Publication Overview CIM-Biomarker

Content:

1.
A pilot study on the use of natural calcium isotope (44Ca40Ca) fractionation in urine as a proxy for the human body calcium balance.
Dec 2009

Published on: 11 December 2009 in Bone Journal
Subject: 2 participants
Content: This pilot study investigated the use of natural calcium isotope variations in urine as a non-invasive method to monitor calcium balance in the human body.
Objective/Findings: To assess whether natural calcium isotope variations in urine can be used as a biomarker for bone mineralisation versus demineralisation. The study established, for the first time, that natural calcium isotopes in urine represent a promising biomarker for bone balance and could revolutionise osteoporosis diagnostics.
Access: Paid

2.
Biological fractionation of stable Ca isotopes in Göttingen minipigs as a physiological model for Ca homeostasis in humans.
Mar 2016

Published on: 21 March 2016 in *Isotopes in Environmental and Health Studies*
Subjects: 18 miniature pigs, divided into 3 groups
Content: The study investigated calcium isotope fractionation in vertebrates as a diagnostic tool for detecting disturbances in calcium metabolism.
Objective/Findings: The study provides important fundamental data on calcium isotope fractionation and confirms its potential for clinical applications in osteoporosis and other bone diseases.
Access: Paid

3.
Calcium isotope ratios in blood and urine: A new biomarker for the diagnosis of osteoporosis.
Mar 2019

Published on: 16 March 2019 in *Bone Reports*
Subjects: 100 postmenopausal women aged 50–75 years, 80 women included (after exclusion of those with vitamin D deficiency and renal failure)
Content: Investigation of whether calcium isotope ratios in blood and urine can be used as novel, non-invasive biomarkers for osteoporosis diagnosis.
Objective/Findings:

- **Significant differences:** Women with osteoporosis showed markedly lower δ44/42Ca values in blood (−0.99‰) and urine (+0.10‰) compared with healthy women (blood: −0.84‰, urine: +0.35‰).
- **Diagnostic accuracy:**
  - Blood isotopes: 100% sensitivity, 54.5% specificity (cut-off: −0.85‰)
  - Urine isotopes: 78.6% sensitivity, 71.2% specificity (cut-off: 0.16‰)
- **Methodological advantage:** The calcium isotope method captures calcium loss from the entire skeleton, whereas DXA measures only individual bones.

- **Early detection:** The isotope method may detect bone demineralisation earlier than radiological changes become visible with DXA.
- **Conclusion:** Calcium isotope ratios offer promising potential as radiation-free, sensitive biomarkers for osteoporosis diagnosis, though further studies are required for confirmation.

Access: Open Access

4.
Early effects of androgen deprivation on bone and mineral homeostasis in adult men: a prospective cohort study.
Aug 2020

Published on: 01 August 2020 in *European Journal of Endocrinology*
Subjects:
26 men, 17 men included after exclusions
All received androgen deprivation therapy (ADT) with cyproterone acetate (CPA)
Content: Investigation of the early effects of androgen withdrawal on bone metabolism and mineral homeostasis in adult men.
Objective/Findings:
The study demonstrates that androgen withdrawal leads to a negative bone balance at a very early stage, mainly through inhibition of bone formation. The calcium isotope method proved to be a promising new biomarker for the early detection of bone changes.
Access: Paid

5.
Naturally Occurring Stable Calcium Isotopes Ratios in Body Compartments Provide a Novel Biomarker of Bone Mineral Balance in Children and Young Adults. Aug 2020

Published on: 12 August 2020 in *Journal of Bone and Mineral Research (JBMR)*
Subjects: 117 participants
Content: Evaluation of natural calcium isotope ratios as a novel biomarker for bone mineral balance in children and young adults.
Objective/Findings: Natural calcium isotope ratios provide an innovative, non-invasive method for real-time assessment of bone mineralisation. They may be particularly valuable for monitoring bone changes in children and for the early detection of bone disorders, as they respond with greater sensitivity than conventional imaging techniques.
Access: Open Access

6.
Calcium isotope fractionation by osteoblasts and osteoclasts, across endothelial and epithelial cell barriers, and with binding to proteins. May 2021

Published on: 21 June 2021 in *American Journal of Physiology – Regulatory, Integrative and Comparative Physiology*
Subjects: Cell cultures of various types
Content: Investigation of the cellular mechanisms of calcium isotope fractionation in bone

cells and epithelial/endothelial barriers to clarify the basis of the δ44/42Ca biomarker method.
Objective/Findings: The study provides fundamental insights into the cellular mechanisms of calcium isotope fractionation. Osteoblasts are identified as the main drivers of fractionation between blood and bone, while renal tubular cells may contribute to the observed blood δ44/42Ca variation. Endothelial and intestinal barriers, as well as protein binding, have only minimal influence on isotope ratios, supporting the application of the δ44/42Ca biomarker method.
Access: Open Access

