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Title:	High Energy Accelerator Production of Actinium-225: Cross Sections for protons on Thorium-232
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ABSTRACT

High Energy Accelerator Production of ^{225}Ac: Cross Sections for ^{232}Th + p

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While the radiotherapy isotopes ^{225}Ac and ^{213}Bi have shown tremendous cancer fighting potential, their widespread use in radiotherapy has been restricted by the limited availability of ^{225}Ac. Presently the worldwide ^{225}Ac supply of around 1 Ci per year comes almost exclusively from two ^{229}Th sources located at Oak Ridge National Laboratory (ORNL) and the Institute for Transuranium Elements (ITU). The anticipated growth in future ^{225}Ac demand has recently led to the investigation of a number of alternative production methods including accelerator production routes. The work presented here is part of a wider evaluation of high energy accelerator production routes, employing intense 100 MeV, 200 MeV and 800 MeV proton beams and thorium targets for the large-scale production of ^{225}Ra, ^{225}Ac and ^{229}Th. Such beams are available at the Los Alamos National Laboratory (LANL) and Brookhaven National Laboratory (BNL).

The presentation describes the experimental efforts associated with the accurate measurement of cross sections relevant to production of Ac-225 via ^{232}Th(p,x) nuclear reactions. Theoretical cross sections obtained using codes such as CEM, Bertini, INCL and ALICE2010 are compared with the measured data as well as with other existing data.

An up-to-date status of the worldwide nuclear cross section data relevant to the production of Ac-225 and other alpha emitting therapy isotopes, such as Ra-223 is given. The presentation provides an overview of all the published data as well as preliminary data from LANL measurements. In addition it provides an overview of data expected from experimental efforts in progress at LANL, ORNL and ANL.

High Energy Accelerator Production of ~~^{225}Ac~~ 225 Actinium: Cross Sections for ~~^{232}Th + p~~ 223- Thorium

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Los Alamos National Laboratory, U.S.A.

Main Driver for this Effort

^{211}At and ^{225}Ac or ^{213}Bi (decay product of ^{225}Ac) are considered for moving forward towards clinical trials

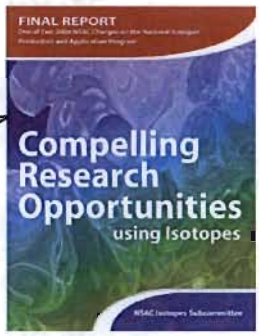
Predicted annual need far exceeds the supply

Year	Amount (mCi)	Program
2008	750	Clinical trials/R&D support
2009	1,600	Clinical trials (1 multi- center) /R&D support
2010	3,100	Clinical trials (2 multi- center) /R&D support
2011	4,600	Clinical trials (2 multi- center) /R&D support
2012	7,400	Clinical trials (3 multi-center)/R&D support
2013	15,000	One approval, Clinical trials(2 multi-center)/R&D
2014	50,000+	Two approvals; Clinical trials/R&D support

Main Driver for this Effort (continued)

First of 6 Recommendations for Charge 1 of NSAC Isotopes Subcommittee

Medicine#1:
Invest in new production approaches of alpha-emitters with highest priority for Ac-225. Extraction of the thorium parent from U-233 is an interim solution that needs to be seriously considered for the short term until other production capacity can become available.



Various ^{225}Ac Production Routes

Facility	Nuclear Reaction
Reactor (thermal neutrons)	$^{226}Ra(3n,\gamma)^{229}Ra \rightarrow ^{229}Ac \rightarrow ^{229}Th$
Reactor (fast neutrons)	$^{226}Ra(n,2n)^{225}Ra \rightarrow ^{225}Ac$
Accelerator (low energy protons)	$^{226}Ra(p,2n)^{225}Ac$ $^{232}Th(p,x)^{229}Th$
Accelerator (high energy protons)	$^{232}Th(p,x)^{225}Ac$ $^{232}Th(p,x)^{225}Ra \rightarrow ^{225}Ac$ $^{232}Th(p,x)^{229}Th$
Accelerator (electrons)	$^{226}Ra(\gamma,n)^{225}Ra \rightarrow ^{225}Ac$

