Medical Isotope Development And Supply Opportunities In The 21st Century

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Abstract

- Medical Isotopes are a significant factor in modern medical diagnosis and therapy
- Supplies are at risk due to:
  - Aged nuclear activation resources
  - Limited specialty production
  - Reduced public funding
- Opportunities are emerging
  - Advanced reactors
  - Advanced compact accelerators
  - Medical and business sectors can join to provide new medical cures

Medical Isotope Supply Side

- 70,000 procedures performed daily in North America at Risk
  - Dec. 2007 sudden lack of Technetium-99m
  - Canadian plant had unexpected prolonged closure
  - Replacement reactors canceled
  - Shutdown of existing expected 2011
- Demand for medical radioisotopes growing 8-20% annually
  - US/world production resources not adequate to meet anticipated needs
  - Most supply reactors reaching end of life cycle
  - Emergent isotopes of interest supply limited/non-existent

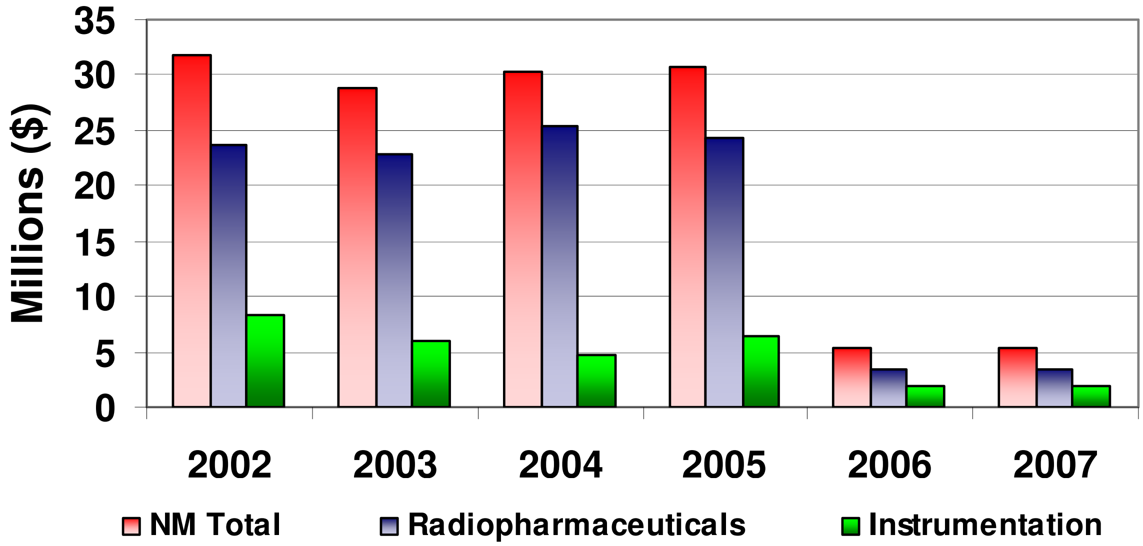
World Nuclear Reactor Medical Isotope Producers

Reactor Facility	% World Supply		Startup
	^{99m}Tc	^{131}I	
NRU at Chalk River, Canada (supplied via MDS Nordion)	40		1957
HFR at Petten in Netherlands (supplied via IRE and Tyco)	30		1962
BR2 at Mol in Belgium (supplied via IRE and Tyco)	12		1964
Osiris & Orphee at Saclay in France (supplied via IRE)	3	75	1967
FRJ-2/ FRM-2 at Julich in Germany (supplied via IRE)	Small		1967
LVR-15 at Rez in Czech Republic			1957
HFETR at Chengdu in China			1979
Safari in South Africa (supplied from NTP)	15	25	1965
Opal in Australia (supplied from ANSTO)	Small	Small	2006

NAS Findings

- The national isotope program is not meeting the needs of the medical research community
- There is an inadequate domestic supply of medical radio-nuclides
- There is a shortage of trained nuclear medicine-related scientists
- There is a need for new technology development and transfer

