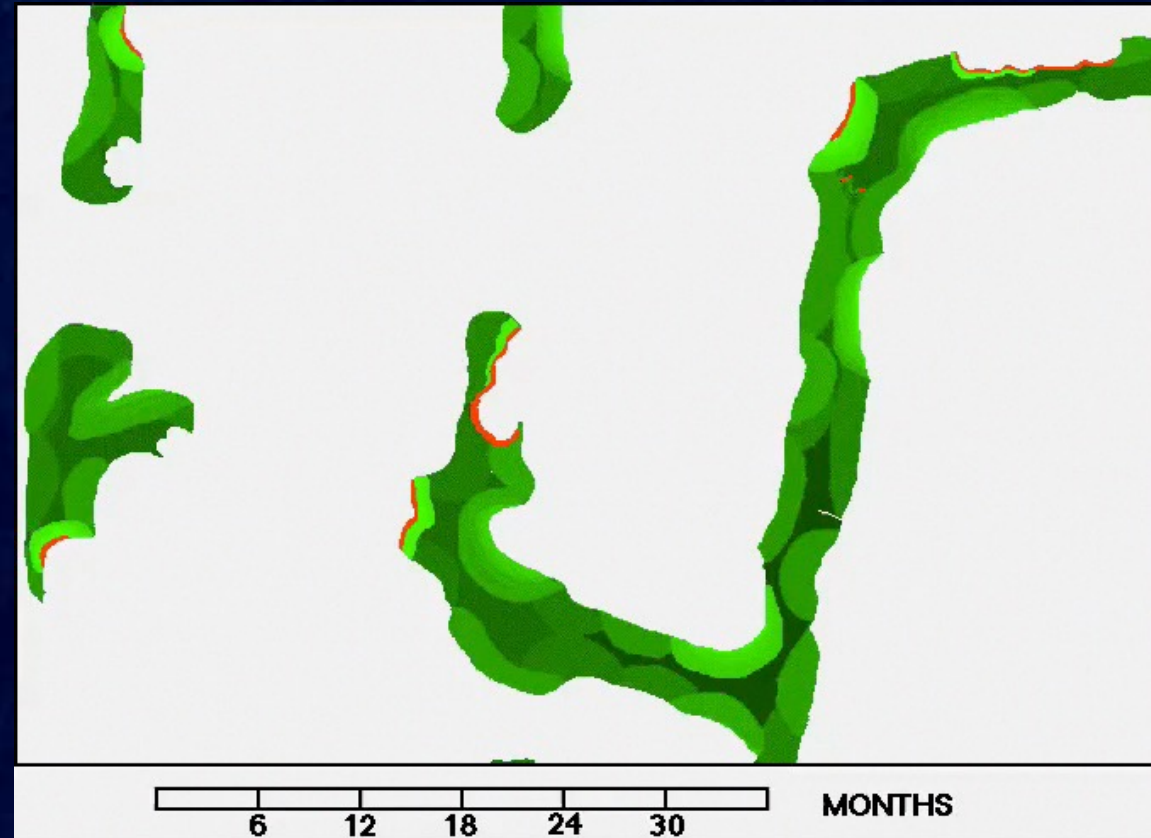
Normal Bone Remodeling



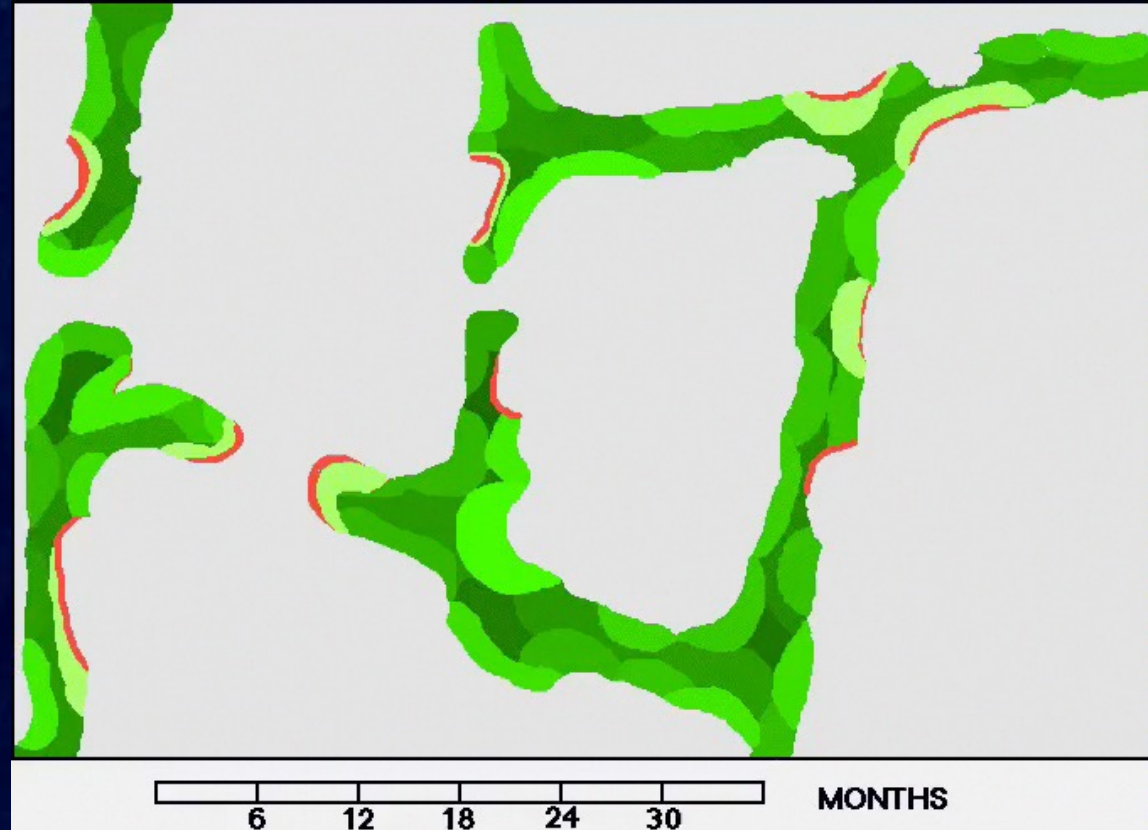
Bone Remodeling at menopause



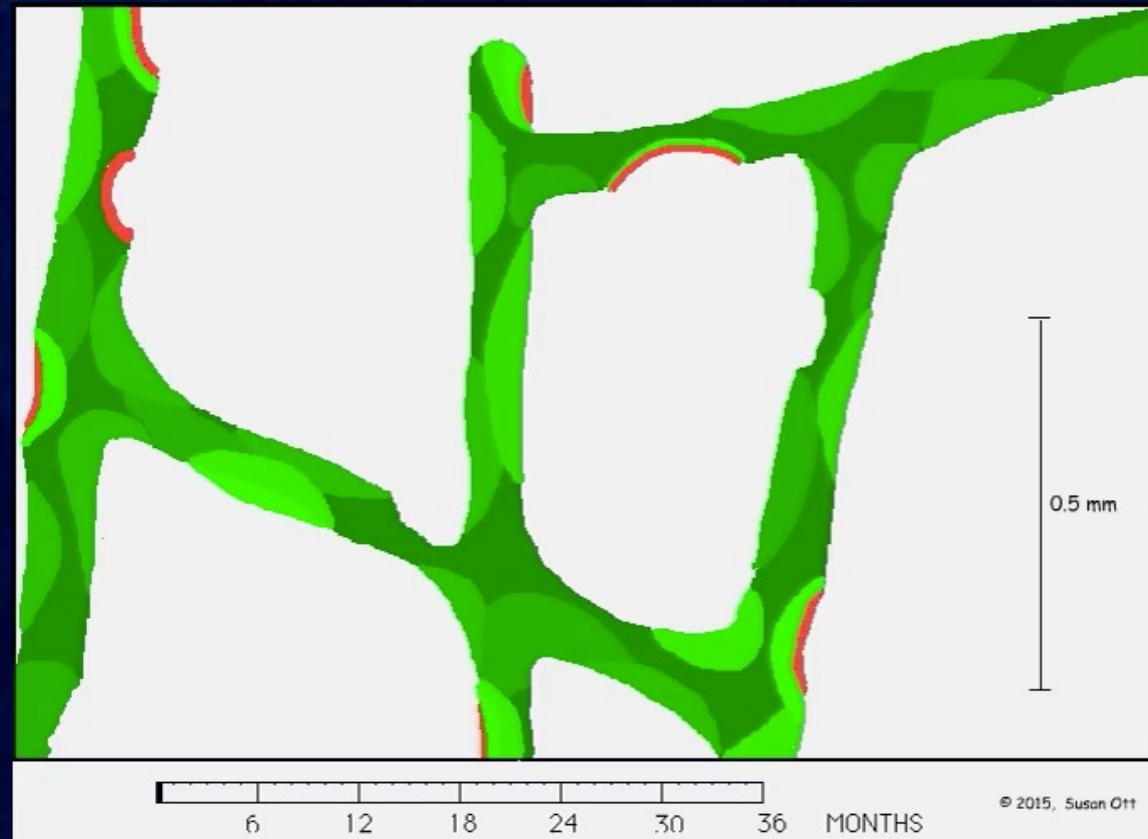
Treatment with estrogen/SERM



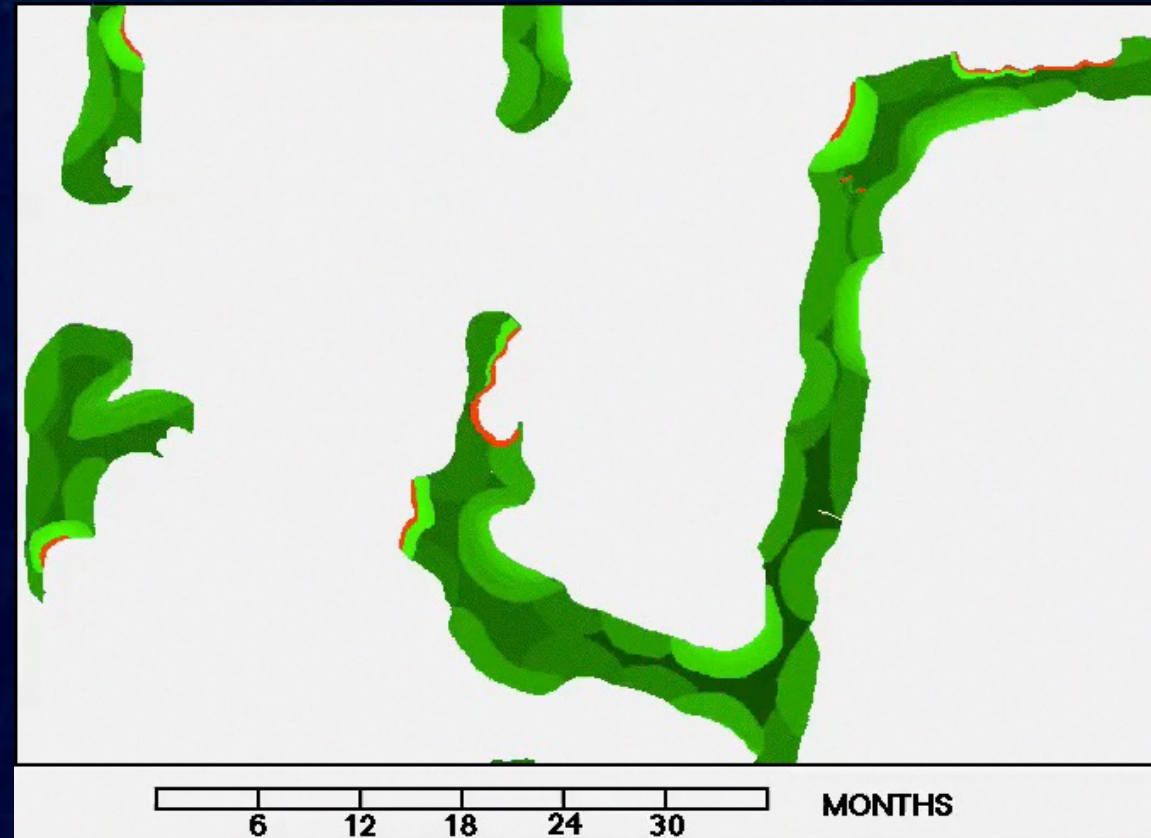
Treatment with bisphosphonate



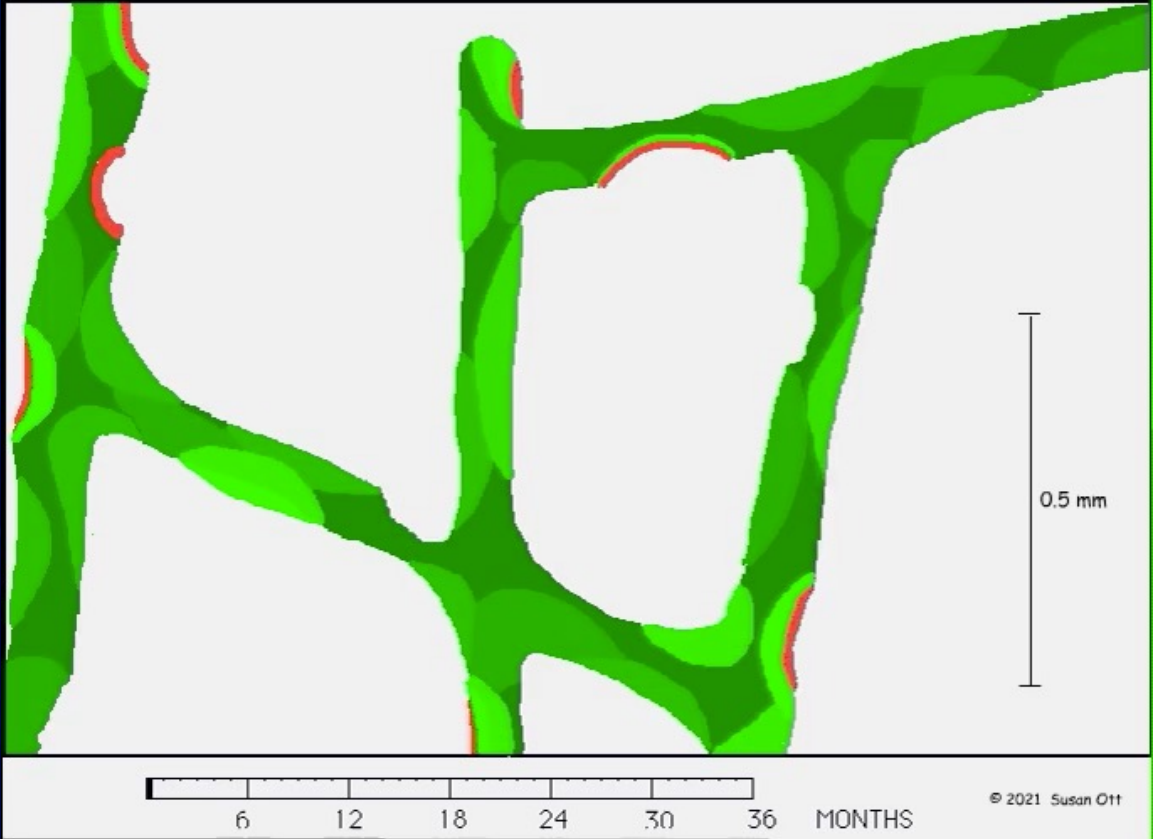
Denosumab



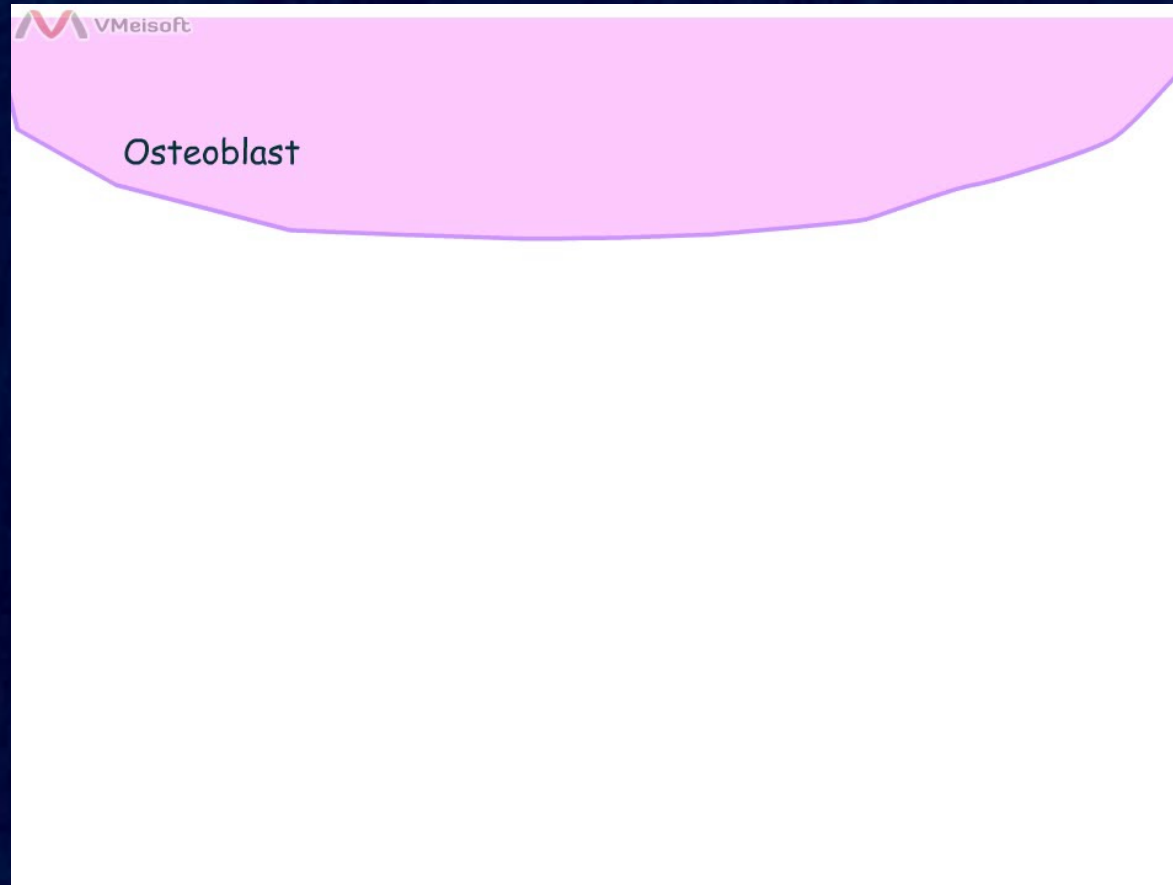
Teriparatide