Evaluate Higher Energy Accelerator Production Routes using thorium targets

Th-229 production

$^{232}Th(p,4n)^{229}Pa \xrightarrow{99.5\%} {}^{229}Th$

$^{232}Th(p,p3n)^{229}Th$

Ra-225/Ac-225 production

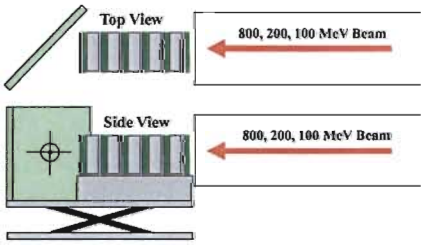
$^{232}Th(p,x)^{225}Ac$

$^{232}Th(p,x)^{225}Ra \xrightarrow{100\%} {}^{225}Ac$

$^{232}Th(p,x)^{229}Th \xrightarrow{10\%} {}^{225}Ac$

$^{232}Th(p,4n)^{229}Pa \xrightarrow{0.5\%} {}^{225}Ac$

Basic Measurement Approach



Isotope	Half Life
Pa-229	1.5 d
Th-229	7880 y
Th-228	1.9 y
Th-227	18.7d
Ac-227	21 y
Ra-225	14.8 d
Ac-225	10 d
Ra-223	11.4 d

- Thorium samples and proton fluence monitor foils are irradiated in three different proton beams
- Samples are assayed via various counting methods
- Decay of isotopes of interest is followed over time to obtain production cross sections

Thorium Sample Irradiations – 100 nA, 30-60 min

800 MeV:

- Single-energy test irradiation completed on December 1st , 2009

200 MeV:

- Very special 200 MeV accelerator tune
- Multi-energy stack irradiation completed on December 7th , 2010

100 MeV:

- Special target holder
- Single-energy test irradiation completed on September 24th , 2010

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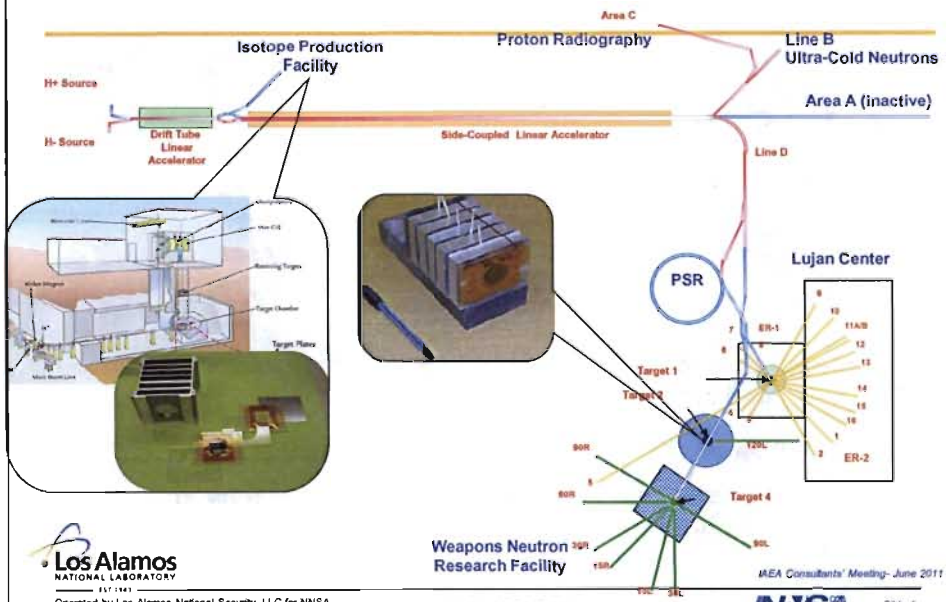
LANSCE Accelerator Complex Overview



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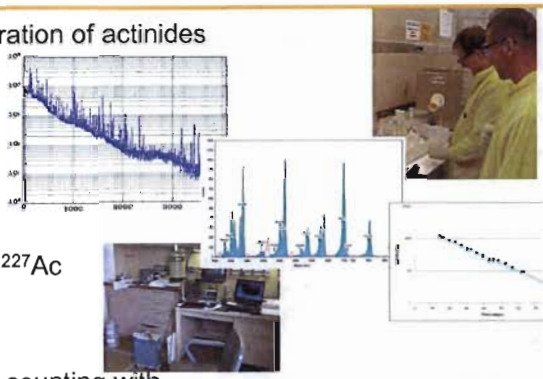
Various Counting and Analysis Approaches

- Exploratory chemistry separation of actinides
- Alpha and gamma counting
- γ-γ coincidence counting of ^{227}Ac
- Exploratory γ-γ coincidence counting with GEANIE in parallel with nondestructive counting
- Chemical separation and α-counting of Ac-227