NAS Finding:
Loss of US Federal Commitment for Nuclear Medicine Research



Common medical isotopes sorted by use category and production method

Purpose	Accelerator-produced	Reactor-produced
Diagnostic Isotopes	^{11}C, ^{13}N, ^{15}O, ^{18}F, ^{55}Fe, ^{57}Co, ^{61}Cu, ^{64}Cu, ^{67}Ga, ^{74}As, ^{76}Br, ^{81m}Kr, ^{82m}Rb, ^{94m}Tc, ^{97}Ru, ^{111}In, ^{123}I, ^{124}I, ^{179}Ta, ^{201}Tl	^{3}H, ^{14}C, ^{51}Cr, ^{64}Cu, ^{97}Ru, ^{99m}Tc, ^{123}I, ^{131}I, ^{133}Xe, ^{153}Gd, ^{195m}Pt
Therapeutic Isotopes	^{64}Cu, ^{67}Cu, ^{77}Br, ^{88m}Br, ^{88}Y, ^{89}Zr, ^{103}Pd, ^{111}In, ^{124}I, ^{186}Re, ^{211}At	^{32}P, ^{47}Sc, ^{60}Co, ^{64}Cu, ^{67}Cu, ^{89}Sr, ^{90}Sr, ^{90}Y, ^{103}Pd, ^{103}Ru, ^{106}Ru, ^{109}Cd, ^{109}Pd, ^{117m}Sn, ^{115}Cd, ^{125}I, ^{131}I, ^{131}Cs, ^{137}Cs, ^{145}Sm, ^{153}Sm, ^{165}Dy, ^{166}Dy, ^{166}Ho, ^{169}Er, ^{169}Yb, ^{180}Tm, ^{175}Yb, ^{177}Lu, ^{186}Re, ^{188}Re, ^{192}Ir, ^{195m}Pt, ^{198}Au, ^{199}Au, ^{211}At, ^{213}Bi, ^{225}Ac, ^{241}Am

Major Medical Isotope Production Neutron Energy Ranges

Neutron Energy	Isotope
Thermal-Epithermal (.01ev-10keV)	^{75}Se, ^{89}Sr, ^{90}Y, ^{103}Pd, ^{125}I, ^{131}I, ^{127}Xe, ^{131}Cs, ^{153}Gd, ^{153}Sm, ^{165}Dy, ^{166}Ho, ^{177}Lu, ^{186}Re, ^{188}W, ^{192}Ir, ^{198}Au, ^{223}Ra, ^{225}Ac
Fast (10keV-1.0MeV)	^{99}Mo, ^{117m}Sn
High Energy (1.0MeV-10MeV)	^{32}P, ^{33}P, ^{57}Co, ^{62}Cu, ^{64}Cu, ^{67}Cu, ^{89}Sr
14MeV	^{99}Mo, ^{225}Ac

