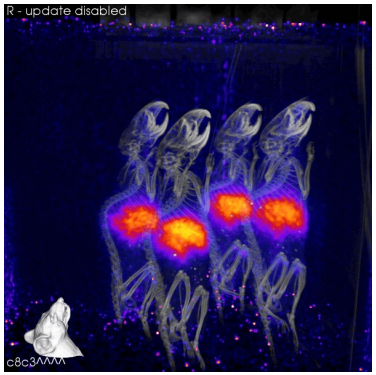
Cerium 134 as an imaging surrogate for ^{225}Ac

This research is supported by the U.S. Department of Energy Isotope Program, managed by the Office of Science.



Mackenzie Malo, MSc & Kevin Allen, PhD

September 19th, 2022

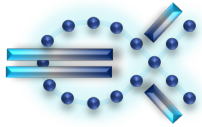
Cerium-134 DOE Users Meeting

Radioimmunotherapy (RIT)

Tumor specific antibodies direct radionuclides to cancer cells

RIT limits the dose to normal tissues

Actinium-225



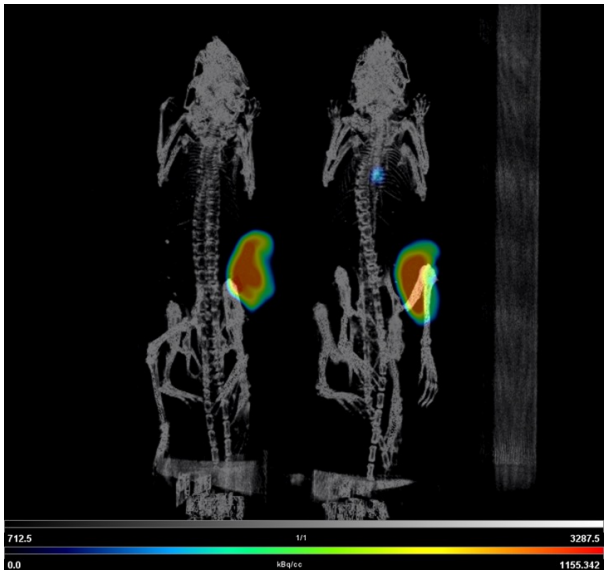
Actinium Pharmaceuticals, Inc.

- Actimab-A® - ^{225}Ac labeled Lintuzumab in phase 1/2 clinical trials. Targets CD33 in patients with relapse/refractory acute myeloid leukemia (AML)
- Positron Emission Tomography (PET) imaging improve pre-clinical evaluation of Ab-radiometal conjugates
- No available PET-enabling radiometals available that match the ^{225}Ac half-life (^{86}Y half-life, 15h, is too short to approximate ^{225}Ac)
- Best option so far has been ^{89}Zr or ^{111}In SPECT

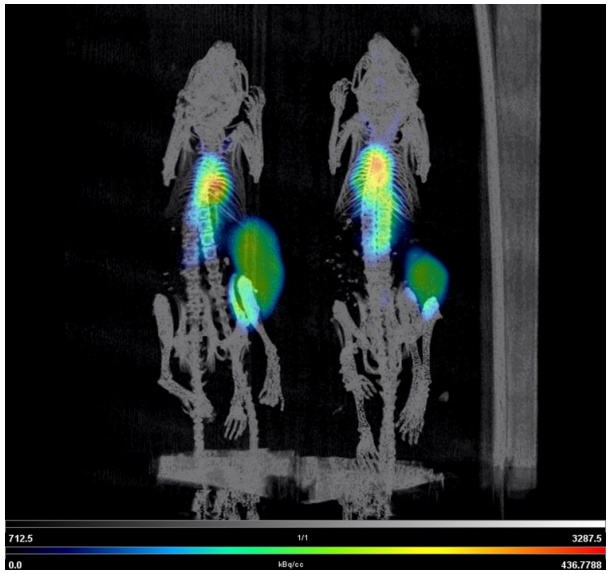
^{89}Zr-DFO-Lintuzumab

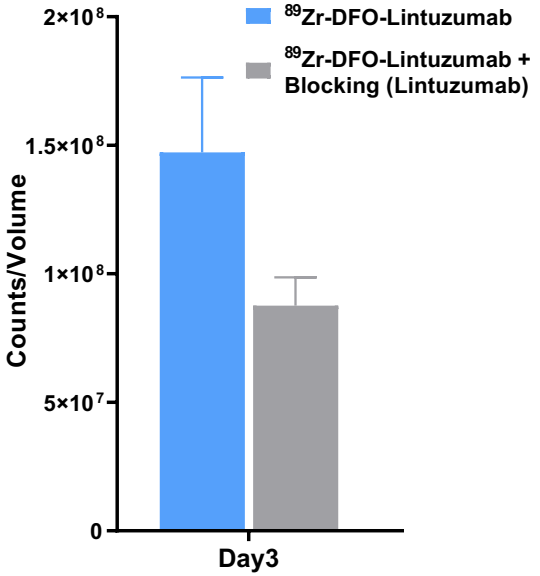
Actinium Pharmaceuticals, Inc.

