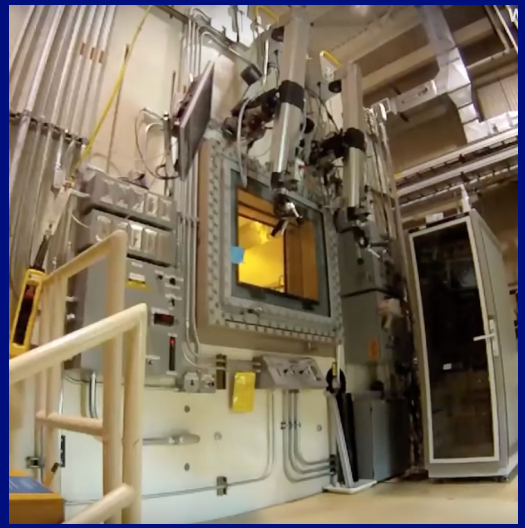
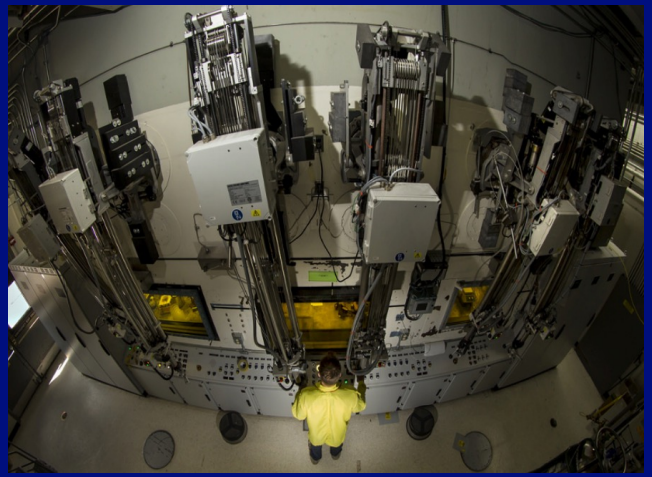
Los Alamos NATIONAL LABORATORY

DOE IP Virtual Seminar Series

Cerium-134





Ce-134 AGENDA

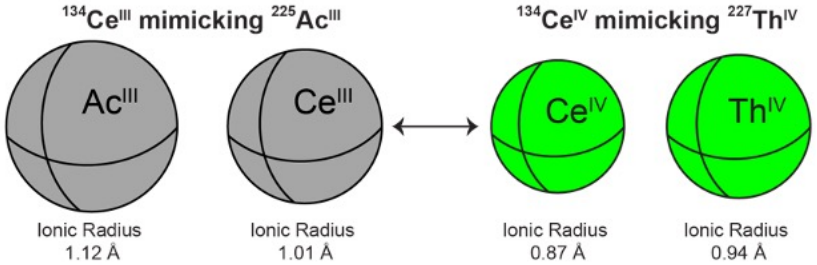
OCTOBER 16, 2023, 1 PM EDT

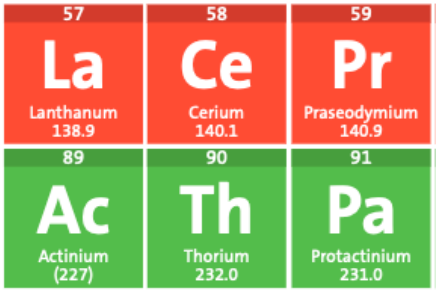
1:00 – 1:15 PM	**Veronika Mocko, PhD** | Los Alamos National Laboratory
1:15 – 1:30 PM	**Robert Flavell, MD, PhD** | University of California San Francisco
1:30 – 1:45 PM	**Timothy Haystead, PhD** | Duke University Center
1:45 – 2:00 PM	**James Kelly, PhD** | Weill Cornell Medicine
2:00 – 2:30 PM	*Moderated Q&A Segment*

