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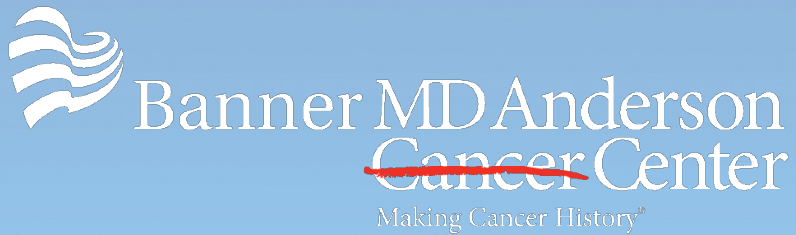
Therapeutic Radiopharmaceuticals and the Emergence of Theranostics in Prostate Cancer



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Radiopharmaceuticals

- Systemic
- Tracer principle
  - A radioactive biologically active substance is chosen in such a way that its spatial and temporal distribution in the body reflects a particular body function or metabolism. (European Nuclear Society)

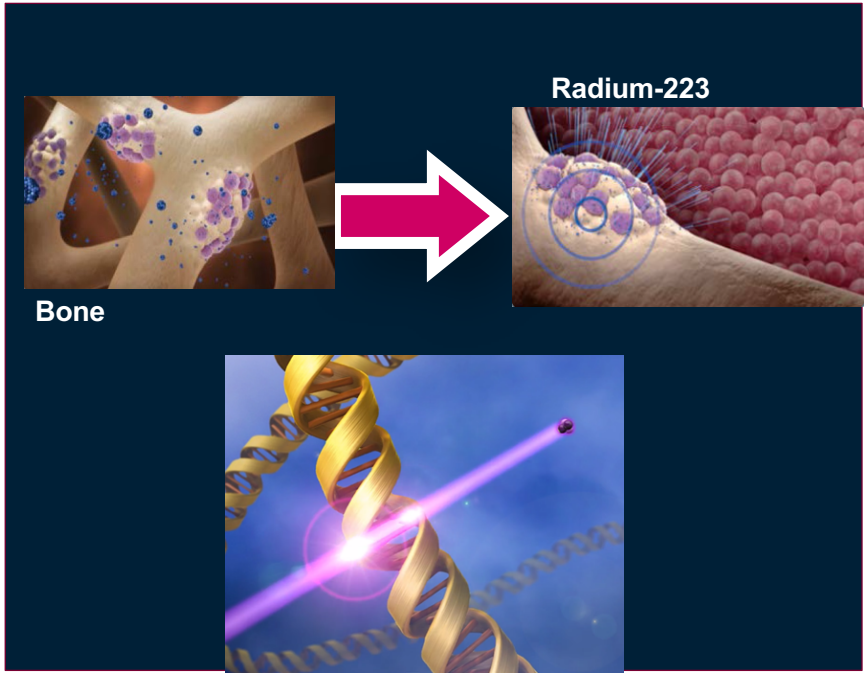
Radium-223 is an alpha particle–emitting pharmaceutical that mimics calcium and locally targets bone metastases

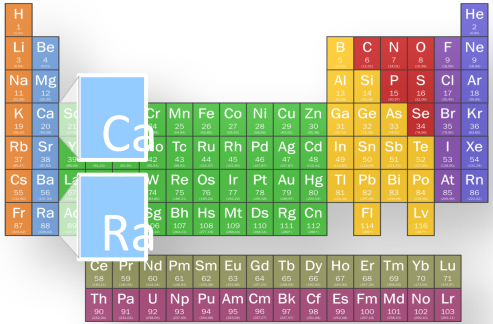
Radium and calcium have the same divalent charge[1]

Radium-223, which mimics calcium, is incorporated into the bone mineral hydroxyapatite in areas of rapidly increased bone turnover[2,3]

Alpha particles cause difficult-to-repair, lethal double-strand DNA breaks, resulting in an antitumor effect on bone metastases[1,2,4–6]

Radium-223 not taken up by bone and bone metastases is excreted through the gut[7]