7.
Naturally occurring stable calcium isotope ratios are a novel biomarker of bone calcium balance in chronic kidney disease.
May 2022
Published on: 26 May 2022 in *Kidney International*
Subjects: 134 children
Content: The study investigated naturally occurring stable calcium isotopes (^{42}Ca and ^{44}Ca) as novel biomarkers for bone calcium balance. Isotopically lighter ^{42}Ca is preferentially incorporated into bone, while heavier ^{44}Ca is excreted. The serum ratio (^{44}/^{42}Ca) increases when bone formation exceeds bone resorption, and decreases in the opposite case. The researchers compared these isotope ratios with conventional bone markers and bone density measurements.
Objective/Findings: Development of a more sensitive, non-invasive method for assessing bone calcium balance in kidney disease. The ^{44}/^{42}Ca serum ratio proved to be the strongest independent predictor of total bone mineral content and correlated more closely with bone health than conventional biomarkers.
Access: Open Access

8.
Nutritional Calcium Supply Dependent Calcium Balance, Bone Calcification and Calcium Isotope Ratios in Rats.
July 2022
Published on: 14 July 2022 in *International Journal of Molecular Sciences*
Subjects: 52 male Sprague–Dawley rats
Content: The study systematically examined how different levels of calcium intake affect calcium isotope ratios (δ^{44}/^{42}Ca) in various body compartments. Isotope ratios were measured in serum, urine, faeces and bone, alongside calcium balance, bone histology, and bone mineral density using µCT.
Objective/Findings: The study demonstrates that dietary differences in calcium isotope fractionation can override the effects of bone mineralisation, which is important for the interpretation of calcium isotope biomarkers.
Access: Open Access

9.
Changes in bone and mineral homeostasis after short-term androgen deprivation therapy with or without androgen receptor signalling inhibitor – substudy of a single-centre, double blind, randomised, placebo-controlled phase 2 trial. Oct 2023

Published on: 05 October 2023 in *eBioMedicine*
Subjects: 87 men
Content: This substudy of the ARNEO trial investigated the early effects of androgen deprivation therapy (ADT) on bone health. Measurements included changes in calcium–phosphate homeostasis, bone biomarkers, and stable calcium isotope ratios ($\delta^{44/42}Ca$) in serum and urine before and after 12 weeks of treatment.
Objective/Findings: Early detection of bone loss in prostate cancer patients undergoing ADT using non-invasive biomarkers. The study shows that bone loss occurs very early after initiation of ADT and that calcium isotope ratios serve as sensitive early indicators of negative bone mineral balance. This underlines the importance of early monitoring of bone health in prostate cancer patients receiving ADT.
Access: Open Access

10.
Calcium isotope composition in serum and urine for the assessment of bone mineral balance (BMB) – The Osteolabs post-market follow-up study. July 2024

Published on: 28 July 2024 in *Bone*
Subjects: 2,320 participants
Content: This large post-market study by osteolabs investigated 2,320 participants to validate the clinical applicability of calcium isotope markers (CIM) for the assessment of bone mineral balance (BMB). The thresholds established in the original OsteoGeo study were confirmed in this larger, more diverse population.
Objective/Findings:
The study confirms CIM as a promising, minimally invasive biomarker for:

- Early detection of bone loss
- Personalised osteoporosis therapy
- Real-time therapy monitoring
- Fracture risk prediction

CIM could serve as an innovative complement to existing diagnostic methods, significantly improving bone health care, particularly through the potential for early intervention and personalised treatment.
Access: Open Access

11.
The effect of calcium supplementation on bone calcium balance and calcium and bone metabolism during load carriage in women: a randomized controlled crossover trial. Jan 2025

Published on: 13 January 2025 in *Journal of Bone and Mineral Research*
Subjects: 48 women
Content: The study investigated the effects of calcium supplementation (1,000 mg) on calcium and bone metabolism during intense physical exertion in women.

Objective/Findings: To examine whether calcium supplementation can prevent exercise-induced disturbances in calcium homeostasis in women.
Access: Paid

12.
Monitoring denosumab therapy using the calcium isotope marker (CIM) technology.
May 2025

Published on: 13 May 2025 in *Bone Journal*
Subjects: 13 postmenopausal women, all with DXA-confirmed osteoporosis and receiving denosumab therapy (60 mg every 6 months)
Content: The study investigated the suitability of CIM technology (Calcium Isotope Marker) for monitoring denosumab therapy in osteoporosis.
Objective/Findings: To assess whether CIM provides a more sensitive and personalised method for monitoring bone health and therapeutic response. CIM represents a promising tool that could significantly enhance osteoporosis treatment through personalised and timely therapy monitoring. Further validation studies, however, are required.
Access: Open Access