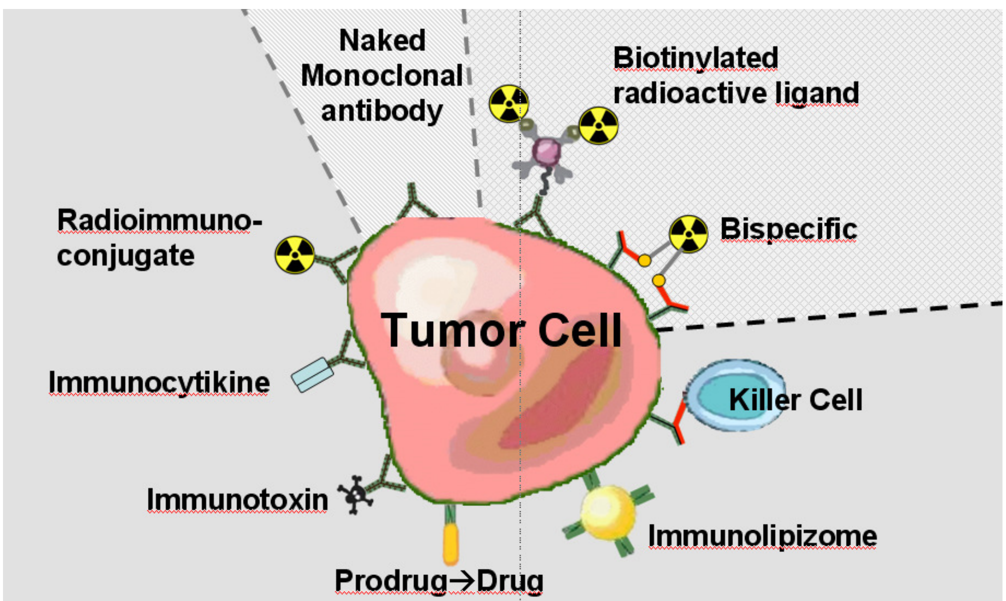
Desirable features of Medical Isotopes

- Moderate half lives –
  - A few hours to a few days
  - Local generation
  - Reactor/accelerator/isotope source
- Diagnostic imaging
  - Direct gamma, positron conversion
  - ^{99m}Tc, ^{18}F
- Therapy
  - Moderate/high energy beta – $^{64/67}$Cu, ^{90}Y
  - Alpha - ^{225}At, ^{211}AT, ^{213}Bi
- Biological compatibility
  - Location seekers – ^{133}I to Thyroid
  - Attachable to cell seekers – monoclonal antibodies

Emerging Opportunities

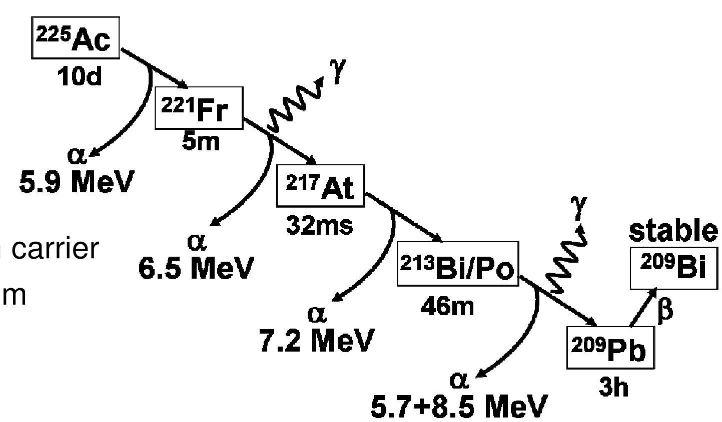
- Radioimmunotherapy (RIT) continuing development
  - Molecular science determining targets
  - Desired isotopes in low supply
    - Short lived alpha emitters
- Branching to diseases other than cancer
  - HIV/AIDS (Albert Einstein College of Medicine)
  - Malaria (IAEA tracer/sterile insect)
  - Bacteria killers
- New resources
  - Small footprint accelerators
  - Modular or retooled reactors
  - Fast reactors

Cell Targeted Therapy With Medical Isotopes



Example challenge – ^{225}Ac

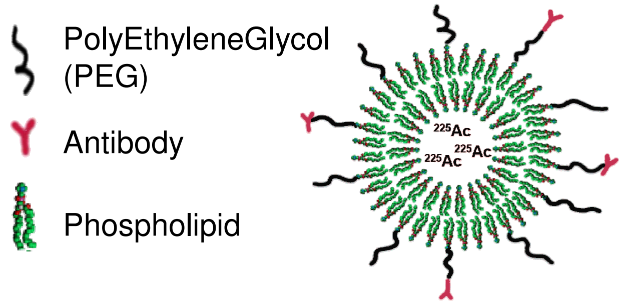
- Short lived alpha emitter
  - 4 alphas in decay chain
  - Hot atoms can breakaway from carrier
  - Hot atom recoil distance ~100nm
  - Alpha particle path ~50-100µm
- Solution: package in a liposome