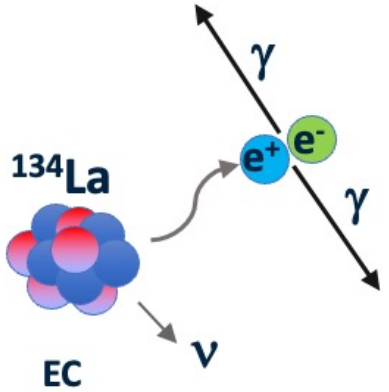
Isotope Program
U.S. Department of Energy

Motivation: ^{134}Ce/^{134}La as imaging companion for α-radiotherapy

- Increased application of targeted alpha therapy ^{225}Ac ($T_{1/2}$ 9.9d), ^{227}Th ($T_{1/2}$ 18.7d)
- PET radiometals: ^{68}Ga ($T_{1/2}$ 67.7min), ^{64}Cu($T_{1/2}$ 12.7h), ^{132}La($T_{1/2}$ 4.8h), ^{133}La($T_{1/2}$ 3.9h)
  - ^{68}Ga, ^{64}Cu – different chemistry and coordination
  - All too short lived to track biological fate over several days







^{134}Ce → ^{134}La → ^{134}Ba + e$^+$ + ν

$T_{1/2}$ 3.16 d. $T_{1/2}$ 6.7 m stable

***In vivo* generator**

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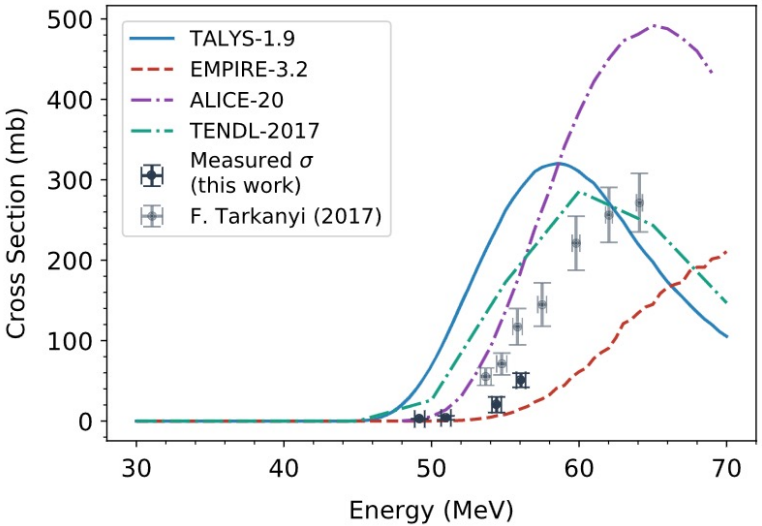
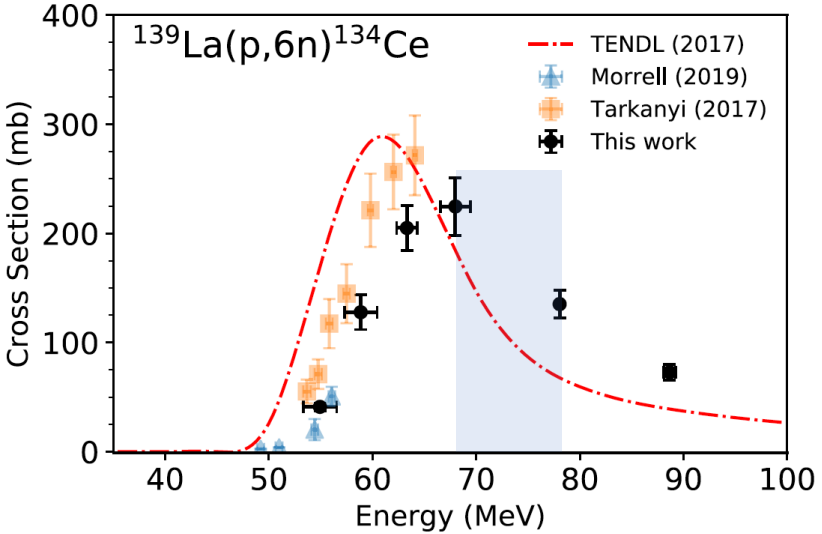
Baily, Mocko, Vermeulen, Kozimor, Abergel, et. al. NATURE CHEM 13. 284 (2021).