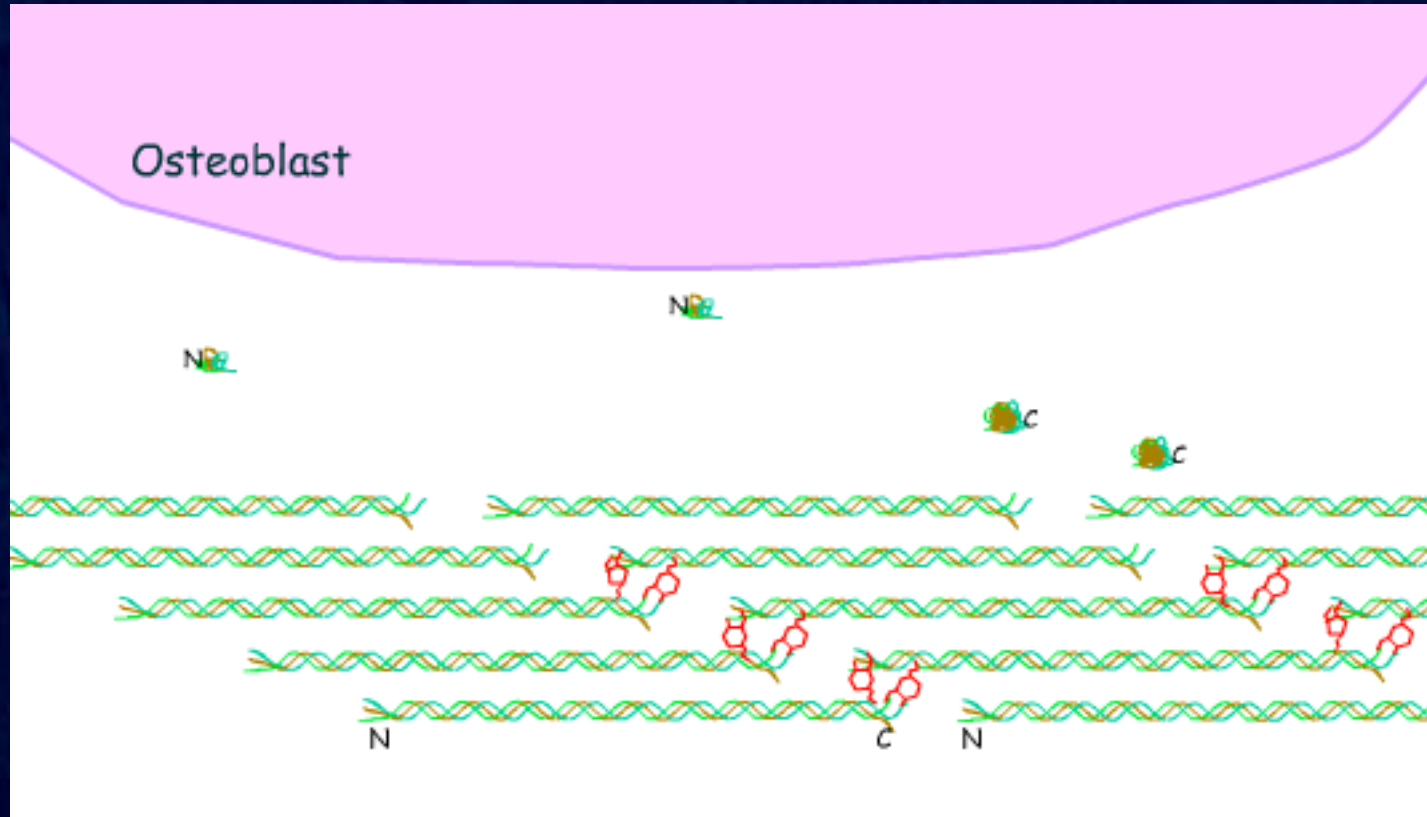
Romosozumab



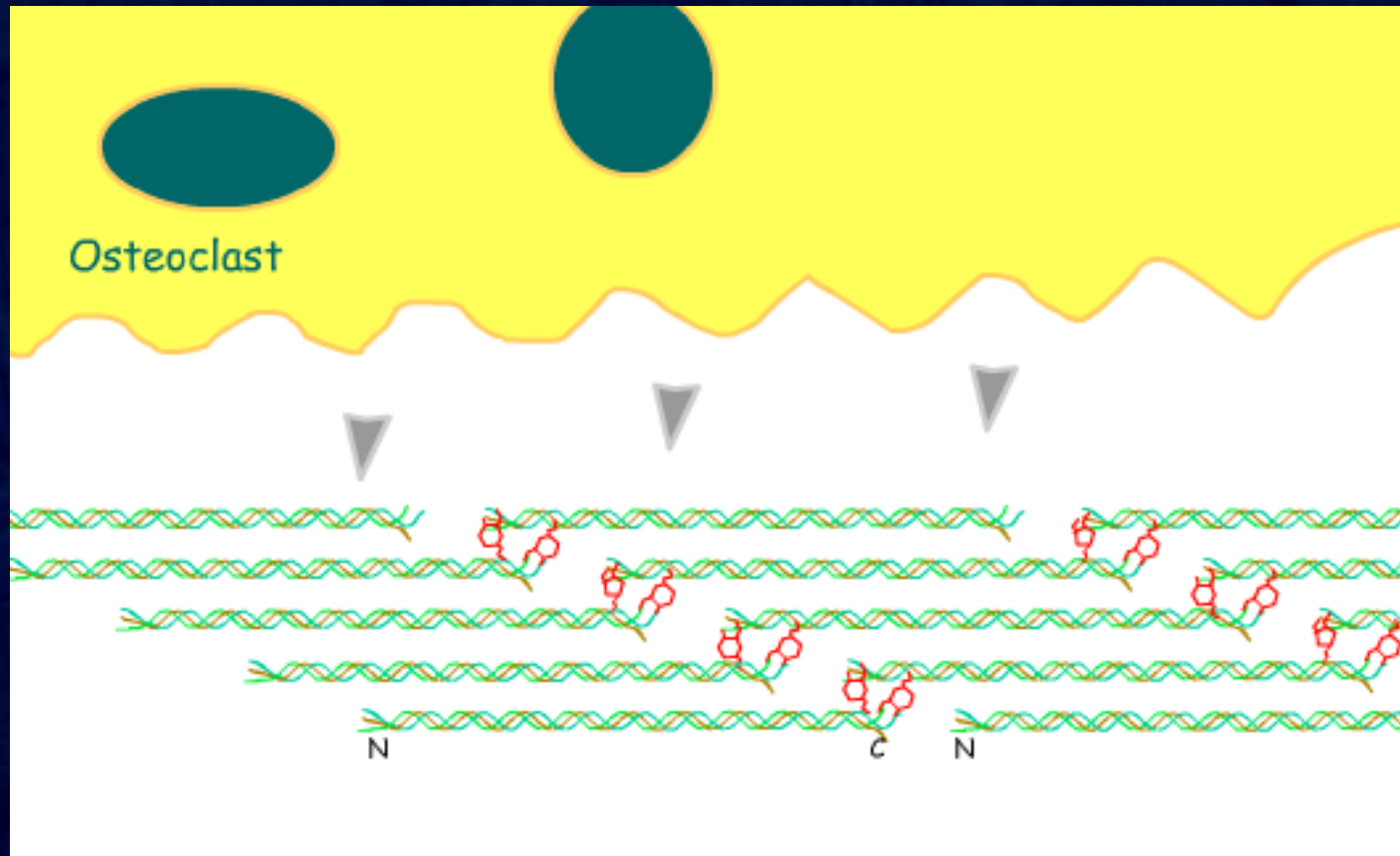
Markers of bone formation



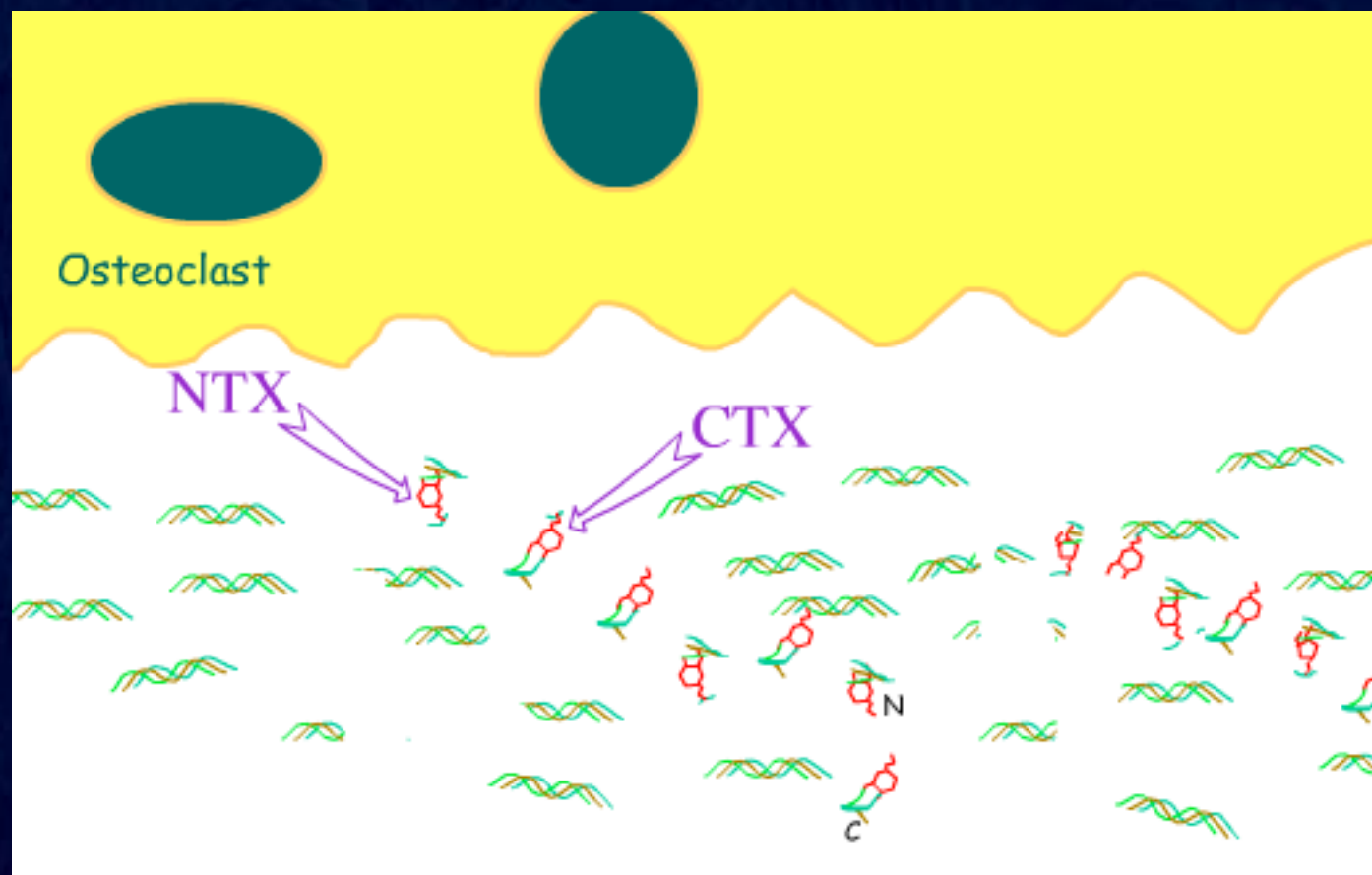
Collagen Crosslinks



Cathepsin K degrades collagen

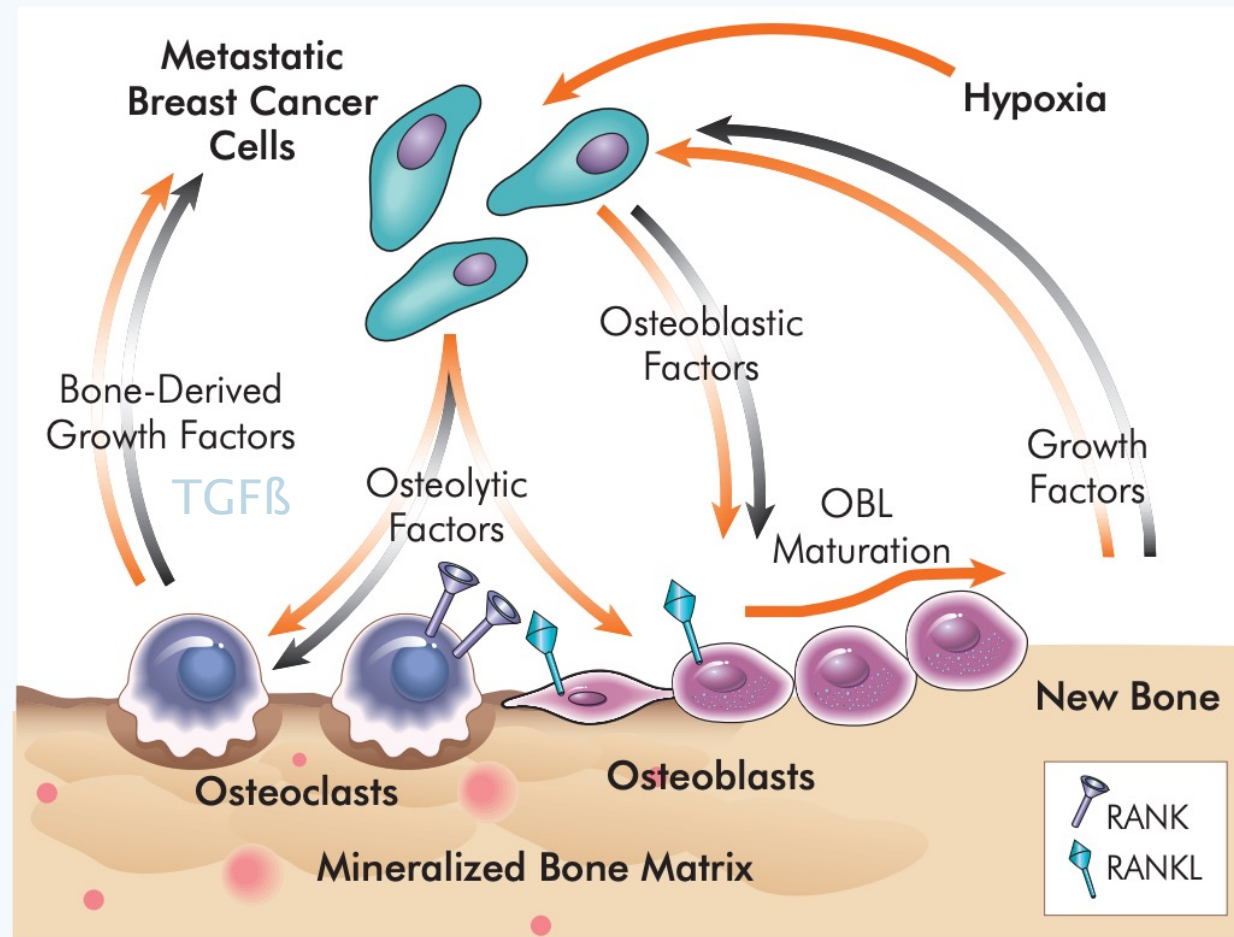


Markers of bone resorption



Bone Metastases

Figure 1 The Vicious Cycle of Bone Metastases



Medications approved for osteoporosis

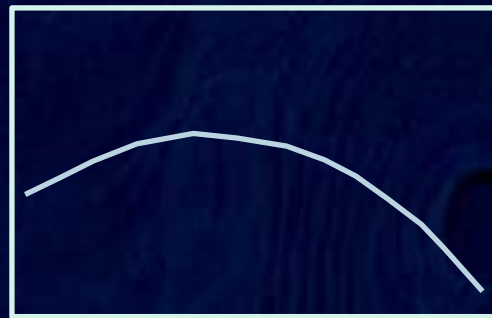
