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Title:	Accelerator production of the therapy isotope Actinium-225 at 800 MeV
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Intended for:	7th Symposium on Targeted Alpha Therapy, Berlin, Germany, July 17-19, 2011

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ABSTRACT

Accelerator production of the therapy isotope ^{225}Ac at 800 MeV

J.W. Weidner, H.T. Bach, L.J. Bitteker, M. Cisneros, A. Couture, D. Dry, M.E. Fassbender, M. Gallegos, G.S. Goff, R. Grizo, K.D. John, S.G Mashnik. J.L. Ullmann, W. Taylor, L.E. Wolfsberg, S. Wender, R.S. Baty and F.M. Nortier,

Los Alamos National Laboratory, Los Alamos, New Mexico, USA

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).

This presentation describes the investigation of a high energy accelerator approach using intense 800 MeV proton beams. Cross sections were measured for production of relevant isotopes via ^{232}Th(p,x) nuclear reactions. Theoretical cross sections using codes such as CEM are compared with the measured data as well as with other existing data. Expected production yields and purity levels derived from the measured cross sections show very promising options for large-scale production with varying levels of product quality.

Additional experiments to measure the ^{232}Th(p,x)^{225}Ac production cross sections in the proton energy range below 200 MeV are still in progress.

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Accelerator Production of the therapy isotope Actinium-225 at 800 MeV

~~Accelerator Production of ^{225}Ac at 800 MeV~~

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and ***F.M. Nortier***

Los Alamos National Laboratory, New Mexico, U.S.A.

Main Driver for this Effort

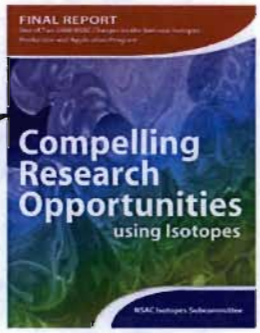
- ^{211}At and ^{225}Ac or ^{213}Bi (decay product of ^{225}Ac) are considered for moving forward towards clinical trials
- Predicted annual need far exceeds the world-wide supply of ~1Ci

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.



Goals

- Evaluate higher energy accelerator production routes using **thorium targets** by means of cross section measurement
- Concentrate on 100 MeV, 200 MeV and 800 MeV beams available at the IPF (LANL), BLIP (BNL) and MTS (LANL)
- Make available accurate production cross sections to the isotope production community.

Two Possible Production Approaches

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

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

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

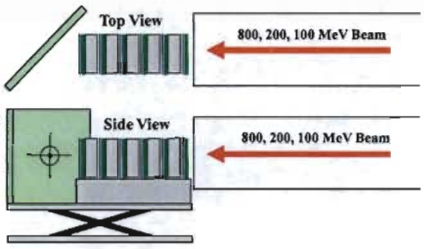
$^{232}Th(p,4n)^{229}Pa \xrightarrow{0.5\%} {}^{225}Ac$

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

Various $^{225}Ac/^{229}Th$ 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 particles)	$^{226}Ra(p,2n)^{225}Ac$ $^{226}Ra(\alpha,n)^{229}Th$ $^{232}Th(p,x)^{229}Th$ $^{230}Th(p,x)^{229}Th$
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)	$^{226}Ra(\gamma,n)^{225}Ra \rightarrow {}^{225}Ac$

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	21.8 y
Ra-225	14.8 d
Ac-225	10 d
Ra-223	11.4 d