^{134}Ce production

- ^{nat}La (p, 6n)^{134}Ce
- Energy range for production optimized



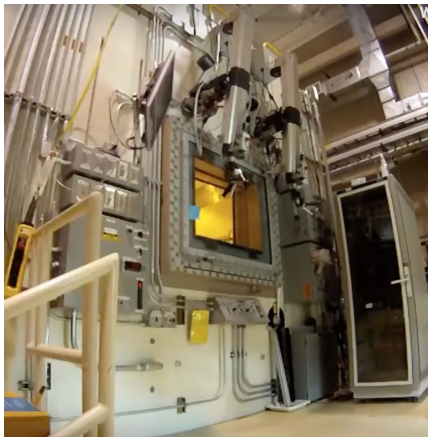


Optimum ^{134}Ce production energy range range: 77.9 – 67.8 MeV

Morrell et al. Eur. Phys. J. A (2020) 56:13; Becker et al. Nucl. Instrum. Meth. B, 468 (2020) 81.

^{134}Ce production

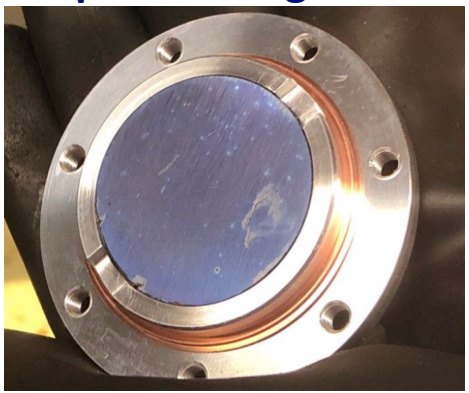
Isotope Production Facility



- ^{nat}La (p, 6n)^{134}Ce
- 32 g of La metal (45.7 x 3 mm)
- Incident energy 77.9 MeV, Exit energy 67.8 MeV H^+
- Beam current 100 μA, Cumulative charge ~3000 μA.h

La metal

La puck in target shell

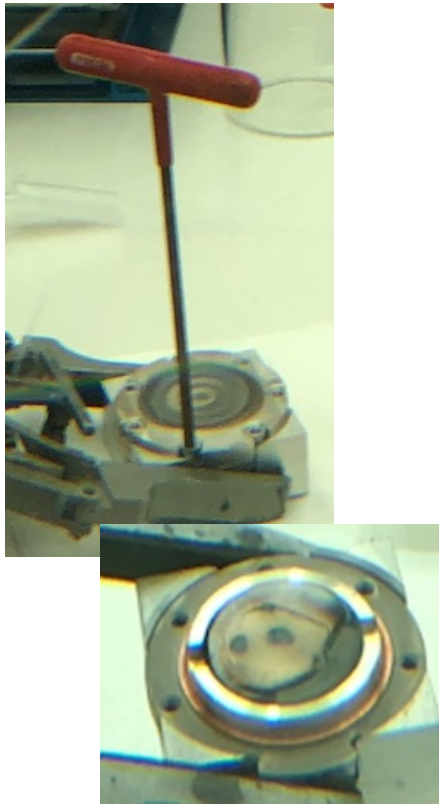


Irradiated target

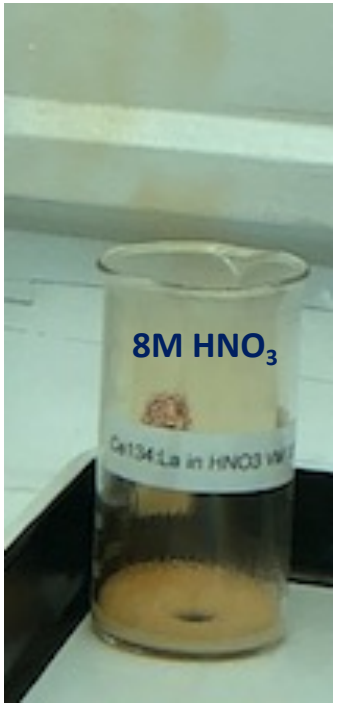
Baily, Mocko, Vermeulen, Kozimor, Abergel, et. al. NATURE CHEM 13. 284 (2021).

