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Monitoring Osteoporosis Therapy Using the Calcium Isotope Marker (CIM) Technology

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Denosumab, a monoclonal antibody targeting RANKL, is a well-established osteoporosis therapy. While DXA and bone turnover markers (BTMs) track changes in bone mineral density (BMD) and turnover, they lack sensitivity to dynamic, individual metabolic changes. Calcium Isotope Markers (CIM: $\delta^{44/42}Ca$) offer a potentially more responsive approach by measuring stable Ca isotope variations in serum (CIM_serum: $\delta^{44/42}Ca_{serum}$) and urine (CIM_urine: $\delta^{44/42}Ca_{urine}$), distinguishing net bone Ca uptake from resorption. This pilot study investigated 13 postmenopausal women with DXA-confirmed osteoporosis undergoing denosumab treatment. Over 24 weeks, CIM_serum and CIM_urine were measured alongside DXA-derived BMD, BTMs (CTX, P1NP), and parathyroid hormone (PTH). Baseline CIM values, adjusted for Ca supplementation (CIM_serum: -1.09±0.15‰, CIM_urine: 0.00±0.22‰), indicated net bone Ca loss, consistent with osteoporosis severity. One week after a 60 mg denosumab injection, all patients showed substantial CIM increases (~+0.4‰), peaking at weeks 4–8 (CIM_serum: ~-0.7‰ to -0.8‰). CIM values correlated positively with PTH, reflecting increased renal Ca reabsorption. Individually, CIM responses varied: some patients rapidly exceeded threshold levels, indicating strong anabolic responses, while others showed only modest or transient improvements. These differences suggest baseline osteoporosis severity influences individual responses to denosumab. While DXA confirmed BMD gains at 24 weeks, it primarily reflected average group trends, lacking insight into individual variability. Similarly, BTMs captured therapy initiation but failed to track patient-specific responses over time. In contrast, CIM provided real-time, individualized data on bone metabolism, offering a more nuanced view of treatment response. This suggests that CIM could enable earlier, patient-specific adjustments to osteoporosis therapy beyond the capabilities of DXA and BTMs. Although further validation in larger cohorts is needed, these findings highlight CIM's potential for enhancing personalized osteoporosis management.