

BONE TURNOVER MARKERS

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BONE TURNOVER MARKES

- What are bone turnover markers (BTM)?
- How do they behave in healthy people?
- What can they tell us in patients with osteoporosis?
- How can we use them for monitoring therapy?

BONE REMODELING CYCLE

Resting / quiescent
Resorption:
osteoclasts
Activation 7-10 days
Formation:
osteoblasts
12 weeks;
mineralization



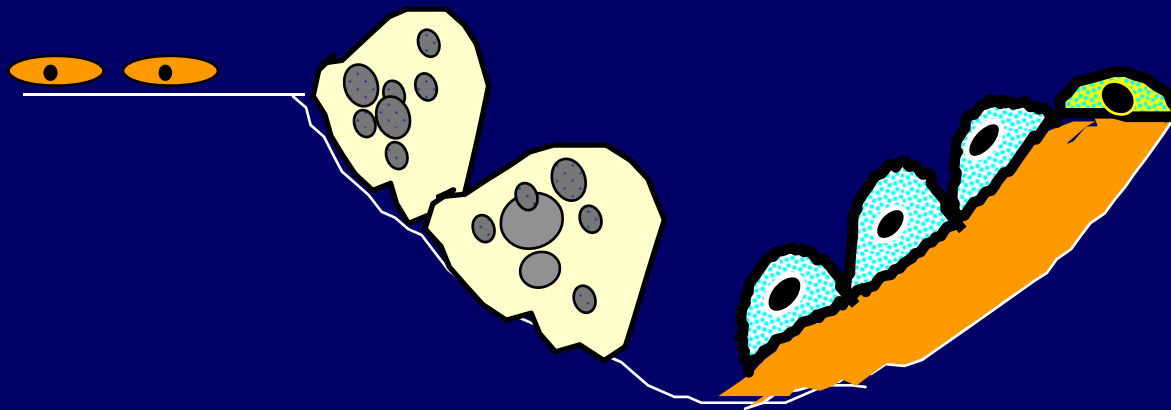
Adapted from Watts NB. *Clin Chem* 1999;45:1359-1368



NORMAL BONE REMODELING

Resorption:
osteoclasts

Formation
osteoblasts



Activation → Resorption → Reversal → Formation

BIOCHEMICAL MARKERS OF BONE TURNOVER

Formation

- Osteocalcin (OC)
- Bone-specific alkaline phosphatase (BAP)
- Amino terminal propeptide of type I collagen (PINP)
- Carboxy terminal propeptide of type I collagen (PICP)

Resorption

- Pyridinoline (Pyr)
- Deoxypyridinoline (dPyr)
- Amino terminal telopeptide of type I collagen (NTX)
- Carboxy terminal telopeptide of type I collagen (CTX)

FACTORS THAT AFFECT REMODELING

- Diet
- Activity
- Season
- Pregnancy/menstrual cycle
- Time of day
- Age, gender, race
- Fracture
- Diseases
- Medications