- ❖ Estrogen – avoid in breast, ovarian or uterine cancer, don't start in women older than 60.
- ❖ Raloxifene – not studied in cancer patients.
- ❖ Calcitonin – safe, but not as effective. May help with pain.
- ❖ Bisphosphonates – effective and safe for first 5 yrs, then increased risks. Tailor dose.
- ❖ Denosumab – effective but dangerous to skip a dose or discontinue.
- ❖ Teriparatide/abaloparatide – not recommended due to theoretical cancer risk.
- ❖ Romosozumab – too new to know.

Raloxifene

- This is a Selective Estrogen Receptor Modulator, similar to tamoxifen.
- Activates estrogen receptors on bone but inhibits them on the breast.
- Decreased fractures in the spine and decreased risk of breast cancer.
- Has not been studied in women who have had breast cancer.

Bone strength with long-term bisphosphonates

- Bone biopsies from ordinary osteoporotic patients on bisphosphonates from 1 to 17 years showed that strength peaked at 7 years and then declined to levels below baseline. Crack density increased progressively.



STRENGTH

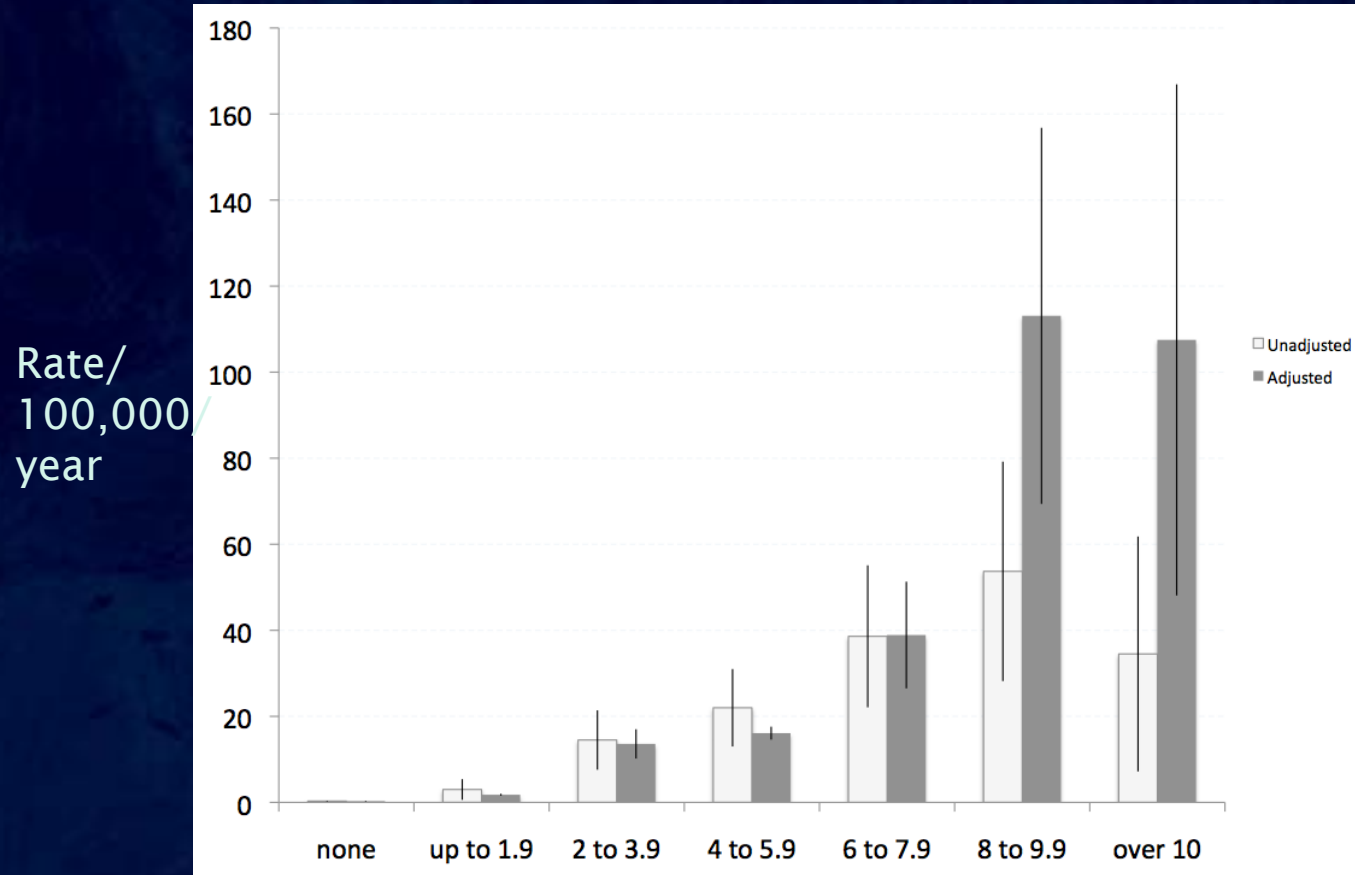


CRACKS



Limit bisphosphonate use to 5 years because long-term use increases risk of fractures, especially in Asians