^{89}Zr-DFO-Lintuzumab



^{89}Zr-DFO-Lintuzumab + Blocking





150 µCi ^{89}Zr-DFO-Lintuzumab in CD33-positive OCI-AML-3 tumors

Allen KA., et al. *Journal of Nuclear Medicine* June 2022, 63 (supplement 2) 4038

Potential of ^{134}Ce

- Improved image quality, shorter imaging protocols over SPECT
- Able to use DOTA
- Longer half-life than other available PET-radiometals

Labeling results

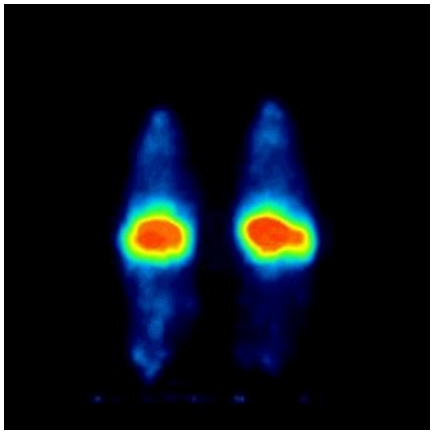
- Initial attempts at 37 °C were unsuccessful at both 1:1 & 5:1 µCi:µg
- Increasing to 50 °C provided near quantitative yield at 1:1 µCi:µg with limited success at 5:1 – likely resulted in some lose of bioreactivity
- Attempts at 42 °C were successful for 1:1 µCi:µg

Antibody	Temperature (°C)	Specific activity (µCi:µg)	Yield (%)
A-DOTA	37	1:1	7
A-DOTA	37	5:1	3
A-DOTA	50	1:1	85
B-DOTA	37	1:1	5
B-DOTA	42	1:1	99
B-DOTA	42	5:1	21
B-DOTA	50	1:1	99
B-DOTA	50	5:1	24

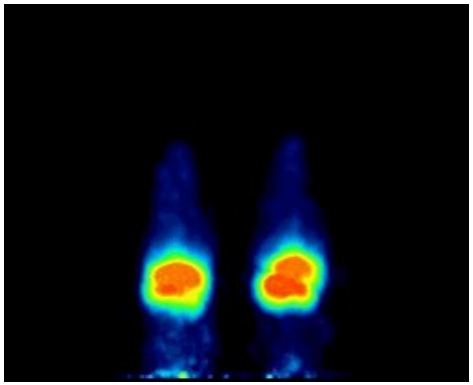
Imaging results

- Labeling was performed at 50 °C with a 1:1 µCi:µg specific activity.
- ^{134}Ce solution pH was adjusted to 7 using 5M ammonium acetate (chelexed).
- iTLC showed near quantitative labeling, however the sample was purified via spin. filtration to maintain constancy with established protocol and ensure highest levels of purity
- 81 µCi (3MBq) of labeled antibody was injected into each mouse.

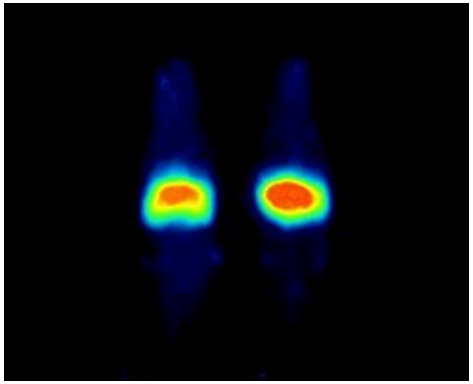
3h



24h



48h



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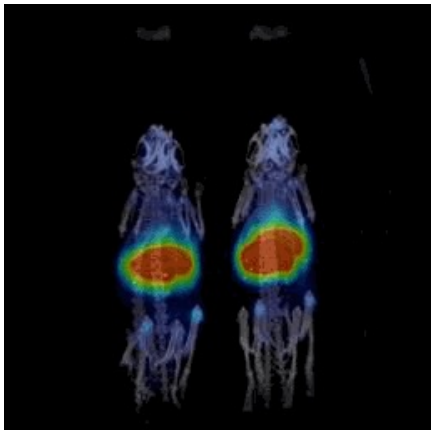

Conclusions

- Labeling is possible at lower activity to antibody ratio.
- Temperature plays a factor in labeling effectiveness, the effect this has on antibodies will be specific to your own antibody
- PET images are readily acquired.
- Longer half-life enables longer labeling times and provide ample opportunity to collect data over multiple days.
- Can act as an imaging surrogate for Ac225

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