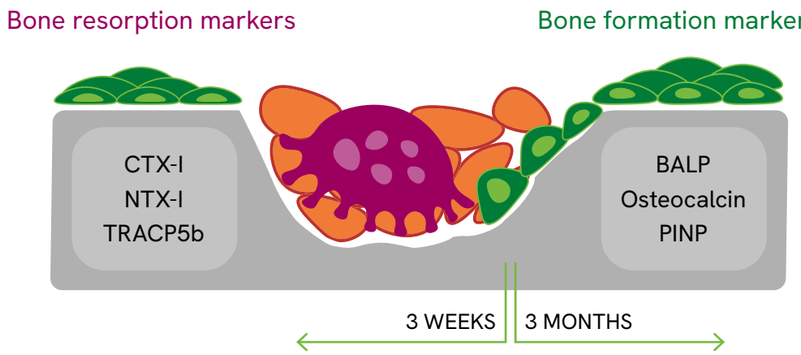
euroimmun
From Revvity

Bone turnover markers: Beyond osteoporosis.

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).

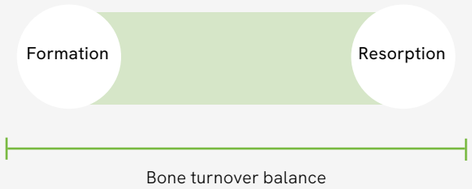
During the bone remodelling process, compounds are released either from bone or from the cells involved (osteoblasts and osteoclasts).



Adapted from Schini M et al, 2023 [1]

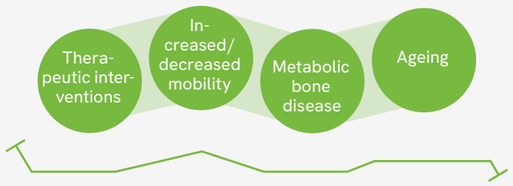
Normal

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 (BALP) – mineralisation of the bone matrix

Bone resorption markers

are all related to osteoclast resorption of the bone matrix:

- Telopeptides of collagen type I (CTX-I and NTX-I) – degradation of the protein matrix
- Tartrate-resistant acid phosphatase 5b (TRACP5b) – dissolution of the mineralised bone 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

Efficiency 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)

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.

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

Possible signs and symptoms:

- Bone pain
- Headache
- Bone deformities
- Fractures

Commonly affected bones:

- Spine
- Legs
- Pelvis
- Skull

Diagnosis [1]

- X-ray
- Blood: BALP, 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:

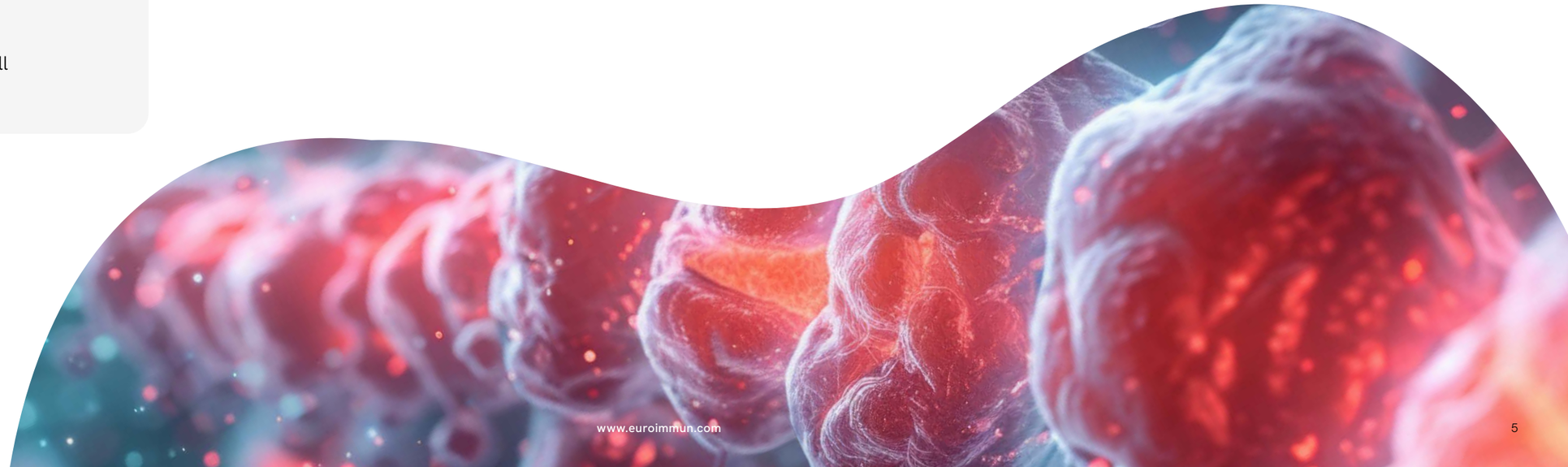
- Bone pain
- Muscle weakness
- Pseudofractures of feet and pelvis
- Affects gait / walk

