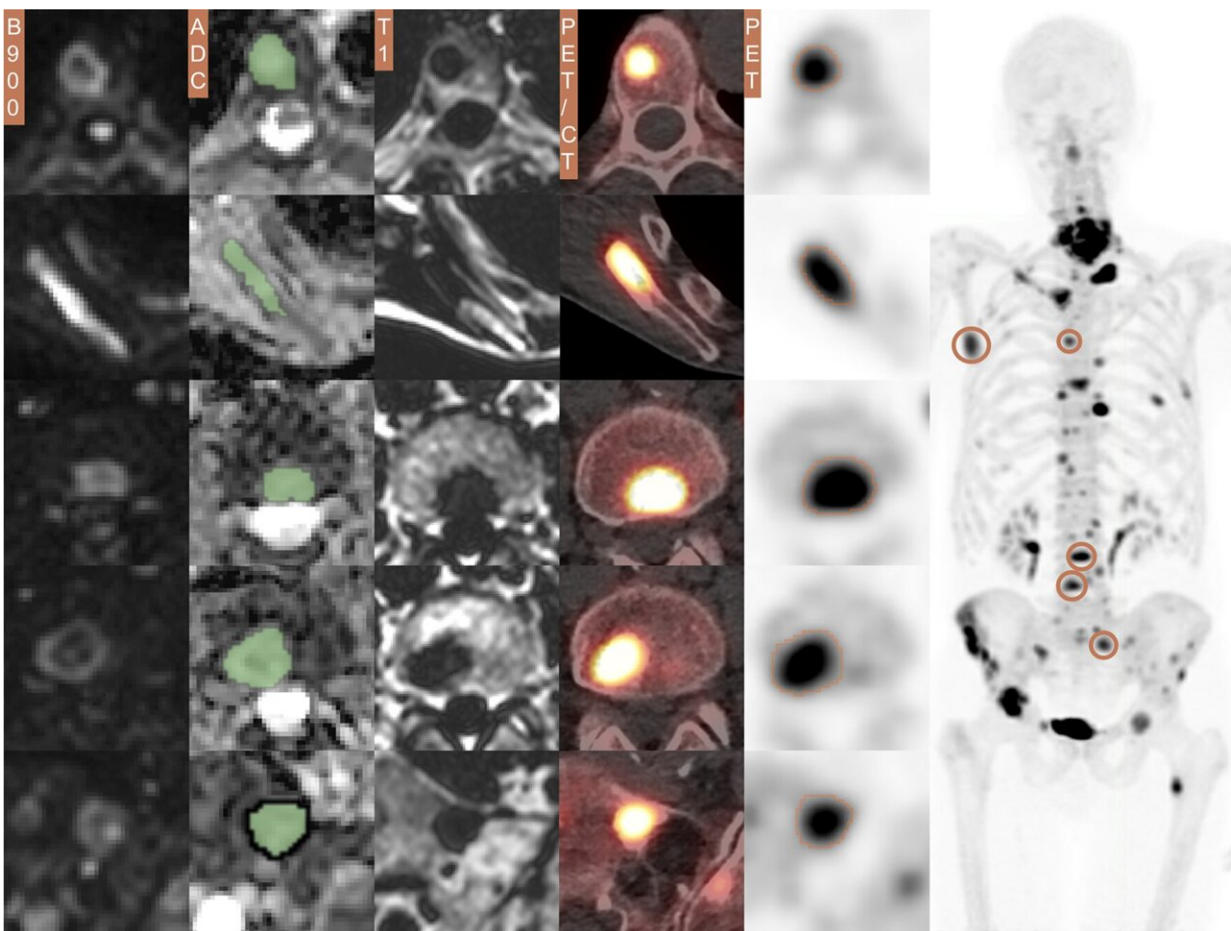


# Scientists now able to predict response to radium-223 treatment in prostate cancer bone metastases

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Target lesion measurements in a 65-year-old metastatic castrate-resistant prostate cancer patient, 5 target lesions on b900 DWI, ADC (with green segmentation), T1-weighted and 18F-NaF PET/CT fusion, and PET (delineated) images; apparent difference in lesion size between DWI and PET images may relate to

the difference in functional properties used to generate image contrast, variance in patient positioning, and slice selection as well as difference in resolution of these two imaging techniques. Credit: *European Radiology* (2023). DOI: 10.1007/s00330-023-10172-7

Researchers have found a way to predict which patients are likely to respond to radium-223, a standard treatment for advanced prostate cancer that has spread to the bones.

By using an [imaging technique](#) called an 18F-sodium fluoride (18F-NaF) PET scan, clinicians could ensure that they are only using this treatment for people who have a good chance of benefitting from it.

Until now, clinicians have had to use the same treatment approach for all patients with this form of cancer, even though it does not always produce results. Being able to better target treatment to the individual could extend survival and improve quality of life.

## **Trialing two different approaches**

In the study, researchers analyzed 133 lesions in 36 patients with castration-resistant prostate cancer that had spread only to the bones. They performed whole-body MRI with diffusion-weighted imaging at the start of the study and every eight weeks throughout, using this proven technique to monitor the change in apparent diffusion coefficient, or ADC, which serves to indicate the movement of water within a tissue.