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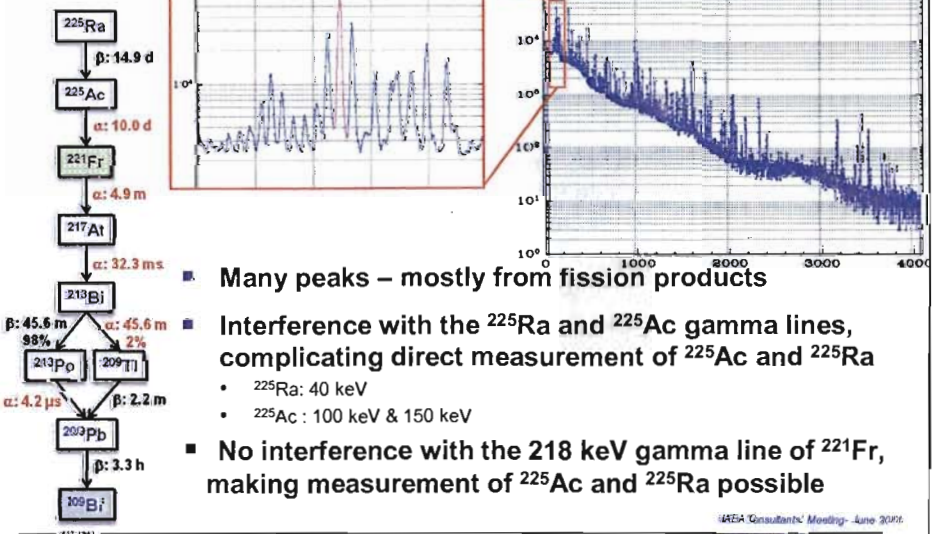
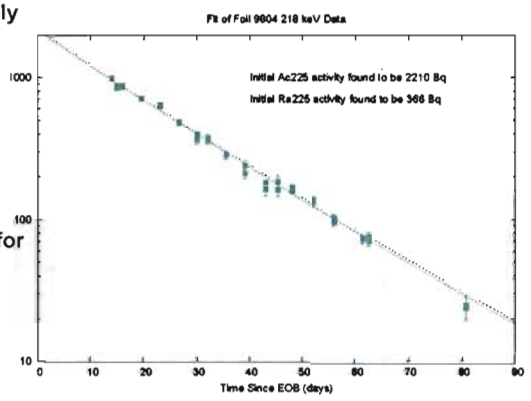
800 MeV γ-counting and analysis: Ra-225 & Ac-225



- **Many peaks – mostly from fission products**
- **Interference with the ^{225}Ra and ^{225}Ac gamma lines, complicating direct measurement of ^{225}Ac and ^{225}Ra**
  - ^{225}Ra: 40 keV
  - ^{225}Ac : 100 keV & 150 keV
- **No interference with the 218 keV gamma line of ^{221}Fr, making measurement of ^{225}Ac and ^{225}Ra possible**

800 MeV γ-counting and analysis: Ra-225 & Ac-225

- Two samples counted nondestructively on two different detectors
  - HPGe coaxial and HPGe planar
- Two analysis software codes
  - RAYGUN and SPECANAL
- Parent-daughter decay/growth curve for $^{225}Ra \rightarrow ^{225}Ac$ fitted to measured ^{221}Fr activity data to obtain ^{225}Ra and ^{225}Ac activities at OEB
- The ^{225}Ra results are considered acceptable but not as accurate as a direct measurement

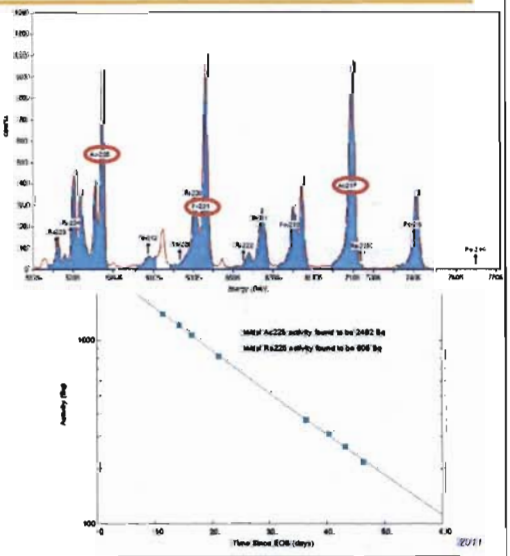


800 MeV α-counting and analysis: Ac-225

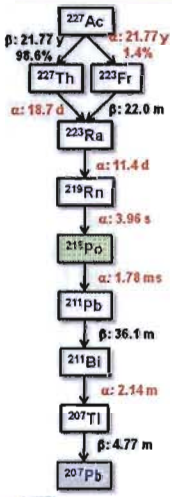
One sample dissolved for preliminary separation chemistry tests