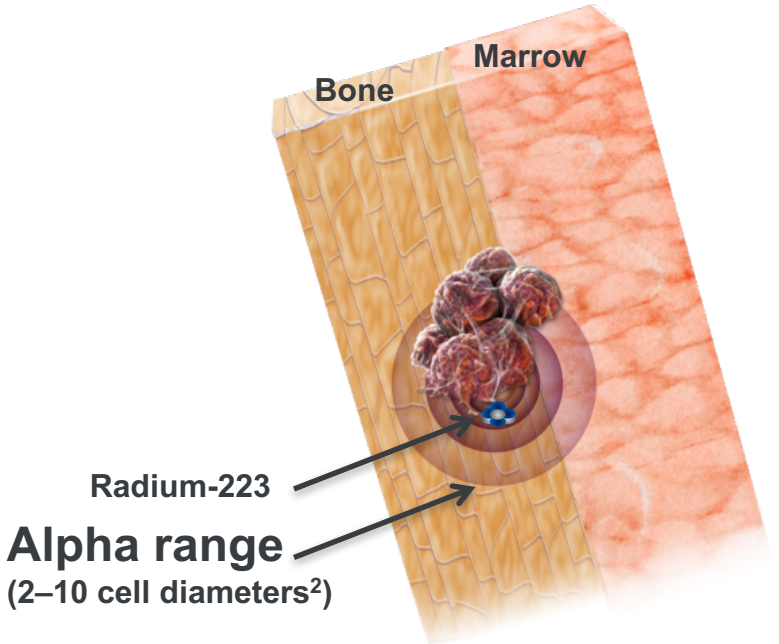


Drawings are not to scale.

1. Agency for Toxic Substances and Disease Registry, US Public Health Service. Toxicological profile for radium. (December 1990). http://www.atsdr.cdc.gov/toxprofiles/tp144.pdf. Accessed March 7, 2014. 2. Henriksen G *et al. Cancer Res* 2002;62:3120–3125. 3. Henriksen G et al. *J Nucl Med* 2003;44:252–259. 4. Liepe K. *Curr Opin Investig Drugs* 2009;10:1346–1358. 5. McDevitt MR *et al. Eur J Nucl Med* 1998;25:1341–1351. 6. Ritter MA *et al. Nature.* 1977;266:653–655. 7. Lewington V et al. *J Clin Oncol.* 2010;28(suppl. abstr e15009).

The short range of alpha particles minimizes damage to surrounding normal tissue

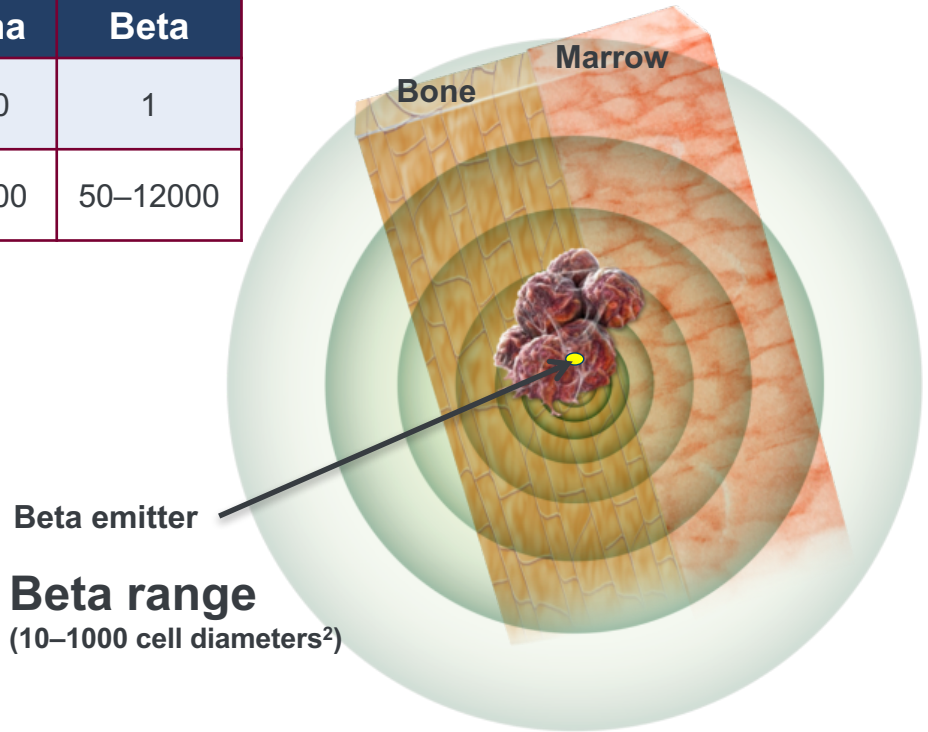
	Alpha
Relative particle mass	7000
Range in tissue (μm)	40–100



Bruland ØS *et al. Clin Cancer Res* 2006;12:6250s–6257s.
Henriksen G *et al. Cancer Res* 2002;62:3120–3125.