Incidence of atypical femur fractures



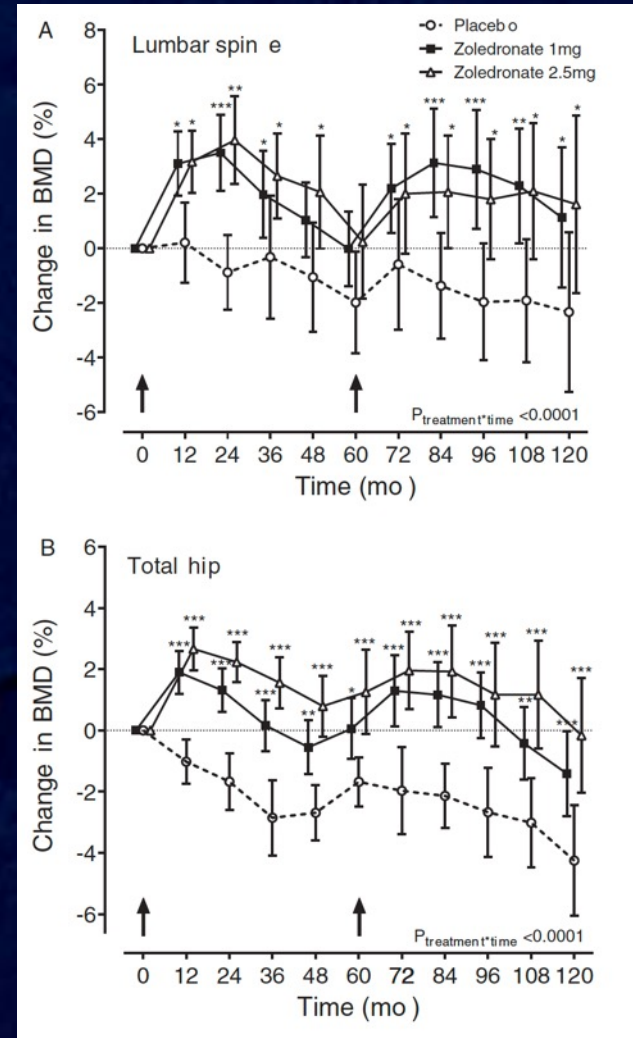
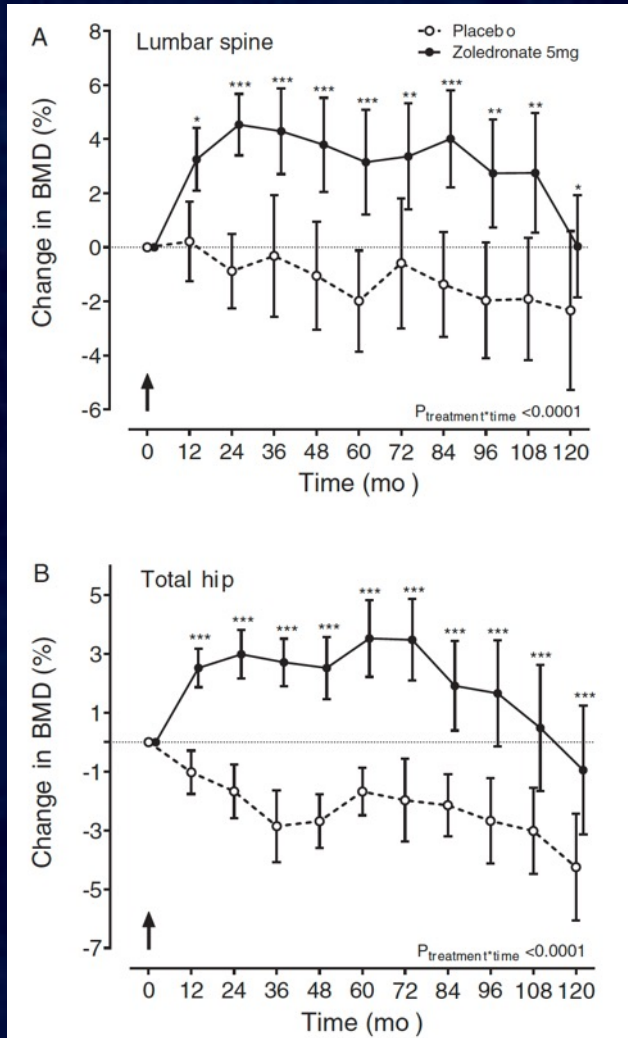