^{134}Ce Isolation

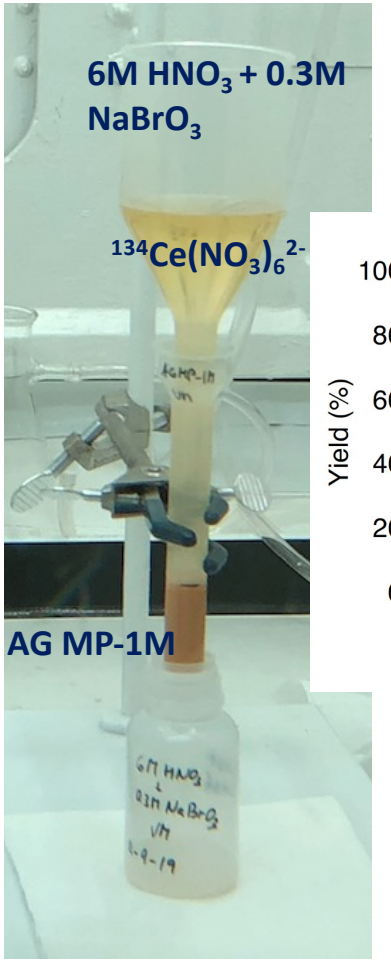
Target opening

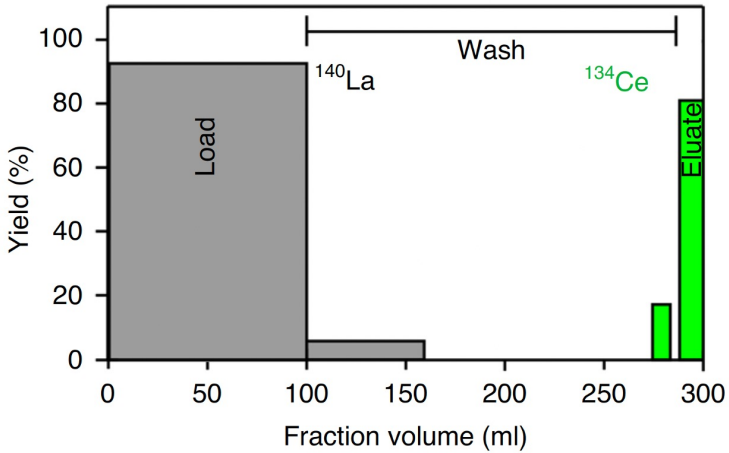


La dissolution



La-Ce separation





^{134}Ce elutes with 50 mM HNO_3

One column rapid separation with high yield > 80%

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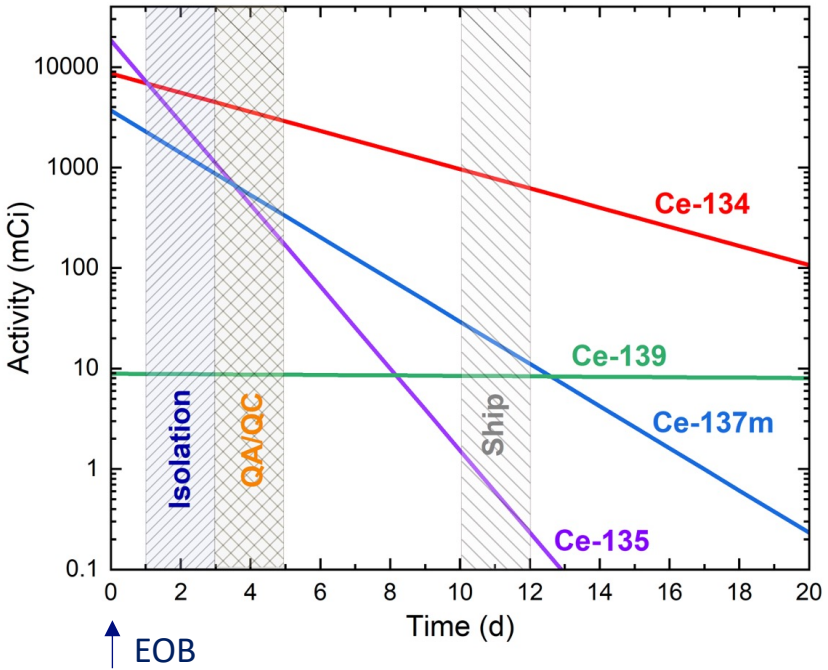
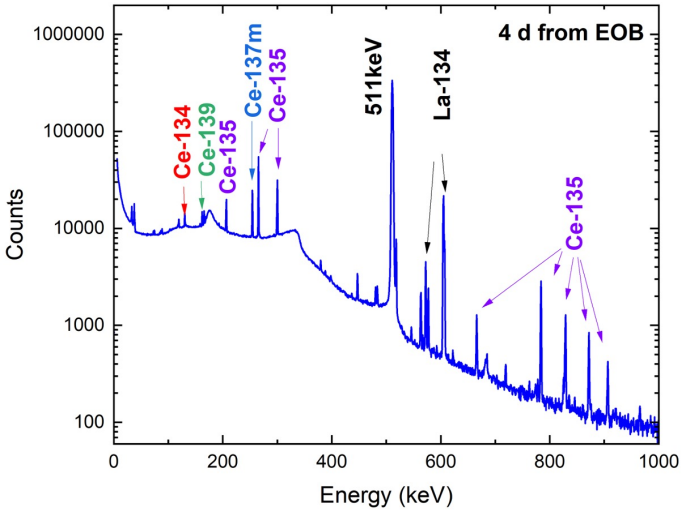
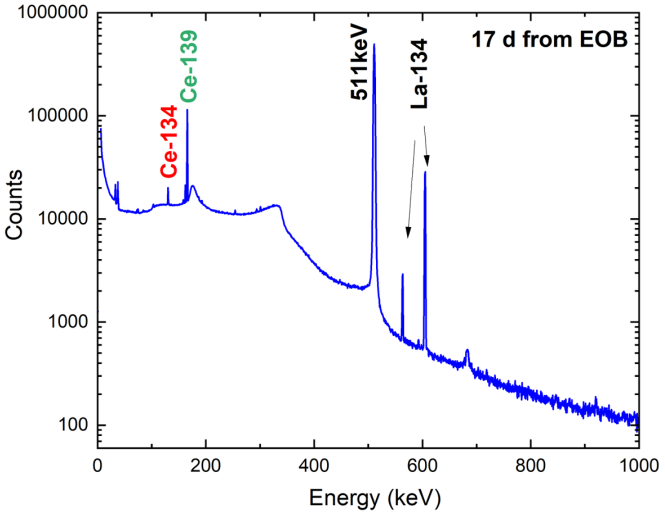
Baily, Mocko, Vermeulen, Kozimor, Abergel, et. al. NATURE CHEM 13. 284 (2021).

^{134}Ce radiochemical purity







^{139}La (p,6n)^{134}Ce ($T_{1/2}$ 3.16 d)

^{139}La (p,5n)^{135}Ce ($T_{1/2}$ 0.74 d)

^{139}La (p,3n)^{137m}Ce ($T_{1/2}$ 1.43 d)

^{139}La (p,n)^{139}Ce ($T^{1/2}$ 137.64 d)

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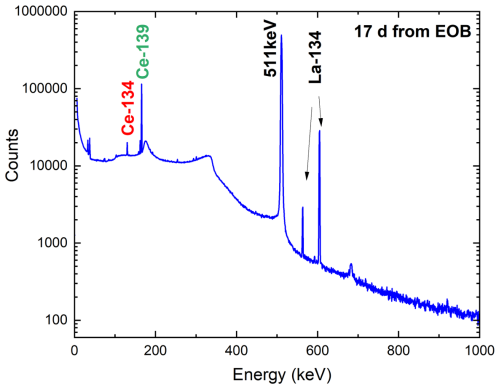
^{134}Ce product

