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EUROIMMUN Medizinische Labordiagnostika AG

Bone turnover markers

Beyond osteoporosis

Providing laboratories with accurate and reliable assays to support the assessment of metabolic bone diseases

Commitment to innovation

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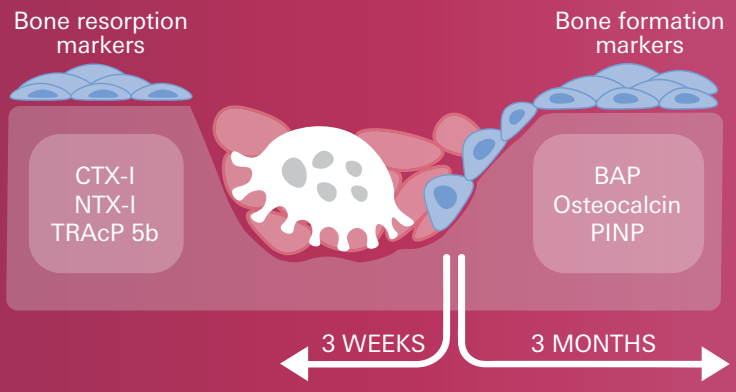
Bone turnover

Bone turnover, also called bone remodelling, is a dynamic, lifelong process in which old bone is removed from the skeleton (resorption) and new bone is added (formation). This process is precisely regulated through the action of various systemic hormones (e. g. parathyroid hormone (PTH) and vitamin D) and local mediators (e. g. cytokines and growth factors).

During the bone remodelling process, compounds are released either from bone or from the cells involved (osteoblasts and osteoclasts).



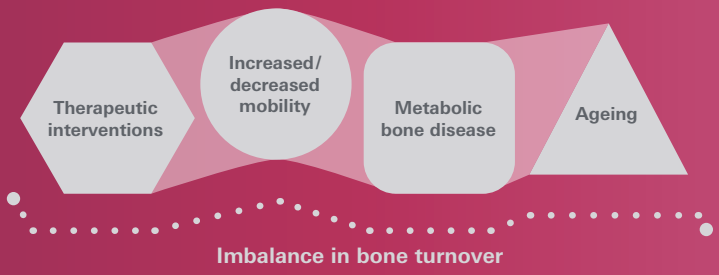
Adapted from Schini M et al, 2023[1].

Normal

Under normal conditions, bone resorption and formation are closely aligned, so that the amount of bone removed is equal to the amount of newly formed bone.

Imbalances

In contrast, ageing, metabolic bone diseases, states of increased or decreased mobility, therapeutic interventions and many other conditions can lead to an imbalance in bone turnover.



Bone turnover markers (BTMs)

Depending on their involvement in the bone remodelling process, BTMs are categorised into **bone formation** and **bone resorption markers**:

Bone formation markers reflect different aspects of osteoblast function and of bone formation:

- **Osteocalcin** and **propeptides of type I collagen (PINP)** – deposition of the protein matrix
- **Bone-specific alkaline phosphatase (BAP)** – mineralisation of the bone matrix

Bone resorption markers are all related to osteoclast resorption of the bone matrix:

- **Tartrate-resistant acid phosphatase 5b (TRAcP 5b)** – dissolution of the mineralised bone matrix
- **Telopeptides of collagen type I (CTX-I and NTX-I)** – degradation of the protein matrix

Supporting the assessment of metabolic bone diseases

- **Comprehensive panel** to support diagnosis and monitoring of metabolic bone diseases
- Measurement possible in **multiple sample types**
- Full bone turnover portfolio **supports translational research**

Paget's disease of bone

Paget's disease is the second most common metabolic bone disorder. It is a chronic, slowly progressing condition with unusually rapid resorption and disorganised formation of bone. Typically, this affects the shape and size of the newly formed bone, resulting in it being structurally dense but also fragile.

Possible signs and symptoms

- Bone pain
- Bone deformities
- Headache
- Fractures

Commonly affected bones

- Spine
- Pelvis
- Legs
- Skull

Occurence [2, 3]

- More common in men than in women
- Affects individuals of all ethnic and racial groups
- Prevalence of 1–2%
- Rarely diagnosed under 40 years, affects 3% of those over 60 years

Diagnosis [1]

- X-ray
- BAP, CTX-I or PINP

Osteomalacia

Osteomalacia is a metabolic bone disorder characterised by altered skeletal mineralisation and weakened bones, predominantly due to vitamin D deficiency. [1, 4, 5] This deficiency causes abnormal mineralisation of the bone matrix (osteoid) resulting in 'softening' of bones.

Possible signs and symptoms

- Bone pain
- Pseudofractures of feet and pelvis
- Muscle weakness
- Affects gait/walk

Causes

- Lack of phosphorus
- Liver disorders
- Coeliac disease
- Genetic factors

Diagnosis [4, 5]

- X-ray
- Calcium, vitamin D, PTH, BAP, CTX-I, PINP, osteocalcin

Hypophosphatasia

Hypophosphatasia (HPP) is a rare inherited condition resulting from mutations within the gene coding for tissue nonspecific alkaline phosphatase (TNSALP). [6] It is characterised by impaired mineralisation (calcification) of teeth and bones resulting from a deficiency of TNSALP in cells involved in the turnover process. [7] HPP is categorised into six clinical forms, most of which are characterised by the age of symptom onset/diagnosis: perinatal, prenatal benign, infantile, childhood and adult HPP. Another form, odontohypophosphatasia, manifests as isolated dental symptoms.