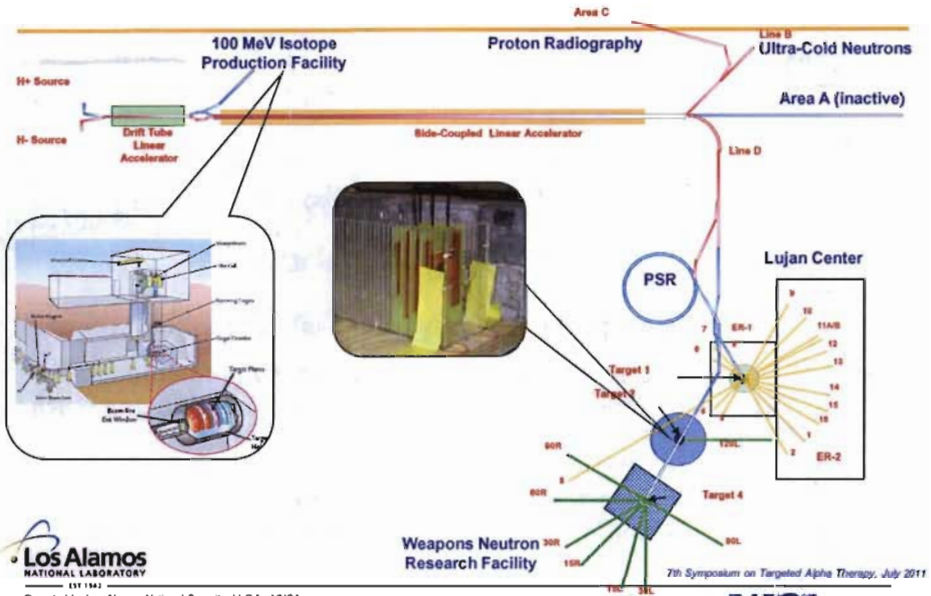
- Thorium samples and proton fluence monitor foils are irradiated in three different proton beams
- Samples are assayed via various counting methods
- Decay of isotopes of interest is followed over time to obtain production cross sections

800 MeV Thorium Sample Irradiations

- Single-energy measurement at 800 MeV
- 3 thorium samples (50 μm thick) and 1 aluminum fluence monitor were activated
- The 1 hour irradiation at proton a current of 80 nA was completed on December 1st , 2009

PhD student, John Weidner

LANSCE Accelerator Complex Overview



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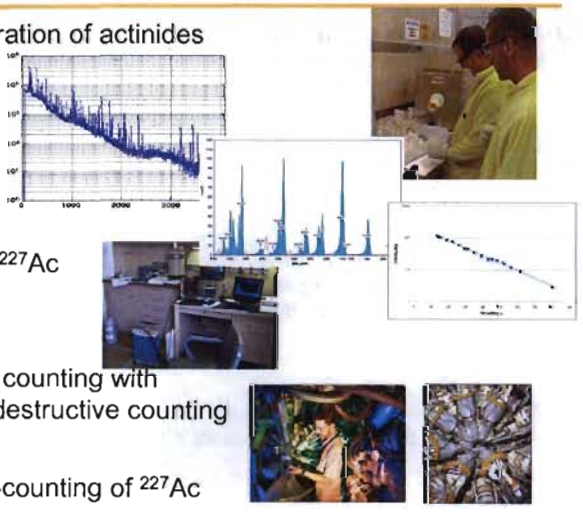
Various Counting and Analysis Approaches

- 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 ^{227}Ac



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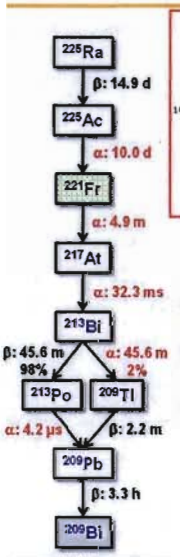
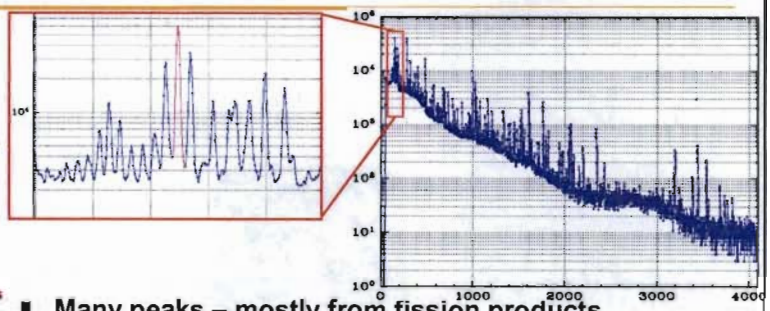
800 MeV γ-counting and analysis: Ra-225 & Ac-225