Intra-individual variation is 20%-30%

SAMPLING FOR BONE TURNOVER MARKERS

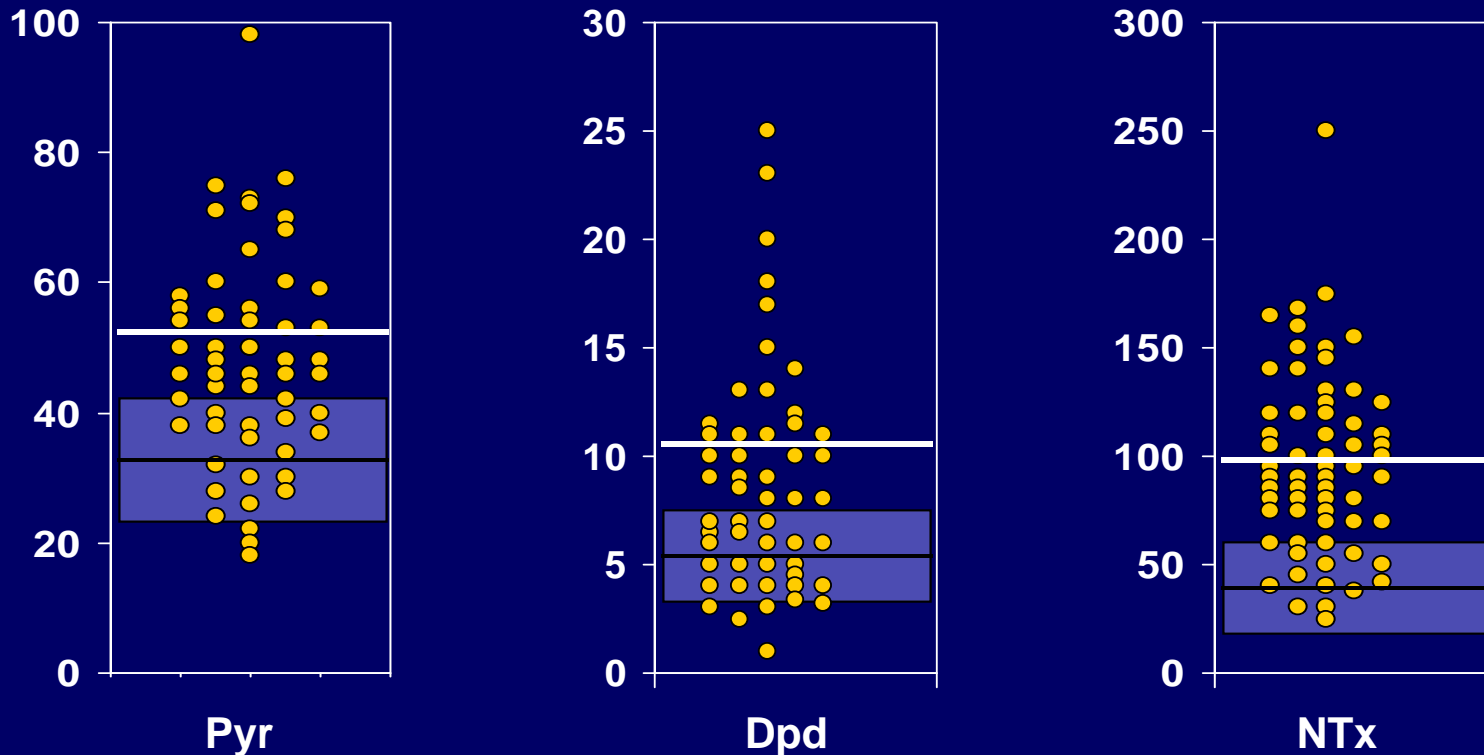
- Because of the diurnal variation (higher in the morning than in the evening) and the decrease after eating, bone turnover markers should be measured on
 - A second-morning fasting urine
 - A fasting blood sample

RELEVANCE OF IMPRECISION (SIGNAL : NOISE RATIO)

<u>Measurement</u>	<u>Variability</u>	<u>Expected Change</u>	<u>Ratio</u>
Spine BMD	~1%	~4%	~4.0
Hip BMD	~2%	~3%	~1.5
Urine NTX	~30%	~60%	~2.0
Serum CTX	~15%	~30%	~2.0