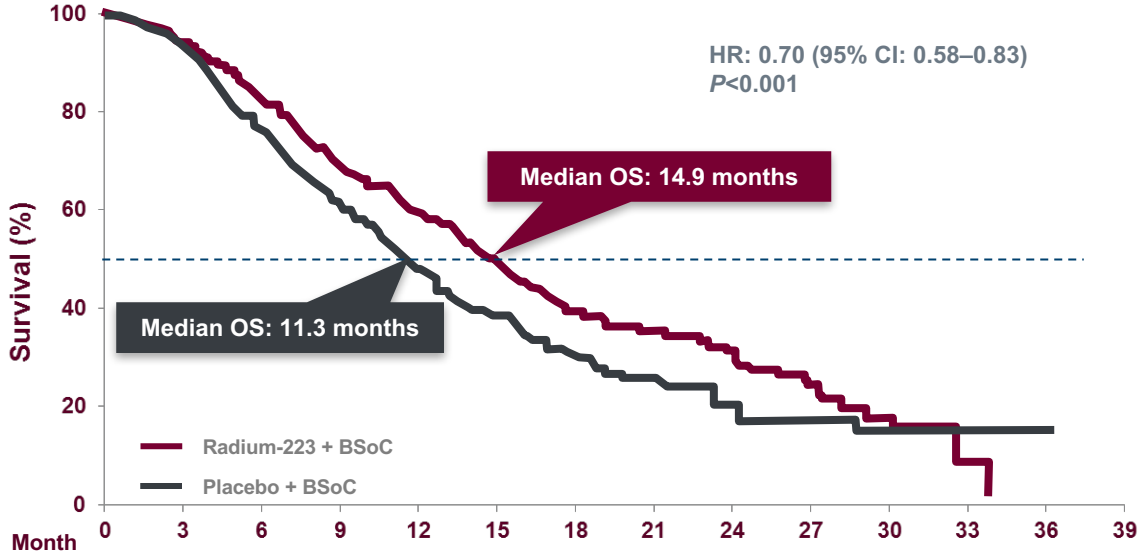
The long range of beta emitters may increase bone marrow exposure and associated toxicities

	Alpha	Beta
Relative particle mass	7000	1
Range in tissue (μm)	40–100	50–12000



Brechbiel M. *Dalton Trans* 2007;43:4918–4928.
Henriksen G *et al. Cancer Res* 2002;62:3120–3125.

Radium-223 significantly improved overall survival



The updated analysis confirmed the interim analysis of a 30% reduction in risk of death for patients in the radium-223 group compared with placebo

HR=hazard ratio.

Parker C *et al. N Engl J Med* 2013;369:213–223.

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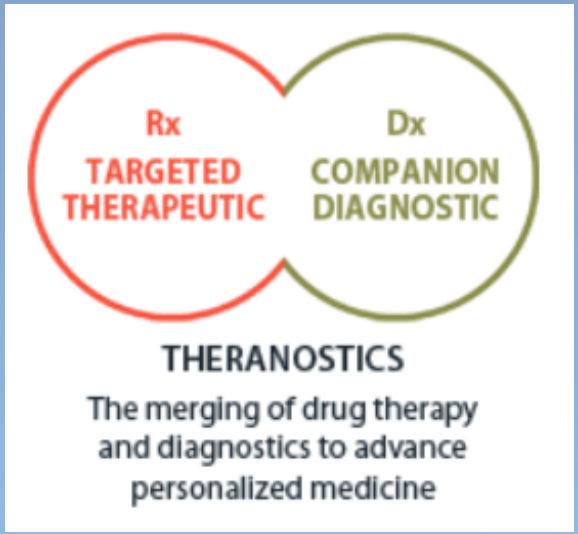
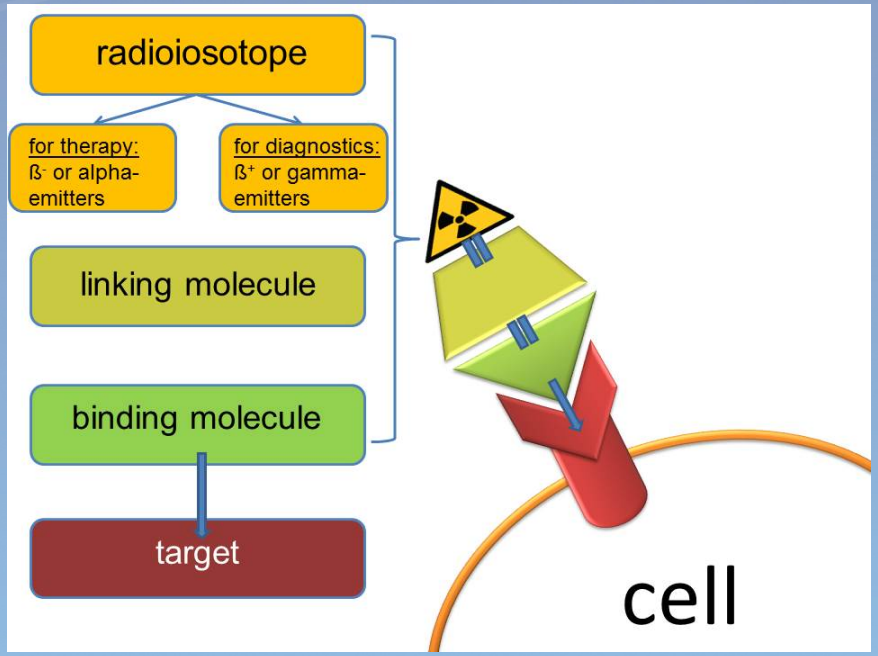
Theranostics