Subjected a near-massless sample, prepared from 50 µL aliquot of Ac/Ra eluant, to α-counting

Despite careful preparation, overlapping peaks still required manual de-convolution in order to determine ^{225}Ac activity

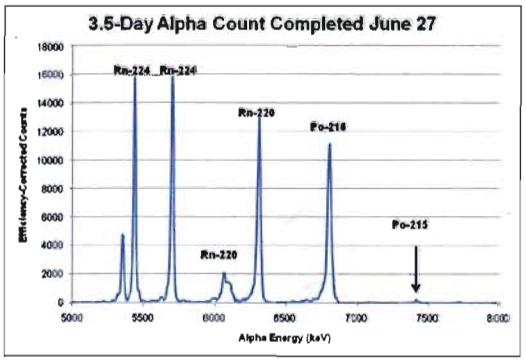


800 MeV α-counting and analysis: Ac-227 (21.7 y)



The α-counting sample was subjected to a 3.5 day long count on June 27th, 2010 (7 months later)

Spectrum shows that the ^{215}Po peak can be used to measure ^{227}Ac activity



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Cross Sections at 800 MeV

Reaction	Cross Section (mb)	Measurement Method	Literature values
^{232}Th(p,x)^{225}Ac	13.3 ± 0.6	γ, α	20.3 ± 5.1*
^{232}Th(p,x)^{225}Ra	4.1 ± 0.2	$\gamma_{indirect}$, $\alpha_{indirect}$	None
^{232}Th(p,x)^{227}Ac	16 ± 1	α	None
^{232}Th(p,x)^{227}Th	12 ± 1	γ	None
^{232}Th(p,x)^{223}Ra	7.0 ± 0.6	γ	None

*Titarenko *et al.* (2002), INDC(CCP)-434

New data for ^{223,225}Ra, ^{227}Ac, & ^{227}Th

Manuscript for publication is in preparation

Production Potential at MTS

Assumptions:
Beam Current; 1250 μA (800 MeV protons)
Target: 3 g/cm^2 thick thorium metal

Expected Yields
^{225}Ac: 1.5 Ci/day (0.18% ^{227}Ac)
^{225}Ra: 313 mCi/day (~200 mCi of pure ^{225}Ac)

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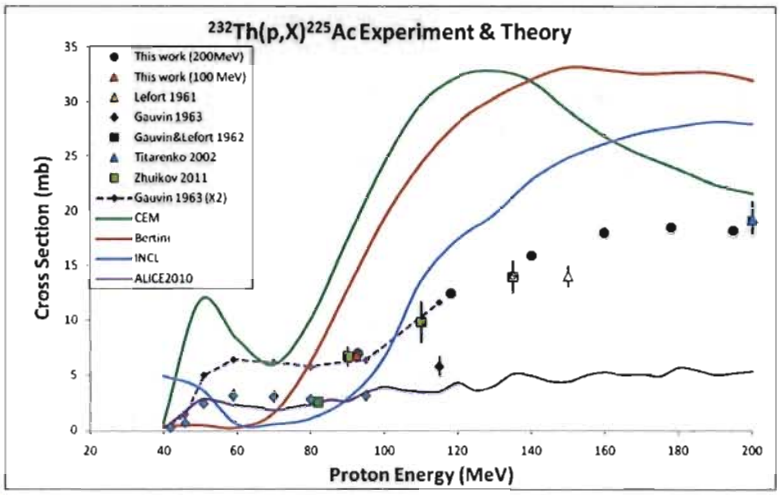
Preliminary ^{225}Ac Cross Sections for 100 MeV - 200 MeV



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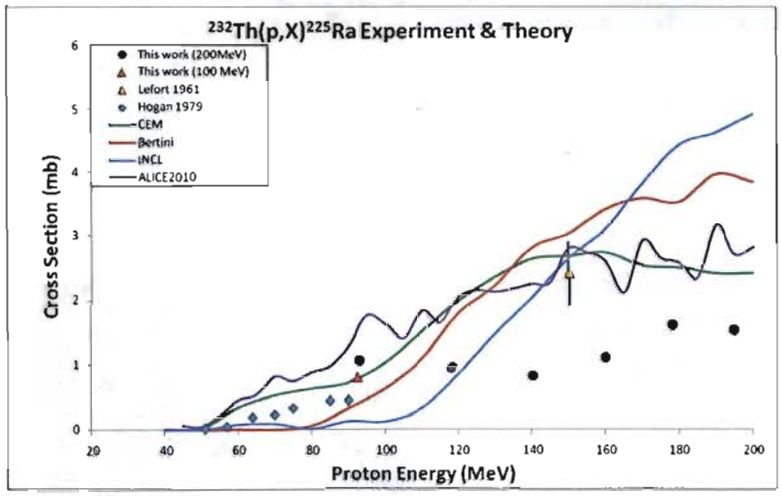
Preliminary ^{225}Ra Cross Sections for 100 MeV - 200 MeV



