

Efficient chelation of ¹³⁴Ce/¹³⁴La using the macrocyclic chelators DOTA and Macropa as potential PET imaging agents

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¹³⁴Ce/La pair

✓ Actinium, cerium and lanthanum have similar chemical properties

- ✓ The ionic radii are similar, La (1.03 Å), Ce (1.01 Å) and Ac (1.12 Å)
- ✓ Thus, ¹³⁴Ce/La pair has been proposed as a PET imaging surrogate for ²²⁵Ac therapy, which is gaining increasing interest in cancer treatment



¹³⁴Ce/La pair (Abergel lab / LANL)



DTPA (+3 metal chelator)



¹³⁴Ce^{III} mimicking ²²⁵Ac^{III}

✓ DTPA & DOTA as chelators

✓ Imaging and biodistribution of [¹³⁴Ce]DOTA-Trastuzumab

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Objective

- ✓ Develop a robust radiolabeling method for chelation with ¹³⁴Ce, which in turn can serve as a surrogate for ¹³⁴Ce/²²⁵Ac theranostic agents.
- Utilize the developed methods for imaging of prostate cancer murine models







Radiolabeling of Macropa.NH₂ & DOTA



✓ Both DOTA and Macropa are efficient ¹³⁴Ce chelators; Macropa is more effective at low L:M ratios



Radiolabeling of Macropa.NH₂ & DOTA

✤ Stability of ¹³⁴Ce-Macropa.NH₂



✓ Both DOTA and Macropa are efficient ¹³⁴Ce chelators; Macropa is more effective at low L:M ratios





TLC : C18, 10% NH₄CI:MeOH (1:1)



PET Imaging and Biodistribution







Imaging prostate cancer using ¹³⁴Ce

- PET imaging with ⁶⁸Ga-PSMA-11 or ¹⁸F-DCFPyL and radionuclide therapy using with ¹⁷⁷Lu-PSMA-617 is standard of care in prostate cancer
- We are developing immunoPET agents targeting CD46, an antigen highly expressed in prostate cancer
- We hypothesized these agents could be labeled with 134Ce and imaged using PET







Radiolabeling of PSMA-617





Radiolabeling of Macropa-PEG₄YS5



Entry	Ab. Qty. (μg)	¹³⁴ Ce (µCi)	RCY TLC (%)	RCP (%)	lsolated Yield (µCi/%)	SA (µCi/µg)	L:M ratio
1	22.14	122	100	-	-		1:1
2	221.4	1300	95.6	100	900 (69%)	4.1	1:1
3	150	749	90.8	-	-		1:1
4	105.6	320	91.9	-	-		1:1



Reaction monitoring by Radio iTLC



iTLC-SG, 50 mM EDTA, pH 5.5



Reaction kinetics by Radio iTLC **Dilution** in =¹³⁴Ce/La saline or PBS 1M NH₄OAc, PD 10 column pH = 8, 25 °C, 1 h. ∙N∽∽∽ H -N~~~ H Н Equilibrium in reaction mixture ¹³⁴La "recoil effect" Similar effect observed t_{1/2}=6.4 m in PSMA-617 labeling



(DOTA chelator)

PET Imaging & BioD of ¹³⁴Ce-Macropa-PEG₄YS5



✓ 22Rv1 xenografts at 7 d p.i.; PET Imaging (n=4) & BioD (n=5)
 ✓ High tumor uptake, low in background tissues except for liver



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Summary

- \checkmark Macropa.NH₂ showed more efficient chelation compared to DOTA
- ✓ ¹³⁴Ce-Macropa.NH₂ was stable in both PBS/saline and serum (95% at 7 d).
- ✓ Free ¹³⁴La may be ejected from chelators in physiologic buffers
- ✓ PET imaging and biodistribution with ¹³⁴Ce-Macropa-PEG₄-YS5 revealed high tumor uptake at 7 d p.i.; [¹³⁴Ce]PSMA-617 showed more modest uptake at 1 and 4h, consistent with prior results with ⁶⁸Ga and ⁸⁹Zr
- \checkmark ¹³⁴Ce labeled radiopharmaceuticals enable imaging of prostate cancer
- ✓ ¹³⁴Ce allows for PET imaging of Macropa-labeled complexes



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