Yordanova A, et al. Theranostics in Nuclear Medicine Practice.

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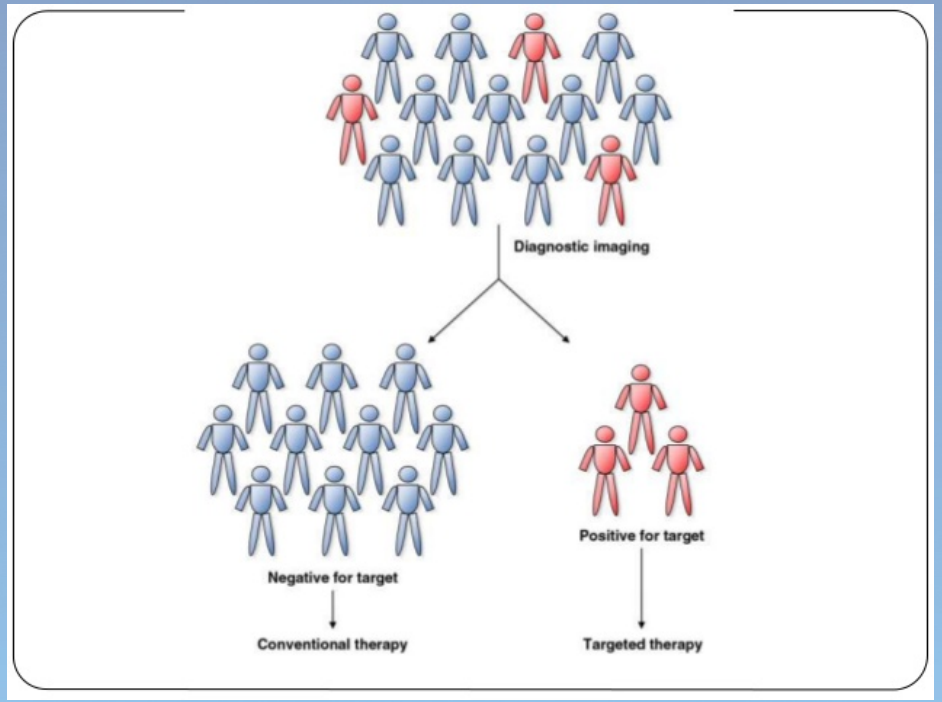
Personalized Medicine