Possible signs and symptoms

Foetuses and newborns (perinatal period)
- Bowed limbs
- Chest deformity
- Stillbirth

Children and infants
- Bone malformation
- Failure to thrive
- Early teeth loss

Adults
- Osteomalacia
- Cartilage damage
- Stress fractures
- Unexplained loss of teeth

Occurence [6]

- Affects men and women equally
- Incidence between 1 in 100,000 and 1 in 300,000 [8]
- Prevalence of adult form between 1:3100 to 1:508 in EU [8]
- Age at onset indicates clinical form

Diagnosis [1, 6, 8]

- X-ray
- Alkaline phosphatase (ALP), BAP, DNA sequencing

Metastatic bone disease

The development of bone metastases (metastatic bone disease) is very common in different forms of organ or tissue cancer such as breast, prostate or thyroid cancer. It is estimated that up to 50% of cancers that start in organs can metastasise to bone. The affected area of the bone is either destroyed or the tumour creates lesions, which weaken or deform the bone.

Possible signs and symptoms

- Bone pain
- Fractures
- Anaemia

Incidence of metastasis [9*]

- 73% Breast cancer
- 68% Prostate cancer
- 42% Thyroid cancer

*** based on post-mortem examinations**

Prospective studies suggest that TRAcP 5b, PINP, BAP and CTX-I levels are significantly higher in patients with metastases than in those without. [1] The combined determination of BAP, PINP and TRAcP 5b has even been recommended for early diagnosis of bone metastasis in the early stages of some cancers. [10] Despite these positive associations between BTMs and the presence of metastases, they are not yet routinely used in clinical practice.

Efficieny and precision

- **Fast results** help prevent delays in diagnosis
- **Broad analytical measuring ranges** allow accurate quantification of markers

Simplified workflow and cost-effective solutions

- **Ready-to-use** reagents
- **Random access** for both samples and reagents (ChLIA)
- Up to 28 days on-board storage and calibration frequency (ChLIA)

Assay information

ChLIA test kits

Product	Product code	Sample type/volume	In-use stability/ calibration frequency
IDS Ostase BAP	IS-2800	Serum, plasma/50 µl	21 days/14 days
IDS N-MID Osteocalcin	IS-2900	Serum, plasma/50 µl	28 days/10 days
IDS CTX-I (CrossLaps)	IS-3000	Serum, plasma/45 µl	4 weeks/14 days
IDS Beta CrossLaps (CTX-I)	IS-3000N	Serum, plasma/90 µl	4 weeks/28 days
IDS Intact PINP	IS-4000	Serum, plasma/20 µl	4 weeks/3 days
IDS TRAcP 5b (BoneTRAP)	IS-4100	Serum, plasma/70 µl	4 weeks/21 days

ChLIA calibrator and control sets

Product	Product code	Product format	In-use stability
IDS Ostase BAP Control	IS-2830	3 levels, 2 vials of 2.5 ml each	Until expiry date
IDS N-MID Osteocalcin Control	IS-2930	3 levels, 4 vials of 1 ml each	21 days*
IDS CTX-I (CrossLaps) Control	IS-3030	3 levels, 2 vials of 2.5 ml each	Until expiry date
IDS Beta CrossLaps (CTX-I) Calibrator	IS-3020N	6 levels, 1 vial of 2 ml each	17 weeks
IDS Beta CrossLaps (CTX-I) Control	IS-3030N	2 levels, 2 vials of 2.5 ml each	17 weeks
IDS Intact PINP Control	IS-4030	3 levels, 2 vials of 1 ml each	14 days*
IDS TRAcP 5b (BoneTRAP) Control	IS-4130	3 levels, 3 vials of 1 ml each	8 hours**

** After reconstitution, at –20 °C*
*** After reconstitution, at 2 to 8 °C*

ELISA kits

Product	Product code	Sample type/volume
Serum CrossLaps (CTX-I)	AC-02F1	Serum, plasma/50 µl
Urine CrossLaps (CTX-I)	AC-03F1	Urine/15 µl
Alpha CrossLaps (CTX-I)	AC-04F1	Urine/25 µl
Urine BETA CrossLaps (CTX-I)	AC-05F1	Urine/20 µl
N-MID Osteocalcin	AC-11F1	Serum, plasma/20 µl
Ostase BAP	AC-20F1	Serum/50 µl
BoneTRAP (TRAcP 5b)	SB-TR201A	Serum, plasma/100 µl

Products manufactured by IDS.

Regulatory status and precise intended use of the products must be verified for the user's individual jurisdiction.
Please contact your country representative for product availability and information.

References

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3. Paget's Disease – Symptoms, Causes, Treatment | NORD (rarediseases.org)
4. Osteomalacia – StatPearls – NCBI Bookshelf (nih.gov)
5. Cianferotti L. Osteomalacia Is Not a Single Disease. Int J Mol Sci 23(23):14896 (2022).
6. Hypophosphatasia – Symptoms, Causes, Treatment | NORD (rarediseases.org)
7. Orimo H. Pathophysiology of hypophosphatasia and the potential role of asfotase alfa. Ther Clin Risk Manag 12:777–86 (2016).
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9. Coleman RE. Clinical features of metastatic bone disease and risk of skeletal morbidity. Clin Cancer Res 12(20 Pt 2):6243s–6249s (2006).
10. Lumachi F, Basso SM, Camozzi V, et al. Bone turnover markers in women with early stage breast cancer who developed bone metastases. A prospective study with multivariate logistic regression analysis of accuracy. Clin Chim Acta ;460:227–30 (2016).

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