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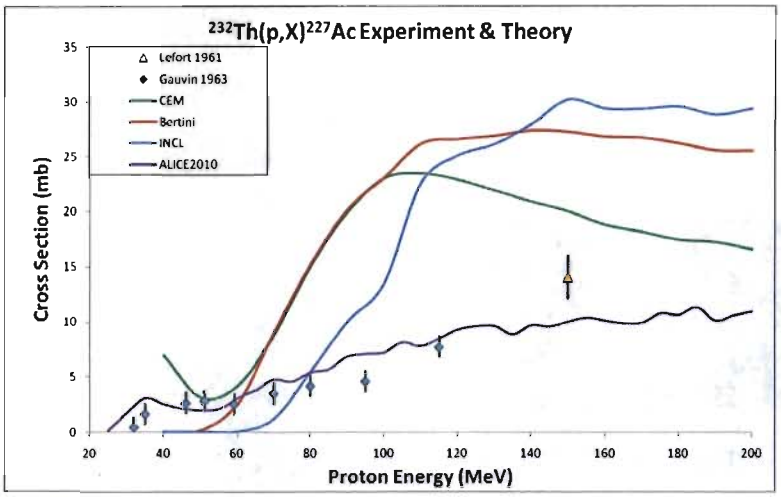
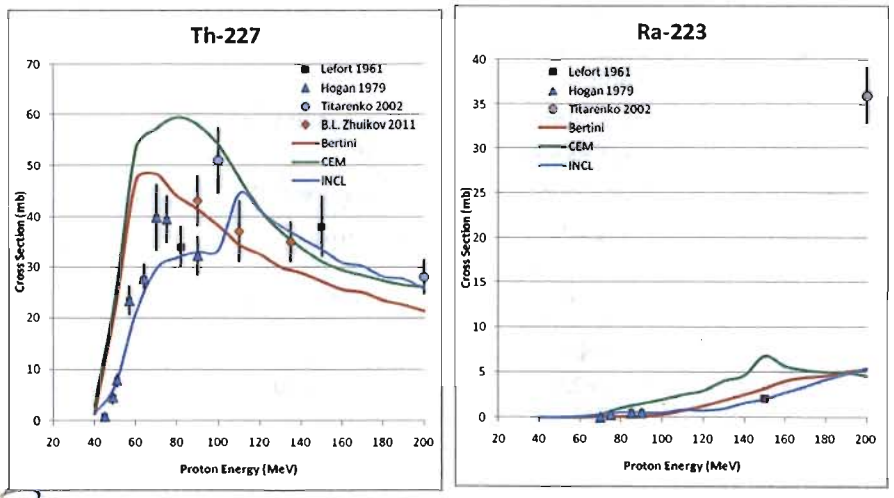
Existing ^{227}Ac Cross Sections below 200 MeV



Existing ^{227}Th & ^{223}Ra Cross Sections below 200 MeV



Other Measurement Efforts at ORNL (low energy) and Fermi Lab (8 GeV)

^{229}Th production at ORNL

^{232}Th(p,4n)^{229}Pa →^{229}Th
^{232}Th(p,p3n)^{229}Th

^{225}Ac production at Fermi Lab

NorthStar
High Energy Proton Spallation of Th232

Slides Courtesy of Jim Harvey, NorthStar

NorthStar
High Energy Proton Spallation of Th232
FNAL beam dump irradiation position

NorthStar
High Energy Proton Spallation of Th232
Copper Th232 target holder

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Summary

- **Measure cross sections to evaluating production potential of ^{225}Ac from natural Th targets using 100, 200, 800 MeV beams – for IPF, BLIP and spallation production routes**
- **800 MeV: Results include new cross section data and show promise from a large scale production perspective**
- **100 MeV - 200 MeV: Counting and analysis are still in progress**
- **Preliminary 100 MeV & 200 MeV results show:**
  - Models generally over estimate cross sections
  - Ac-225 – LANL data are in good agreement with recent data. Measurements below 100 MeV must be done.
  - Ra-225 – LANL data are in reasonable agreement with literature data
  - Ac-227, Th-227 & Ra-223 – LANL measurements should substantial new data in the100-200 MeV range

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