The less the water can move, meaning a low ADC value, the higher the cellular density of the tumor—a hallmark of a more aggressive cancer. Based on data from other research, the team considered an increase in ADC of 30% or more as indicative of a real treatment benefit.

Alongside this known method, the researchers carried out PET scans with  $^{18}\text{F}$ -NaF and  $^{18}\text{F}$ -choline. They found that the uptake of  $^{18}\text{F}$ -NaF by metastases at baseline was significantly higher in those that went on to produce an increase in ADC of 30% or more. This means that a higher uptake of  $^{18}\text{F}$ -NaF prior to treatment correlates with a better response to treatment. However, there was no association between treatment response and  $^{18}\text{F}$ -choline uptake.

The team chose to trial this technique on the basis that radium-223, an internal form of radiotherapy, tends to be most effective in areas where the [bone](#) turnover rate is high. Cancer cells in bone metastases raise the turnover rate by releasing proteins that interfere with healthy bone cells, overactivating the cells that break down bone. As  $^{18}\text{F}$ -NaF is very similar in structure to calcium, which is key for bone development and metabolism, the uptake of the marker is significantly higher in bones with a high turnover rate.

A PET scan can reveal the areas with the highest uptake of  $^{18}\text{F}$ -NaF, thereby showing where radium-223 is most likely to work.

The study involved researchers from the Institute of Cancer Research, London, and the Royal Marsden NHS Foundation Trust, and it was [published](#) in the journal *European Radiology*.

## **The difficulty of monitoring treatment response adds to the challenge of treating bone metastases**

Advanced prostate cancer often spreads to the bones, causing bone metastases. Unlike with tumors or malignant lymph nodes, which shrink if treatment is effective, it is not possible to assess response to treatment by observing bone metastases. Instead, clinicians have to determine the effectiveness of treatment by considering survival and quality of life.

A different Royal Marsden and ICR-led study recently demonstrated that it was possible to use diffusion-weighted MRI, an imaging technique that studies the movement of water molecules in a tissue, to assess response to radium-223.

In addition, the researchers showed that some patients seemed to benefit much more than others from radium-223 treatment. Furthermore, different metastases within the same patient did not all respond in the same way. The most surprising finding, though, was that in some patients, new bone metastases developed during treatment. The study was [published](#) in the journal *JNCI Cancer Spectrum*.

First author Professor Chris Parker, Consultant in Clinical Oncology and Prostate Cancer at The Royal Marsden and Professor of Prostate Oncology at the ICR, said, "This is exciting from a clinical point of view. Radium-223 has been used globally for more than a decade, but we've never before had a good way to assess response. We have tended to assume that all patients benefit to a similar extent, but we now know that's not the case. What's next is to try to predict response so that we can identify who might respond well to treatment."

## **Bringing together recent findings**

In combination, these two pieces of research represent a significant step forwards in the treatment of [advanced prostate cancer](#) that has spread to the bones.

Clinicians with access to the required technology could, subject to approval, use 18F-NaF PET to determine which patients are likely to respond to radium-223. They could then use diffusion-weighted MRI to monitor their response to treatment and confirm that it is proving effective.

This could potentially benefit all patients, as those who 18F-NaF PET did not identify as candidates for radium-223 treatment could receive an alternative treatment that may work better for them.

Senior author of the European Radiology paper Professor Dow-Mu Koh, who is Consultant Radiologist in Functional Imaging at The Royal Marsden and Professor in Functional Cancer Imaging at the ICR, said, "This trial was innovative in its ambition to look at advanced imaging techniques side by side to see which can best inform decision-making around disease management. Our findings demonstrate how sensitive imaging is and how it can be used for targeted treatments. We hope that the study will be part of a paradigm shift in terms of how we monitor treatment for people with this form of [cancer](#)."

Dr. Matthew Blackledge, leader of the Computational Imaging Group at the ICR, brought his imaging expertise to this study. He said, "We are pleased to confirm the predictive power of using PET, which might allow clinicians to stratify patients at an earlier timepoint. Alongside this, thanks to other work at the ICR, we can now use quantitative MRI to assess whether individual tumors are responding rather than the patient as a whole. This is particularly important when using radium-223. We hope that our findings will translate to wider clinical use so that as many patients as possible can benefit."

**More information:** Ricardo Donners et al, The value of baseline 18F-sodium fluoride and 18F-choline PET activity for identifying responders to radium-223 treatment in castration-resistant prostate cancer bone metastases, *European Radiology* (2023). [DOI: 10.1007/s00330-023-10172-7](https://doi.org/10.1007/s00330-023-10172-7)

Chris Parker et al, Radium-223 in metastatic castration-resistant prostate cancer: whole-body diffusion-weighted magnetic resonance imaging scanning to assess response, *JNCI Cancer Spectrum* (2023). [DOI:](#)

[10.1093/jncics/pkad077](https://doi.org/10.1093/jncics/pkad077)

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