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Researchers use calcium isotope analysis to predict myeloma progression

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A team of researchers from Arizona State University and Mayo Clinic is showing how a staple of Earth science research can be used in biomedical settings to predict the course of disease.

The researchers tested a new approach to detecting bone loss in cancer patients by using calcium isotope analysis to predict whether myeloma patients are at risk for developing bone lesions, a hallmark of the disease.

They believe they have a promising technique that could be used to chart the progression of multiple myeloma, a lethal disease that eventually impacts a patient's bones. The method could help tailor therapies to protect bone better and also act as a way to monitor for possible disease progression or recurrence.

"Multiple myeloma is a blood cancer that can cause painful and debilitating bone lesions," said Gwyneth Gordon, an Associate Research Scientist in ASU's School of Earth and Space Exploration, and co-lead author of the study. "We wanted to see if we could use isotope ratio analysis, a common technique in geochemistry, to detect the onset of disease progression."

"At present, there is no good way to track changes in bone balance except retrospectively using x-ray methods," said Ariel Anbar, a President's Professor in ASU's School of Earth and Space Exploration and the Department of Chemistry and Biochemistry. "By the time the x-

rays show something the damage has been done."

"Right now, pain is usually the first indication that cancer is affecting the bones," added Rafael Fonseca, Chair of the Department of Medicine at the Mayo Clinic and a member of the research team. "If we could detect it earlier by an analysis of urine or blood in high-risk patients, it could significantly improve their care," he added.

The research team – which includes Gordon, Melanie Channon and Anbar from ASU and Jorge Monge (co-lead author), Qing Wu and Fonseca from Mayo Clinic – described the tests and their results in "Predicting multiple myeloma disease activity by analyzing natural calcium isotopic composition," in an early on-line edition (July 9) of the Nature publication *Leukemia*.

The technique measures the naturally occurring calcium isotopes that the researchers believe can serve as an accurate near-real-time detector of bone metabolism for multiple myeloma patients. Bone destruction in myeloma manifests itself in bone lesions, osteoporosis and fractures. The ASU-Mayo Clinic work builds on a previous NASA study by the ASU team. That research focused on healthy subjects participating in an experiment.

"This is the first demonstration that the technique has some ability to detect bone loss in patients with disease," said Anbar, a biogeochemist at ASU.

With the method, bone loss is detected by carefully analyzing the isotopes of calcium that are naturally present in blood. Isotopes are atoms of an element that differ in their masses. Patients do not need to ingest any artificial tracers and are not exposed to any radiation for the test. The only harm done with the new method, Anbar said, is a pinprick for a blood draw.

The technique makes use of a fact well known to Earth scientists but not normally used in biomedicine – different isotopes of a chemical element can react at slightly different rates. The earlier NASA study showed that when bones form the lighter isotopes of calcium enter bone a little faster than the heavier isotopes. That difference, called isotope fractionation, is the key to the method.

In healthy, active humans bone is in "balance," meaning bone is forming at about the same rate as it dissolves (resorbs). But if bone loss is occurring, then the isotopic composition of blood becomes enriched in the lighter isotopes as bones resorb more quickly than they are formed.

The effect on calcium isotopes is very small, typically less than a 0.02 percent change in the isotope ratio. But even effects that small can be measured by using precise mass spectrometry methods available at ASU. With the new test, the ASU-Mayo Clinic researchers found that there was an association between how active the disease was and the change in the isotope ratios. In addition, the isotope ratios predicted disease activity better than, and independent from, standard clinical variables.

Anbar said that while the method has worked on a small set of patients, much still needs to be done to verify initial findings and improve the efficiency of analysis.

"If the method proves to be robust after more careful validation, it could provide earlier detection of bone involvement than presently possible and also provide the possibility to monitor the effectiveness of drugs to combat bone loss."

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