NOT EVERYONE WITH OSTEOPOROSIS HAS HIGH BONE TURNOVER

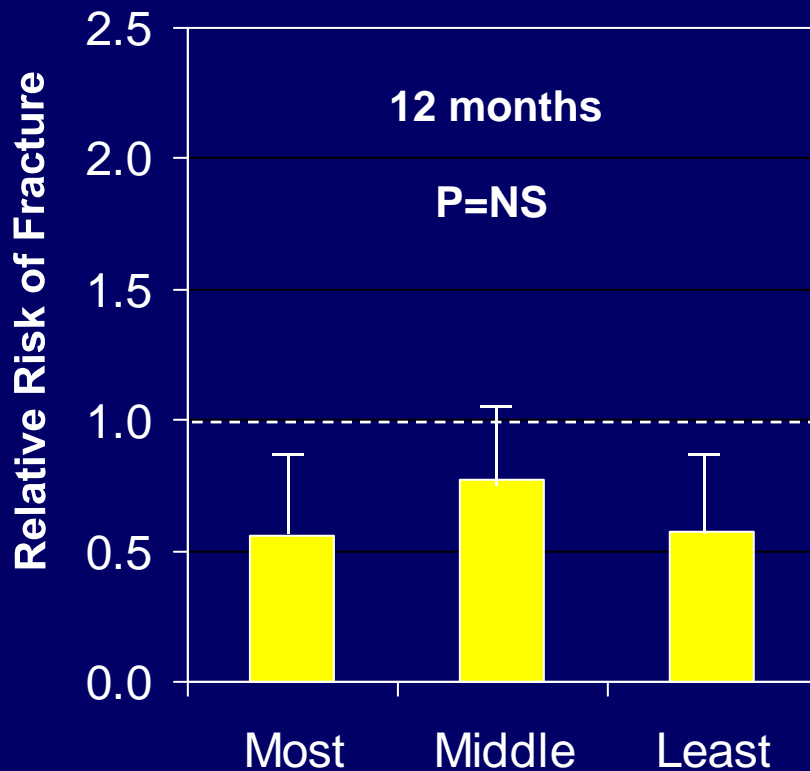
89 Elderly Women with Osteoporosis



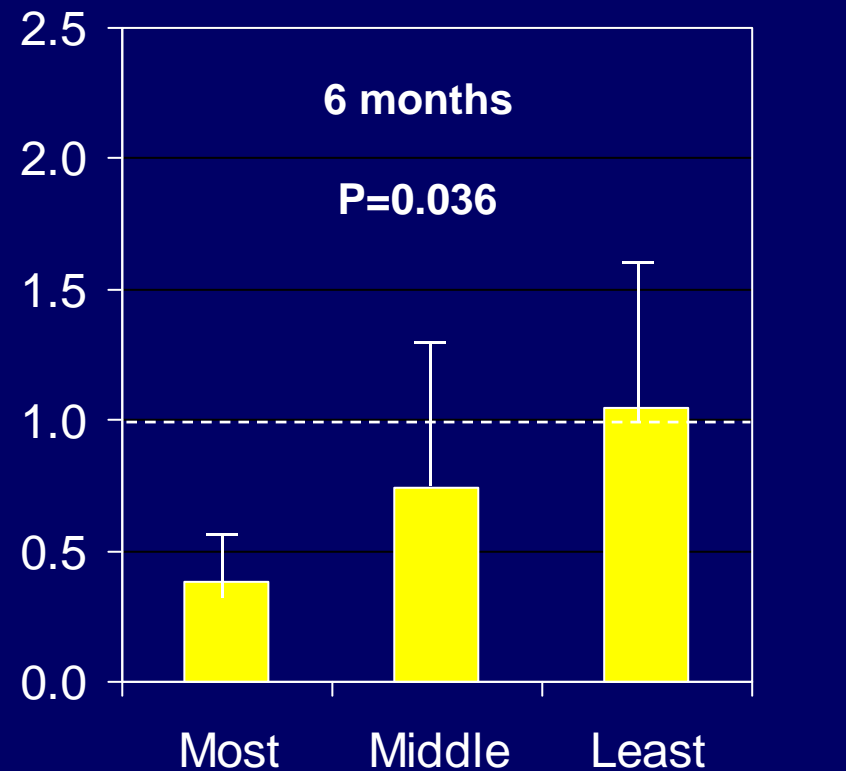
Garnero P et al, *J Clin Endocrinol Metab* 1994;79:1693