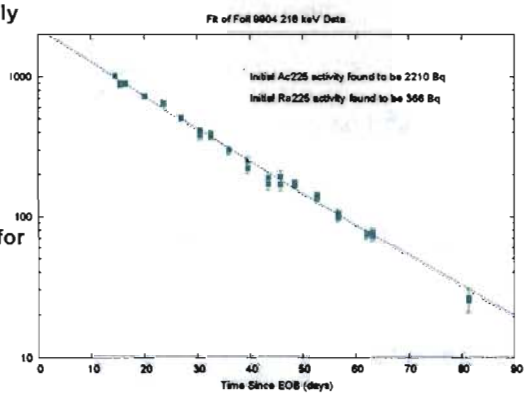




- Many peaks – mostly from fission products
- Interference with the ^{225}Ra and ^{225}Ac gamma lines, complicating direct measurement of ^{225}Ac and ^{225}Ra
  - ^{225}Ra: 40 keV
  - ^{225}Ac : 100 keV & 150 keV
- No interference with the 218 keV gamma line of ^{221}Fr, making measurement of ^{225}Ac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

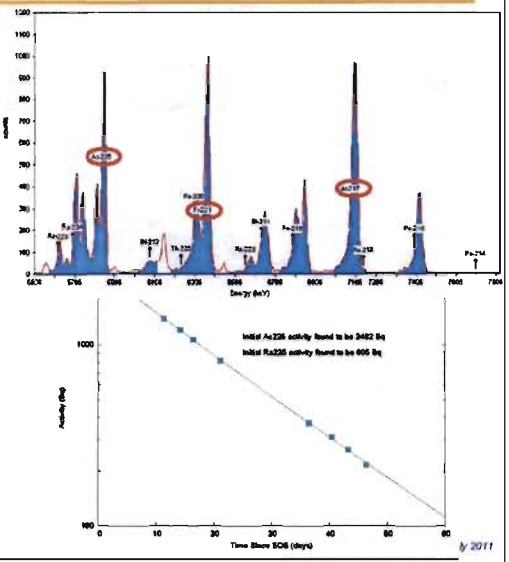


800 MeV α-counting and analysis: Ac-225

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



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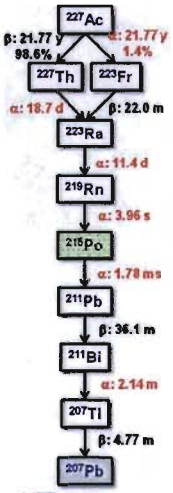
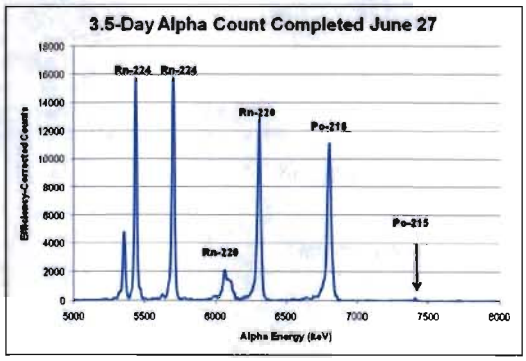
800 MeV α-counting and analysis: Ac-227 (21.7 y)



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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Production Cross Sections at 800 MeV