One dose of zoledronate prevents bone loss for a decade

5mg once

1 or 2.5mg twice

Spine



Postmenopausal women with osteopenia

N = 180

25-35/group in extension

Hip

Exaggerated Increases in Bone Mass 2-Year Rat Study of PTH

Control



5 mcg/kg



30
mcg/kg

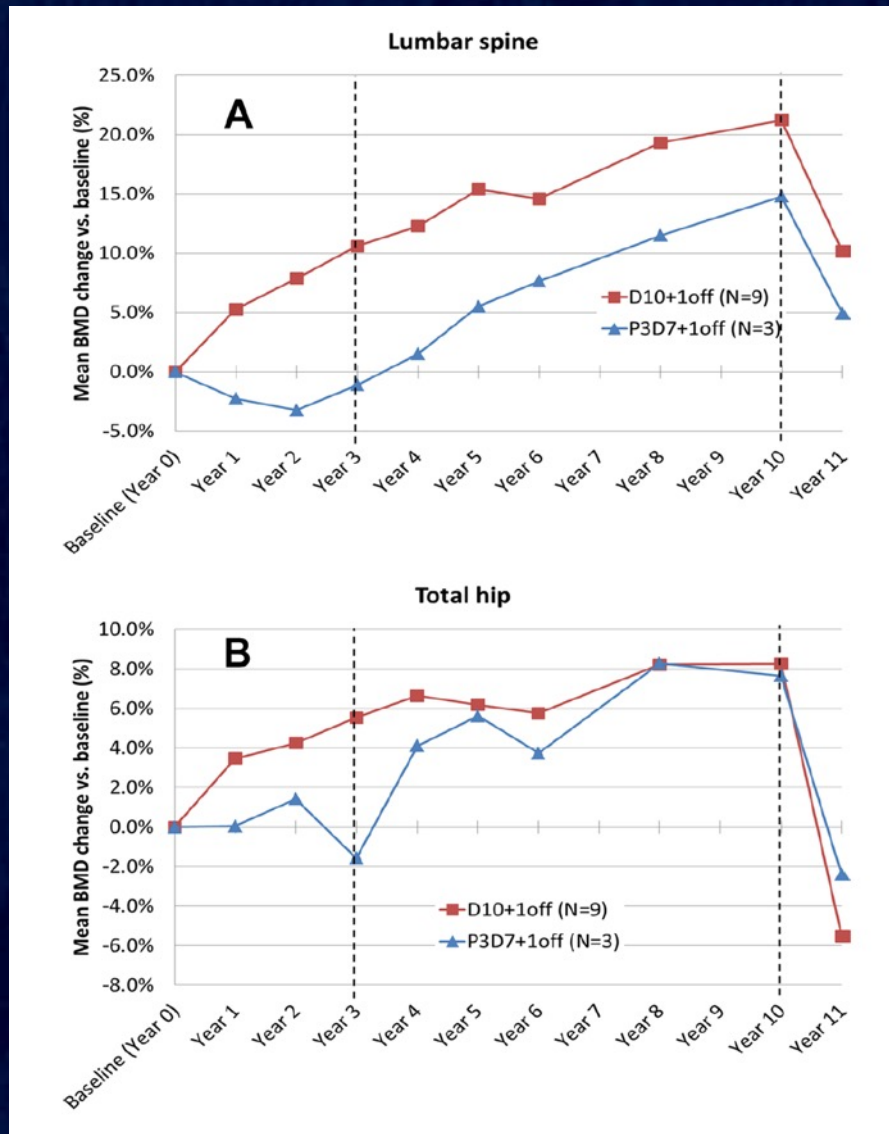


75
mcg/kg



But 31% of the rats got
osteosarcoma

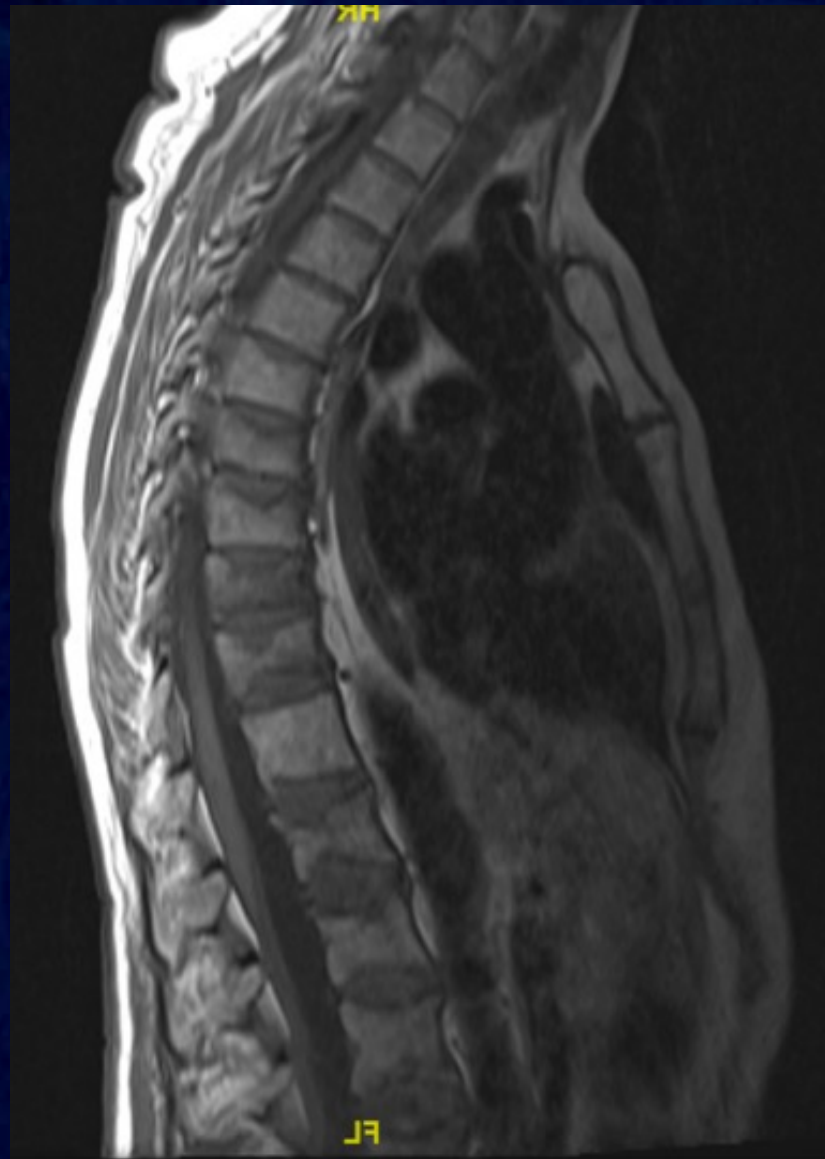
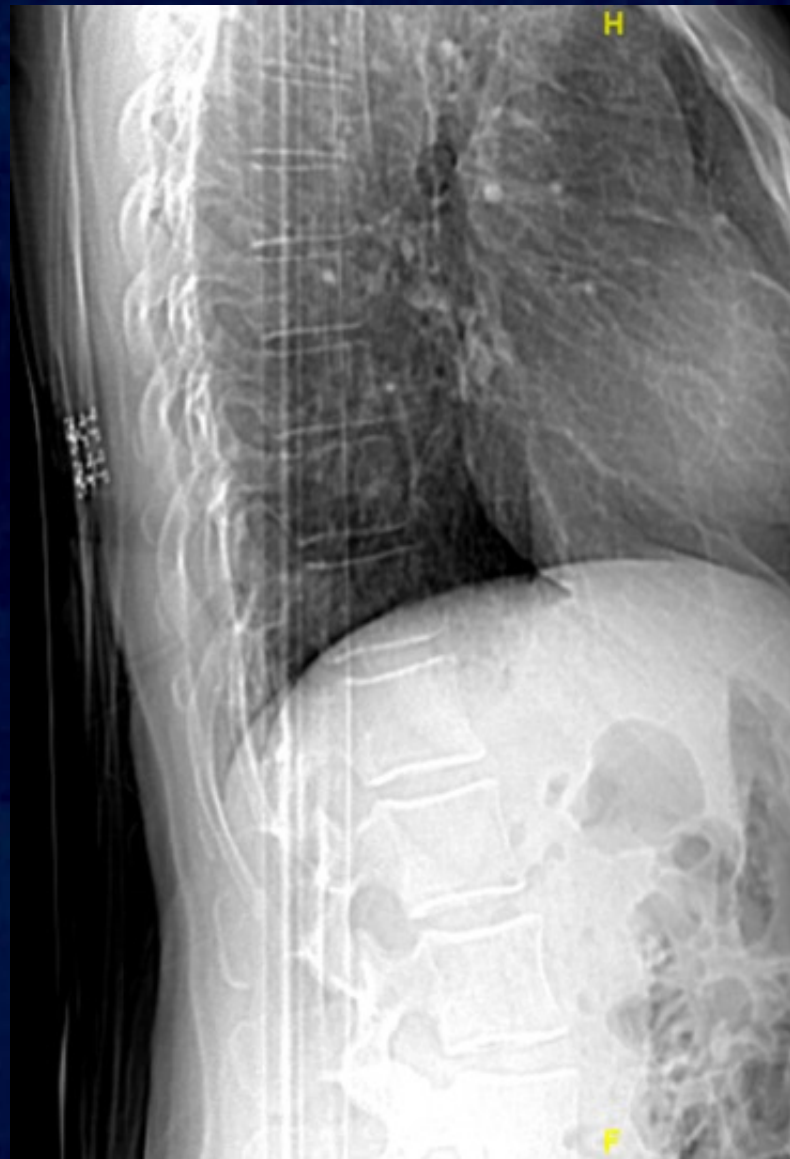
Bone density after long-term denosumab