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Lu-177 PSMA

- Beta emitter
- Gamma emitter
- 6.7 days

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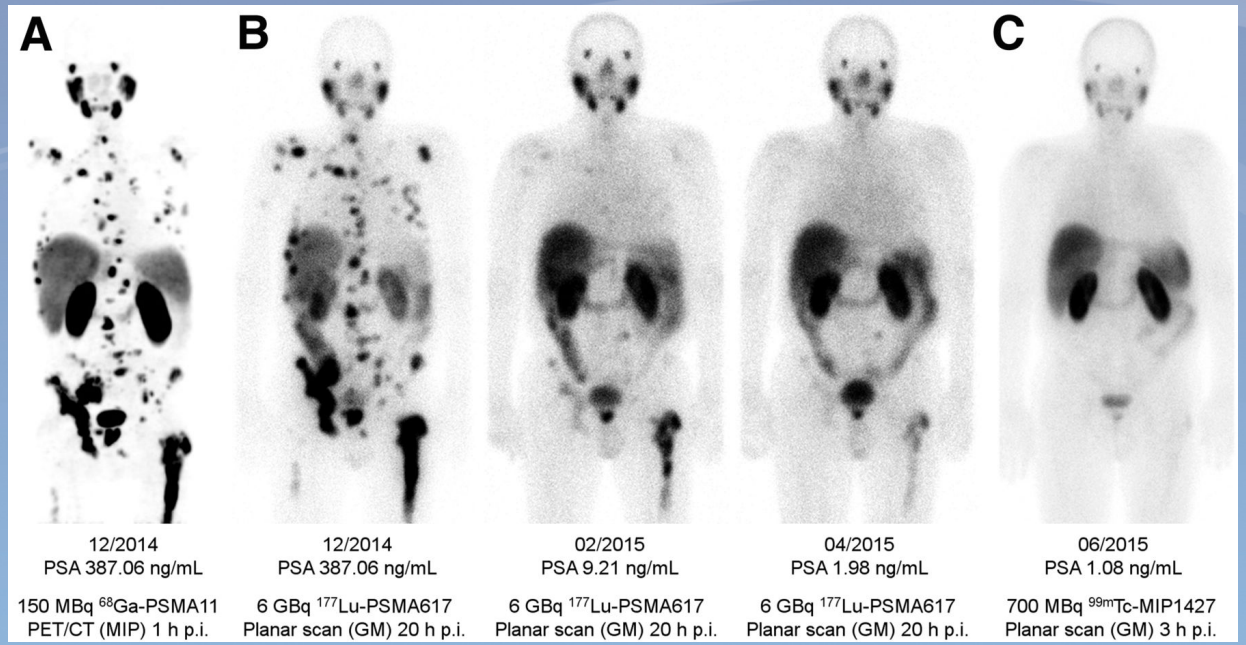
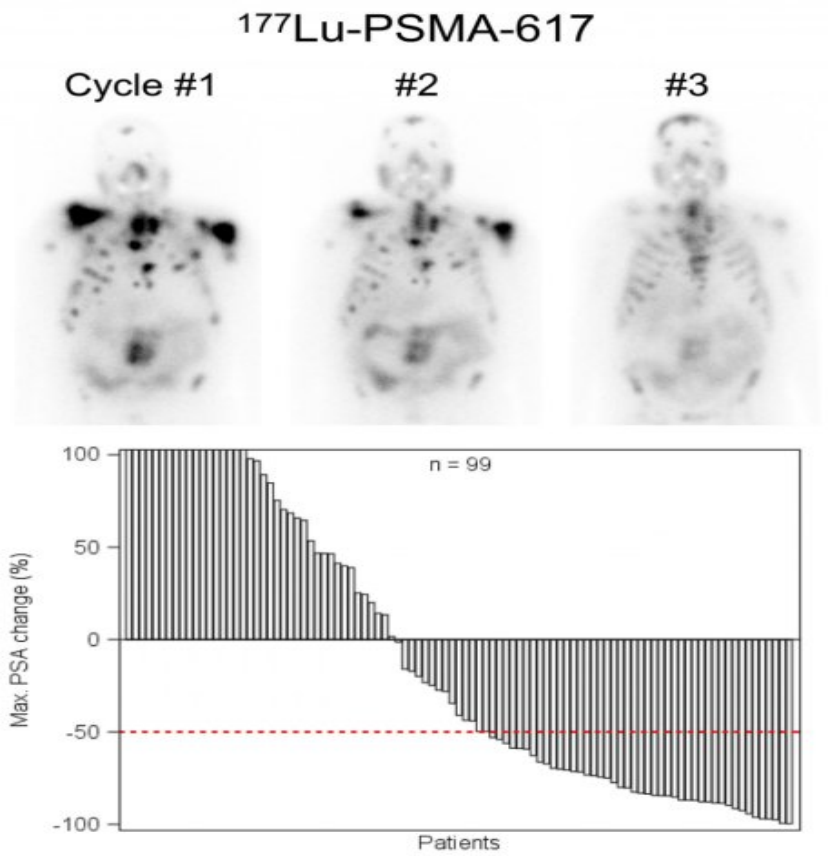