Reaction	Cross Section (mb)	Measurement Method	Literature values (mb)	Theoretical values (CEM) (mb)
$^{232}Th(p,x)^{225}Ac$	13.5 ± 0.7	γ, α	20.3 ± 5.1*	15.0
$^{232}Th(p,x)^{225}Ra$	3.0 ± 0.3	$\gamma_{indirect}$, $\alpha_{indirect}$	None	1.54
$^{232}Th(p,x)^{227}Ac$	15.2 ± 1.1	α	None	11.0
$^{232}Th(p,x)^{227}Th$	12 ± 1	γ	None	18.6
$^{232}Th(p,x)^{223}Ra$	7.0 ± 0.6	γ	None	11.6

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

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

Manuscript for publication is in preparation

800 MeV production potential at the future MTS

Assumptions:
MTS Design Beam Current: 1250 μA (800 MeV protons)

Target: 3 g/cm² thick thorium metal

Isotope	$T_{1/2}$	Expected Yields
^{225}Ra	14.8 d	230 mCi/day (~140 mCi of pure ^{225}Ac)
^{225}Ac	10 d	1.5 Ci per day (0.14% ^{227}Ac)
^{223}Ra	11.4 d	700 mCi per day
^{227}Th	18.7 d	730 mCi per day
^{227}Ac	21.7 y	800 mCi per year

Summary

- **LANL measurements are aimed at evaluating production potential of ^{225}Ac in natural Th targets using 100, 200, 800 MeV beams – for IPF, BLIP and spallation production routes (MTS).**
- **800 MeV results include new cross section data for ^{223,225}Ra, ^{227}Ac, and ^{227}Th.**
- **Production cross sections for ^{225}Ra and ^{225}Ac show promise from a large scale production perspective.**
- **Assuming the MTS design beam current:**
  - Expected daily production of ^{225}Ra is 230 mCi from which ~140 mCi of pure ^{225}Ac can be recovered.
  - Expected daily production of ^{225}Ac is 1.5 Ci, with a ^{227}Ac contamination level of 0.14%.
- **The usefulness of the directly produced ^{225}Ac is still uncertain.**
- **Promising production options for ^{223}Ra also exists.**

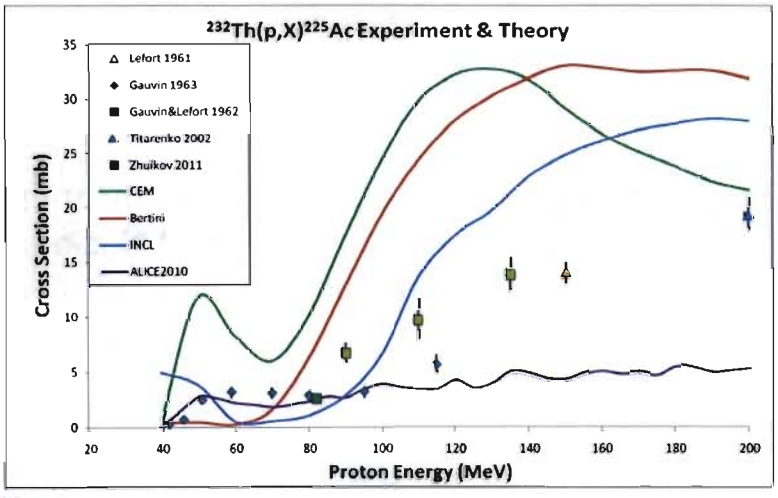
Acknowledgements

This work is supported by U.S. Department of Energy, Office of Science, Office of Nuclear Physics