Causes:

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

Diagnosis [4, 5]

- X-ray
- Blood: Calcium, vitamin D, PTH, BALP, CTX-I, PINP, osteo-calcin



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.

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

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

Diagnosis[1, 6, 8]

- X-ray
- Blood: Alkaline phosphatase (ALP), BALP, 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.

Incidence of metastasis[9*] (based on post-mortem examinations):

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

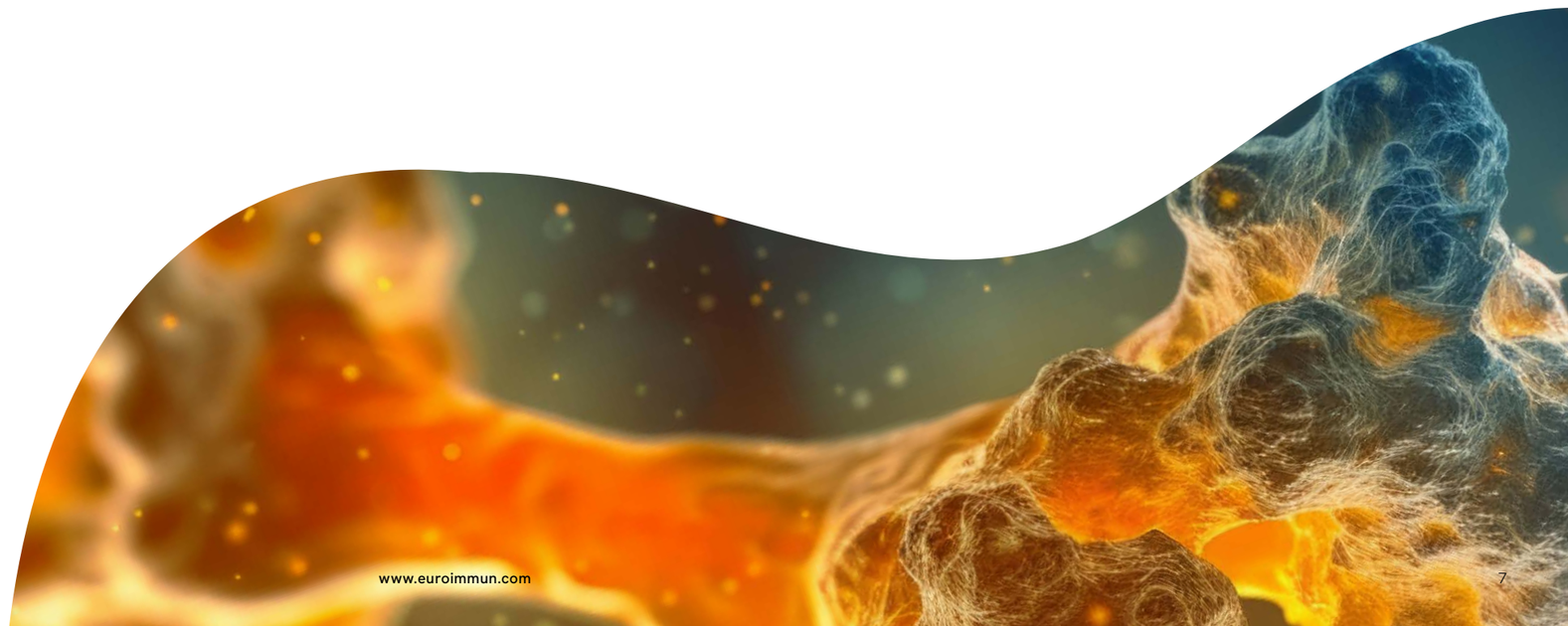
Possible signs and symptoms:

- Bone pain
- Fractures
- Anaemia

Prospective studies suggest that TRACP5b, PINP, BALP and CTX-I levels are significantly higher in patients with metastases than in those without.[1]

The combined determination of BALP, PINP and TRACP5b 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.



Assay information

ChLIA kits *

Product	Product code	Sample type/volume	In-use stability/calibration frequency
IDS Ostase BAP**	IS-2800	Serum, plasma/50µl	21 days/14 days
IDS N-MID Osteocalcin**	IS-2900	Serum, plasma/50µl	28 days/10 days
IDS Beta CrossLaps (CTX-I)**	IS-3000N	Serum, plasma/90µl	4 weeks/28 days
IDS Intact PINP	IS-4000	Serum, plasma/20µl	28 days/3 days
IDS TRAcP 5b (BoneTRAP)	IS-4100	Serum, plasma/70µl	28 days/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 2.5ml each	Until expiry date
IDS N-MID Osteocalcin Control**	IS-2930	3 levels, 4 vials of 1ml each	21 days[a]
IDS Beta CrossLaps (CTX-I) Calibrator**	IS-3020N	6 levels, 1 vial of 2ml each	17 weeks
IDS Beta CrossLaps (CTX-I) Control**	IS-3030N	2 levels, 2 vials of 2.5ml each	17 weeks
IDS Intact PINP Control	IS-4030	3 levels, 2 vials of 1ml each	14 days[a]
IDS TRAcP 5b (BoneTRAP) Control	IS-4130	3 levels, 3 vials of 1ml each	8 hours[b]

a After reconstitution, at -20°C b After reconstitution, at 2 to 8°C

ELISA kits *

Analyte	Product code	Sample type/volume
Serum CrossLaps (CTX-I)**	AC-02F1	Serum, plasma/50µl
Urine CrossLaps (CTX-I)**	AC-03F1	Urine/15µl
Alpha CrossLaps (CTX-I)**	AC-04F1	Urine/25µl
Urine BETA CrossLaps (CTX-I)**	AC-05F1	Urine/10µl
N-MID Osteocalcin**	AC-11F1	Serum, plasma/20µl
Ostase BAP**	AC-20F1	Serum/50µl
BoneTRAP (TRAcP 5b)	SB-TR201A	Serum, plasma/100µl

* Products manufactured by Immunodiagnostic Systems Limited (IDS), available to order from your local contact (availability may be restricted in certain countries).
** CrossLaps and N-Mid are trademarks of IDS, Ostase is a trademark of Hybritech Incorporated.

References

1. Schini M, Vilaca T, Gossiel F, et al. Bone Turnover Markers: Basic Biology to Clinical Applications. Endocr Rev 44(3):417-473 (2023).
2. Appelman-Dijkstra NM, Papapoulos SE. Paget's disease of bone. Best Pract Res Clin Endocrinol Metab 32(5):657-668 (2018).
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).
8. Tournis S, Yavropoulou MP, Polyzos SA, Doulgeraki A. Hypophosphatasia. J Clin Med 10(23):5676 (2021).
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).

Find out more about bone turnover disorders at www.euroimmun.com or contact us directly: www.euroimmun.com/contact

EUROIMMUN Medizinische Labordiagnostika AG
Seekamp 31 · 23560 Lübeck (Germany) · Phone: +49 451 20 32-0
www.euroimmun.com

euroimmun
From Revvity