N=12
Subjects from
FREEDOM trial

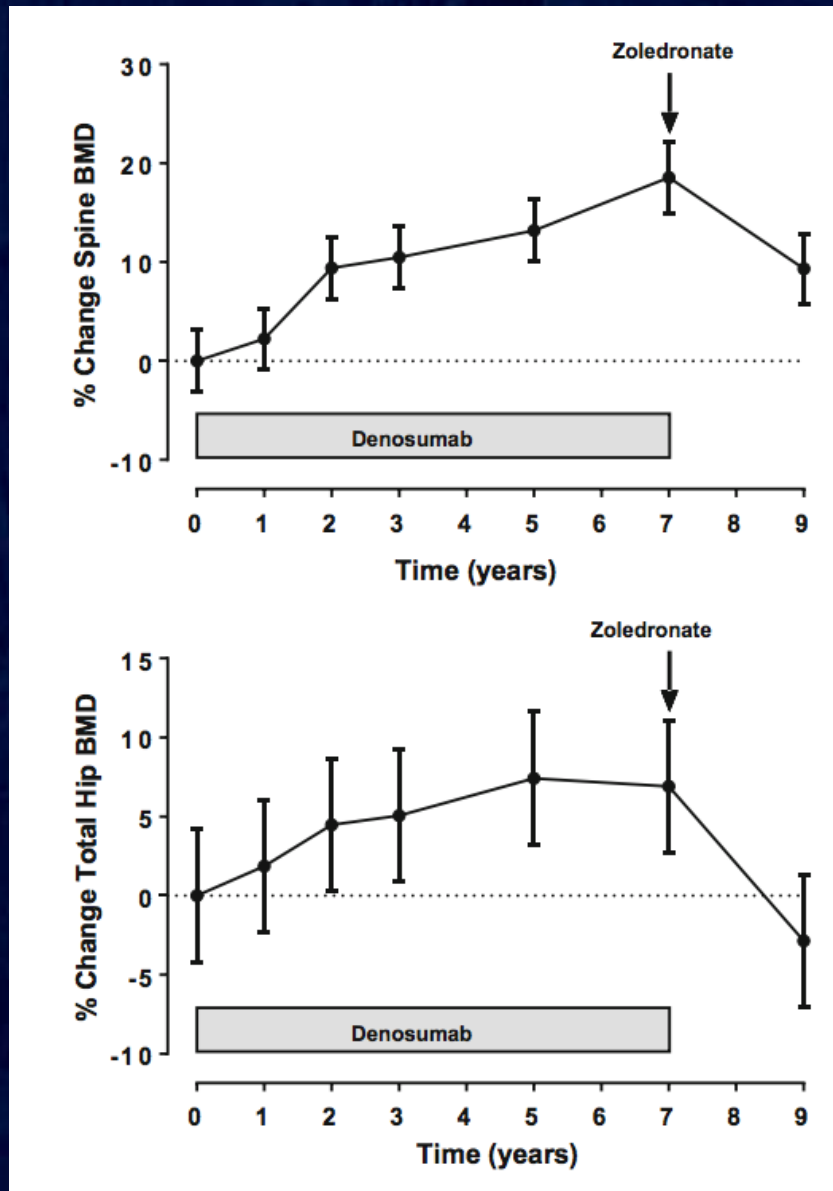


48 yr old woman with breast cancer treated with AI from 2010 to 2015 and denosumab from 2012-2015 with improvement in BMD. Within 6 months after stopping she developed multiple spine fractures.

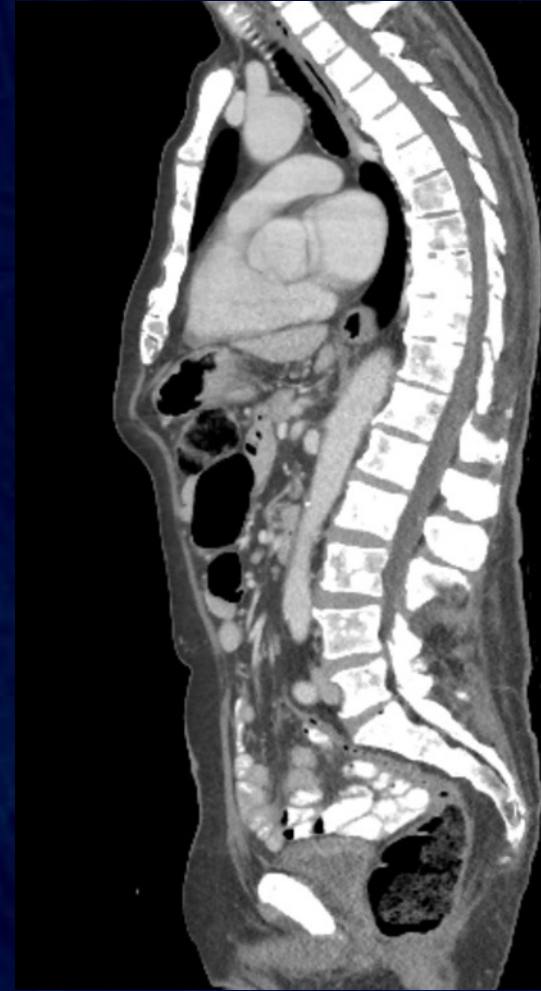


Before
and after
skipping a
dose of
denosumab

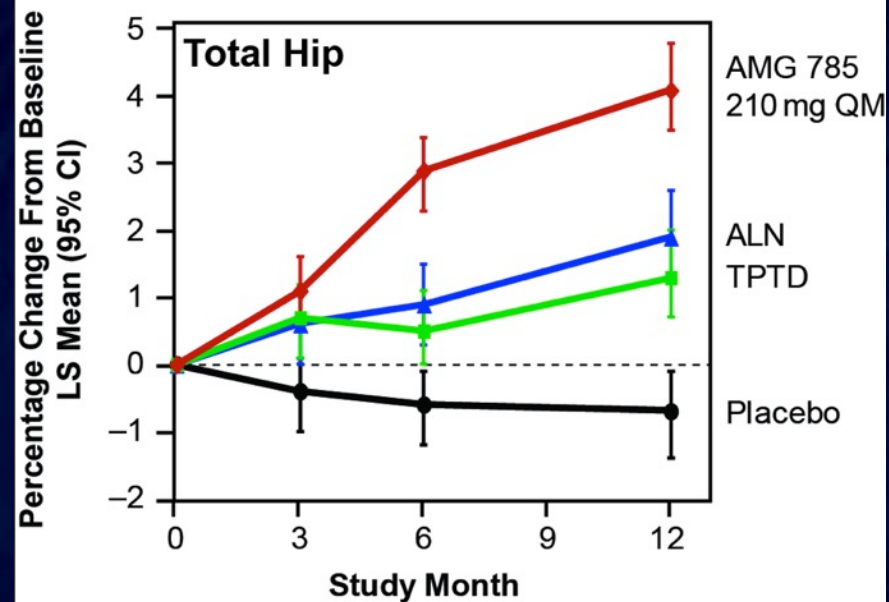
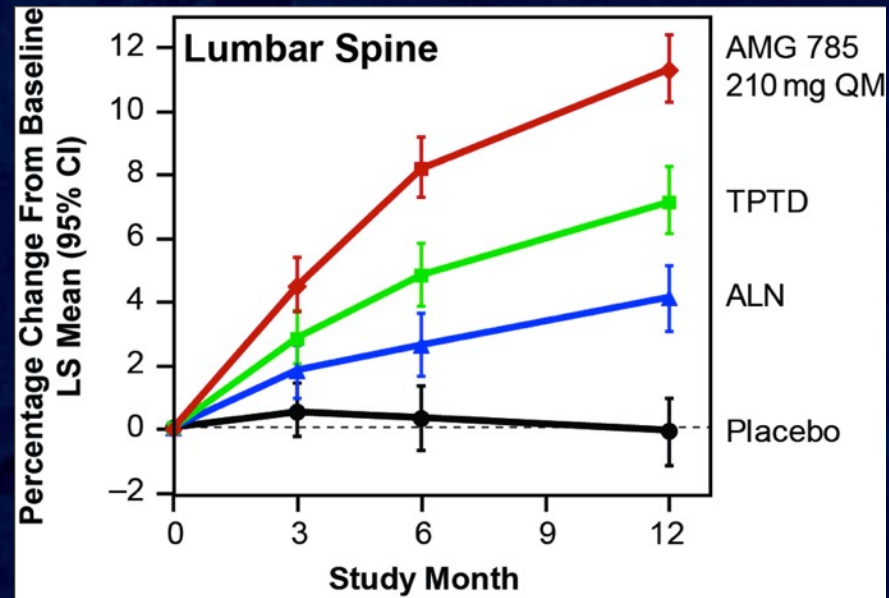
Zoledronate may not prevent BMD loss after denosumab



When to use denosumab



Romosozumab



Presented 2012
ASBMR