Additional slides

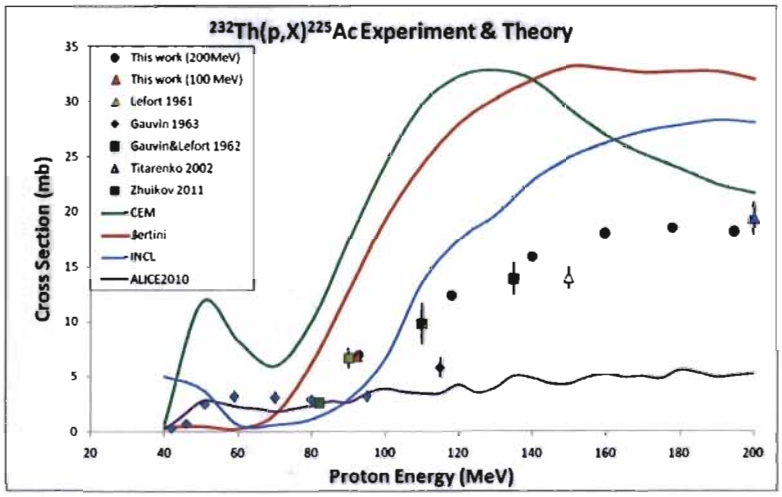
Cross Section Data below 200 MeV

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



Cross Section Data below 200 MeV

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



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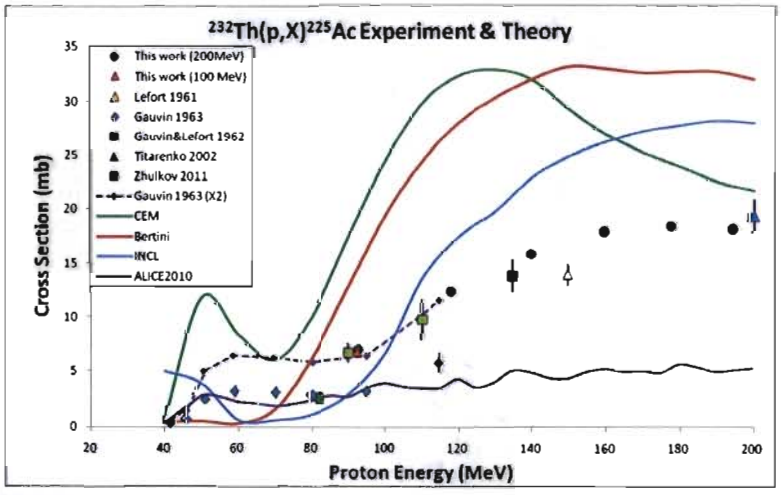
Cross Section Data below 200 MeV

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



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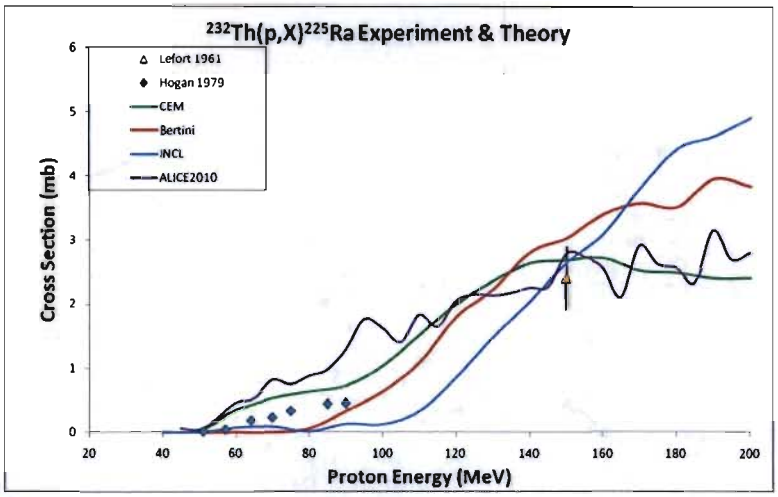
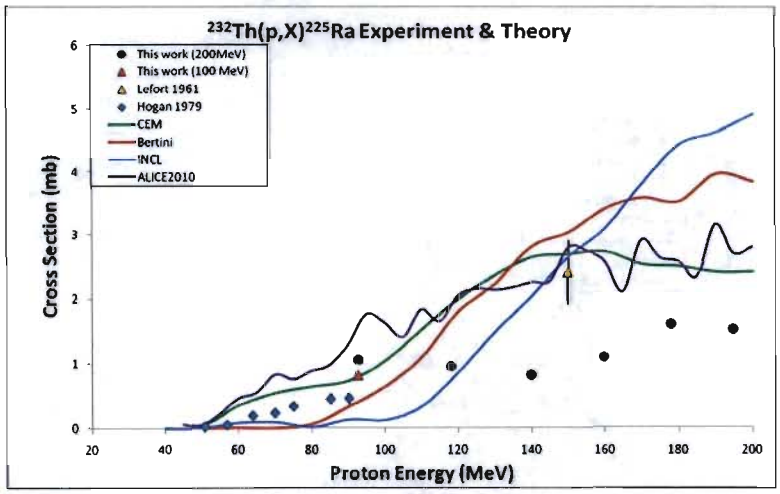
Cross Section Data below 200 MeV