DECREASE IN BTM CORRELATES WITH DECREASE IN FRACTURE RISK



Femoral Neck BMD



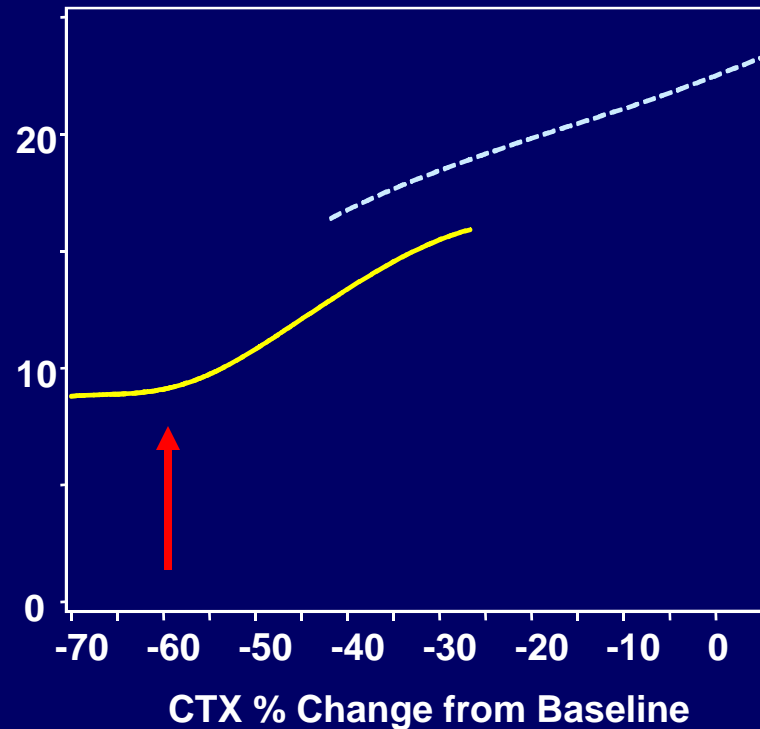
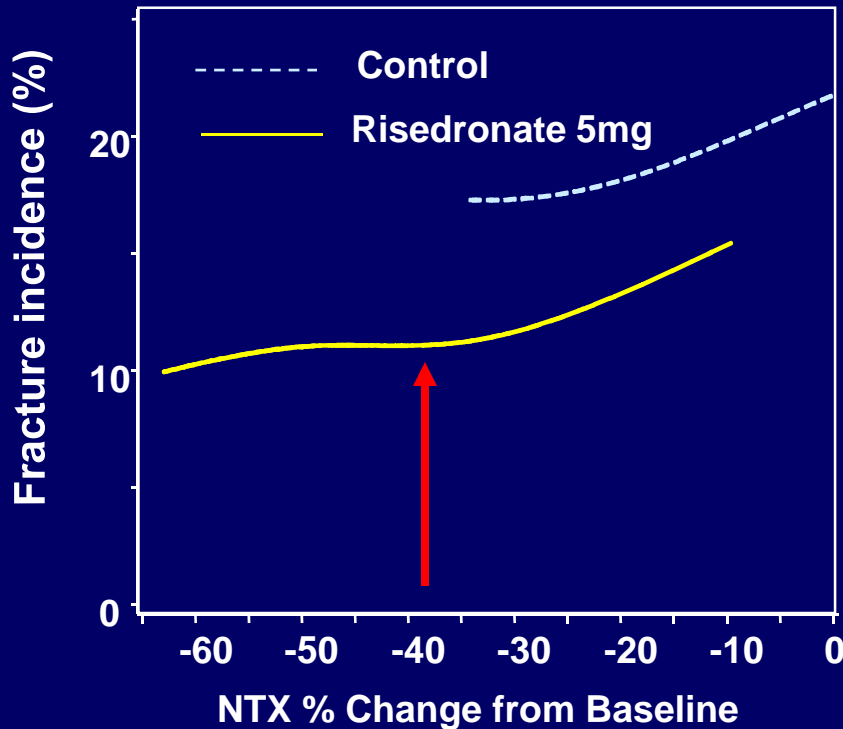
Bone-Specific Alkaline Phosphatase

Bjarnason NH et al. *Osteoporos Int* 2001;12:922-930



RELATIONSHIP BETWEEN CHANGE IN BONE TURNOVER MARKER AND FRACTURE INCIDENCE

New Vertebral Fractures over 3 Years
vs. 3 to 6 Month Marker Change from Baseline



Eastell R et al, *J Bone Miner Res* 2003;18:1051-1056



BONE TURNOVER MARKERS

- Bone turnover markers...
 - Predict bone loss and fracture risk in untreated patients
- With treatment...
 - Change sooner than BMD
 - Identify more “responders” than BMD
 - Explain a greater proportion of fracture reduction than change in BMD
- Can be useful in monitoring the response to treatment