Product characterization: gamma spectroscopy & ICP-OES

- Radionuclidic purity >99.8% (excluding ^{135}Ce, ^{137}mCe, ^{139}Ce and daughters)
- ^{135}Ce < 1%, ^{137m}Ce < 5%, ^{139}Ce < 3%
- Specific activity >4,000 Ci/g, typical 8,000-12,000 Ci/g on ship date
- Form: Ce(III) in 0.1 M HCl
- Concentration > 5 mCi/mL, typical 10-20 mCi/mL
- Total Ce 42-101 μg, total Ce concentration 1.4-10.4 μg/mL
- Total La 50-169 μg, total La concentration 1.7- 17.4 μg/mL



Isotope Program
U.S. Department of Energy

NIDC NATIONAL ISOTOPE DEVELOPMENT CENTER
MANAGED BY THE U.S. DEPARTMENT OF ENERGY ISOTOPE PROGRAM

Product Information

Specifications

Radioisotope	Ce-134
Half-Life/Daughter	3.16 days to lanthanum-134
Decay	Decay Radiation Information (NNDC)
Chemical Form	Ce(III) in 0.1M HCl
Available Specific Activity	> 4000 Ci/g
Activity Concentration	> 5 mCi/ mL
Radionuclidic Purity	> 99.8% (excluding Ce-135, Ce-137m, Ce-139 and La daughters), Ce-135 < 1%, Ce-137m <5%, Ce-139 <3%
Production Route	Proton irradiation of La target
Processing	Dissolution and ion exchange
Primary Container	Glass crimp- top V-vial
Availability	Monthly
Unit of Sale	Millicuries

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^{134}Ce application *in vivo*

nature chemistry
ARTICLES
https://doi.org/10.1038/s41557-020-00598-7
Check for updates

Developing the ^{134}Ce and ^{134}La pair as companion positron emission tomography diagnostic isotopes for ^{225}Ac and ^{227}Th radiotherapeutics

Tyler A. Bailey[1,2,5], Veronika Mocko[3,5], Katherine M. Shield[1,2,5], Dahlia D. An[2], Andrew C. Akin[3], Eva R. Birnbaum[3], Mark Brugh[3], Jason C. Cooley[3], Jonathan W. Engle[4], Michael E. Fassbender[3], Stacey S. Gauny[2], Andrew L. Lakes[2], Francois M. Nortier[3], Ellen M. O'Brien[3], Sara L. Thiemann[3], Frankie D. White[3], Christiaan Vermeulen[3]✉, Stosh A. Kozimor[3]✉ and Rebecca J. Abergel[1,2]✉

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journal homepage: www.elsevier.com/locate/nucmedbio
ELSEVIER

Evaluation of ^{134}Ce as a PET imaging surrogate for antibody drug conjugates incorporating ^{225}Ac

Tyler A. Bailey[a,b], Jennifer N. Wacker[a], Dahlia D. An[a], Korey P. Carter[a,1], Ryan C. Davis[c], Veronika Mocko[d], John Larrabee[a,b], Katherine M. Shield[a,b], Mila Nhu Lam[d], Corwin H. Booth[a], Rebecca J. Abergel[a,b,*]

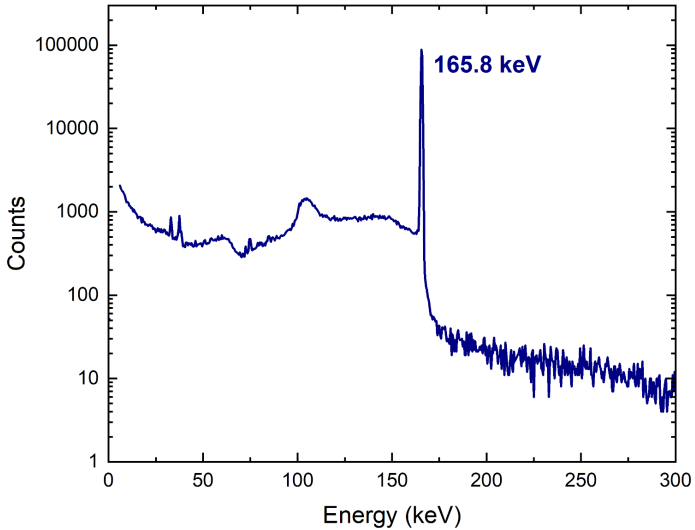
- First application of ^{134}Ce *in vivo*
- ^{134}Ce(III) DTPA mimics ^{225}Ac
- ^{134}Ce(IV) HOPO mimics ^{227}Th