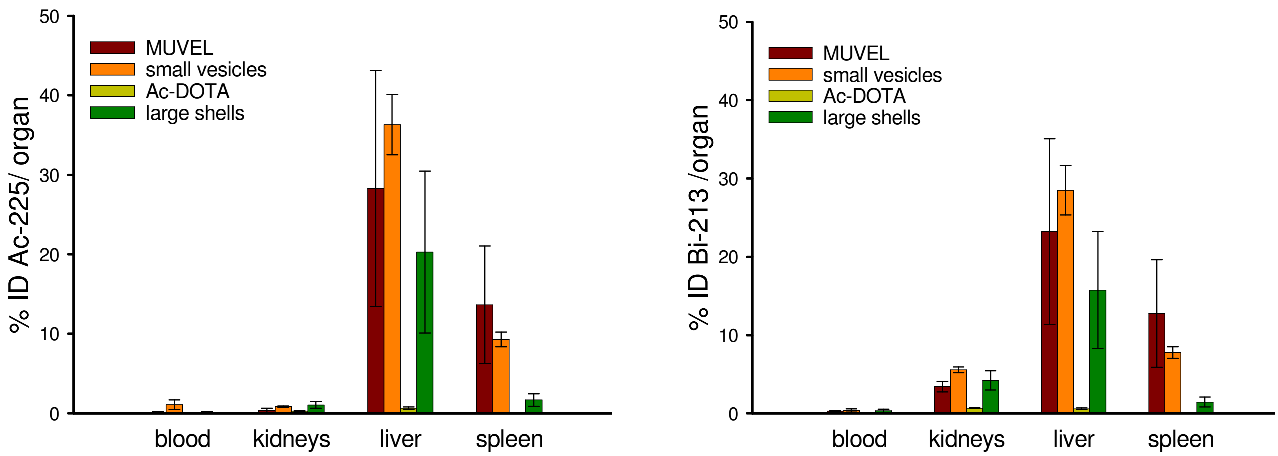
Lipisomal packaging

- Lipisome diameter on order of 800 µm
- Attachable to monoclonal antibody
- Outer/inner sheath design
- Majority of decay progeny maintained at target cell

Multivesicular Liposomes (MUVEL) Isotope Encapsulation



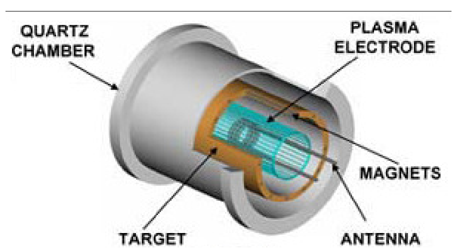
Biodistributions of intraperitoneally administered ^{225}Ac-liposomes (@24hr)

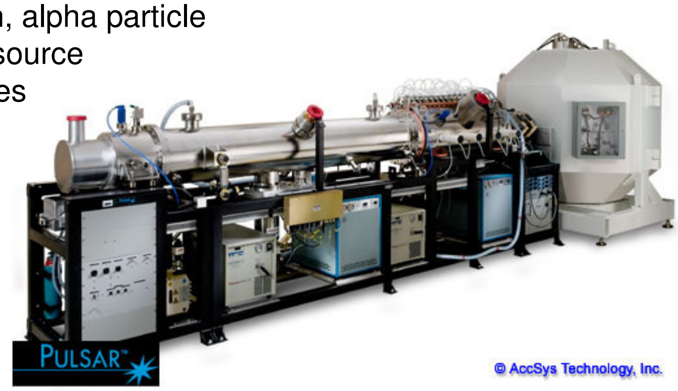


G SGOUROS, et al, *Liposomal Encapsulation of 225Ac for Targeted Nanogenerator Therapy of Cancer*, 4th Alpha-Immunotherapy Symposium, 28-29 June 2004, Düsseldorf, Germany.

Emerging isotope production methods

- Fast spectrum reactors – unavailable isotopes
- Compact linear accelerators – proton, alpha particle
- Electron-beam high-energy gamma source
- Plasma purifier for rare stable isotopes
- Compact Neutron generator





Conclusions

- The field of nuclear medicine is at a crossroads of need and opportunities. Continued development of cell targeted research is showing advancement in therapy beyond traditional cancer treatments and common diagnostic methods using limited supplies of useful isotopes such as short lived beta and alpha emitters. The challenges of supply and delivery to patients may be addressed with recent developments in compact isotope production devices. However, it will take a concerted effort on the part of the medcal industry, business, and government funding to achieve the needed isotopes and approved procedures.