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

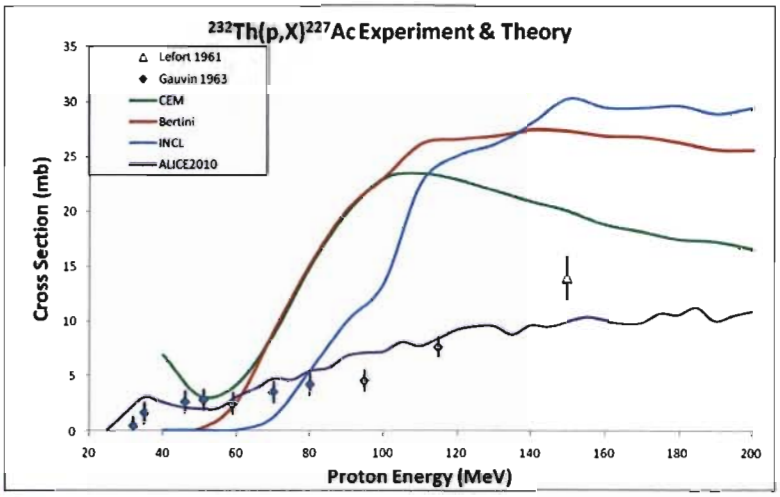


Cross Section Data below 200 MeV

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



Existing ^{227}Ac Cross Sections below 200 MeV



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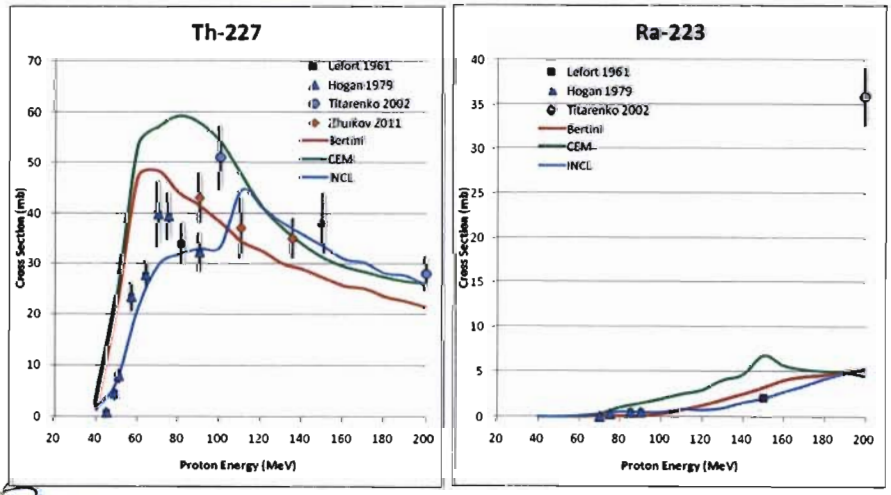
Existing ^{227}Th & ^{223}Ra Cross Sections below 200 MeV



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