- ^{134}Ce allows for long-term tumor targeting with DOTA-based antibody drug conjugates
- ^{134}Ce better match for ^{225}Ac/^{227}Th due to longer half life than ^{132}La($T_{1/2}$ 4.8h), ^{133}La($T_{1/2}$ 3.9h)

Baily et al. NATURE CHEM 13. 284 (2021), Bailey et al. Nucl. Med. Biol. 110-111 (2022)

^{139}Ce

- New product available through NIDC
- $T_{1/2}$ = 137.641 d
- Production from La, **^{nat}La (p,n)^{139}Ce**
- Radionuclidic purity >99.9%
- Specific activity >25 Ci/g, when produced 600 Ci/g
- Form: Ce(III) in 0.5 M HCl
- Concentration > 1 mCi/mL



Announcing domestic supply chain of Cerium-139

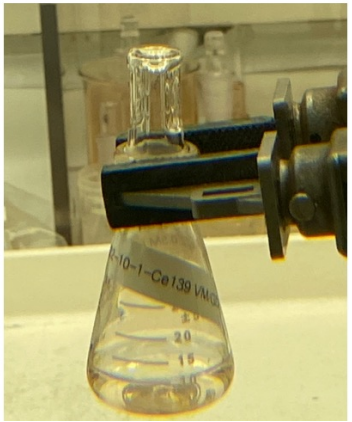
November 4, 2022

The U.S. Department of Energy Isotope Program is pleased to announce cerium-139 (Ce-139) has been added to our catalog and is available for purchase.

Ce-139 is used in mixed calibration sources and to determine attenuation maps for SPECT medical diagnostic tomography. It also can be used as a tracer instead of short lived Ce-134. Historically, Russia has been the world's primary producer of this isotope. Ce-139 is being produced in the Isotope Production Facility at Los Alamos National Laboratory.

For further inquiries about Ce-139 please contact the NIDC at contact@isotopes.gov or click the link below to request a quote.

Request a quote



Summary and outlook

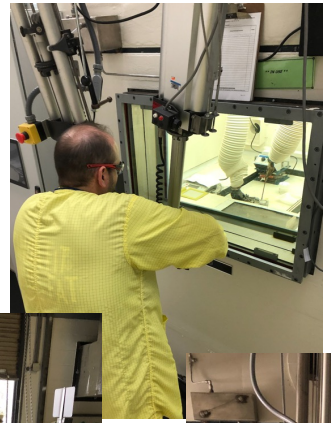
- In 2021&2022 LANL produces 2 evaluation batches
- Production and processing procedures for ^{134}Ce transferred to BNL
- Both LANL and BNL demonstrated production of Ci-level ^{134}Ce to provide year-round steady supply
- High specific activity and radioisotope purity ^{134}Ce product
- Collaborators demonstrated that ^{134}Ce allows for long-term tumor targeting
- In case of growing demand, La encapsulation in welded target shells can provide larger batches of ^{134}Ce and likely also improved ^{134}Ce/^{139}Ce ratio
- ^{139}Ce can be potentially used as longer-lived ^{134}Ce surrogate

The team

Program manager:

Kirk Rector

Team lead:
Carl Iverson



Adelman Sara, Archuleta Joseph, Bhardwaj Kirti, Capon Ross, Cummins Lisa, Dutech Guy, Fassbender Michael, Henning Christopher, Kedge Anthony, Kollarik Nathan, Kozimor Stosh, Martinez Christopher, Mocko, Veronika, Morrell Jonathan, Nadeau Kenneth, O'Brien Ellen, Ortiz Beverly, Romero Nicole, Vermeulen Etienne, Wade Heath

LANL colleagues: Cooley Jason

University of Wisconsin: Engle Jonathan, LBNL/Univ. of California: Abergel Rebecca