(A) PSMA PET/CT delivers highest resolution. Clemens Kratochwil et al. J Nucl Med 2016;57:1170-1176

JNM The Journal of NUCLEAR MEDICINE



Waterfall plot of maximum PSA change (%) from baseline over total follow-up period. Kambiz Rahbar et al. J Nucl Med 2017;58:85-90

JNM The Journal of NUCLEAR MEDICINE

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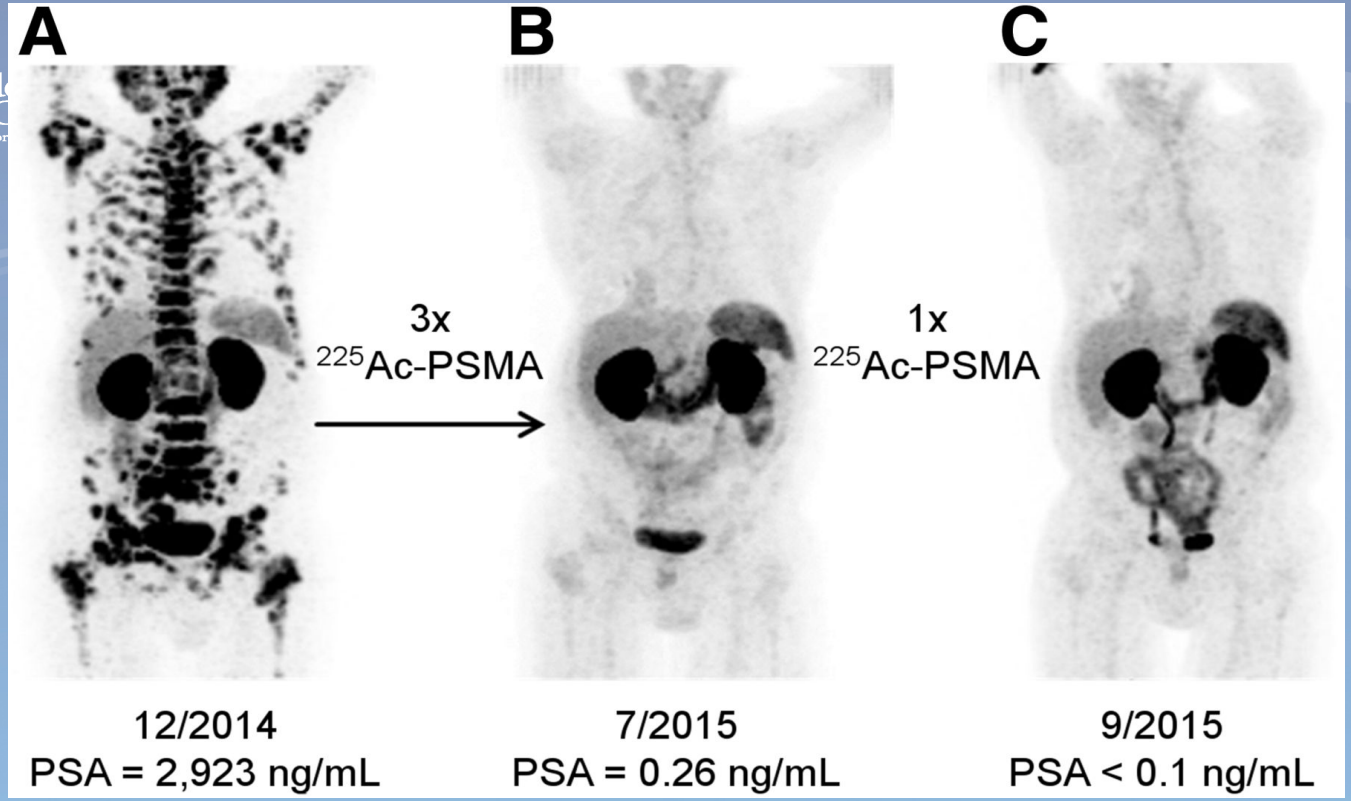
Actinium

- Alpha emitter
- 9.9 days



68Ga-PSMA-11 PET/CT scans of patient A. Pretherapeutic tumor spread (A), restaging 2 mo after third cycle of 225Ac-PSMA-617 (B), and restaging 2 mo after one additional consolidation therapy (C). Clemens Kratochwil et al. J Nucl Med 2016;57:1941-1944

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Take Home Points

- Therapeutic radiopharmaceuticals
  - Safe
  - Effective