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The LASL Medical Radioisotope Research Program: Radiochemistry Problems and New Developments

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Introduction

Within the Medical Radioisotope Research Program, the major areas of activity include: (1) spallation reaction research; (2) chemistry problems; (3) cooperative biomedical research; (4) remote process development; and (5) target and irradiation facility development. Earlier in this meeting, I discussed the current status and projected scheduling of the LAMPF and the Isotope Production Facility (IPF). In this paper a brief summary of the more recent developments in cross section and yield measurements, radiochemical separation studies, and radionuclide generator developments are presented.

Spallation Reaction Research

Incident nucleons in excess of 100 MeV cause a complex series of nuclear events within a target, including knock-on cascade, evaporation, fragmentation, and, for sufficiently high Z target materials, fission processes. In addition, secondary nuclear reactions can occur between emitted particles and other target nuclei. Thus one can expect the formation, to a greater or lesser extent, of every element from Z + 2 or 3 above the target to Z = 1. This is illustrated schematically in Figure 1, where the approximate formation cross sections are plotted against the mass number of products of the reactions of 480-, 800-, and 3000-MeV protons with bismuth. At 800 MeV, three distinct regions can be discerned: a) spallation product peak near the target mass; b) fission product peak between mass numbers 60 and 140; and c) fragmentation products below mass number 40. A similar complex distribution is evident from the data in Figure 2, where cross sections for the formation of products from the reaction of 590-MeV protons with vanadium are given. It is important to recognize that the complexity of nuclear processes induced by energetic projectiles results in the formation of numerous spallogenic elements in a given target, leading to formidable radiochemical recovery problems.

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With increasing beam energy during the start-up of the LAMPF accelerator, spallation reaction studies were performed at 100, 211, 302, 496, and 800 MeV (1,2). Also numerous irradiations were conducted using the 590-MeV proton beam at the Space Radiation Effects Laboratory (3,4). A summary of recent spallation cross section data is contained in Table 1, where values given in parantheses represent preliminary results. Projected yields of selected radionuclides were calculated using these data and are shown in Table 2. Note that the EOB yields at half saturation are based on an assumed current of 500 μA, the beam intensity anticipated at the IPF when LAMPF achieves its full designed operating parameters.

Radiochemical Separation Studies

Radiochemical separation schemes for several target-isotope systems have been developed at the bench-scale level, and these have been or are in the process of being scaled to permit in-cell processing of production-sized targets (7.6 cm dia. x 2.3 cm thick). The following is a brief summary of this work.

Potassium-43 --- is synthesized in V targets, which are subsequently dissolved in 8 M HNO_3, diluted to 4 M, and loaded onto a hydrated antimony pentoxide (HAP) inorganic exchanger. Following elutions with 4 M HNO_3 and 1 M HCl, the major fraction of radiopotassium is stripped from the column with 12 M HCl. Stable Sb present in the strip solution results from a partial breakdown of the inorganic exchanger. This is removed by diluting to 8 M HCl and passing the solution through an AG1-X8 anion resin. The final cleanup step consists of making the solution basic with NH_4OH (pH = 9-10) and loading onto a 100-200 mesh Bio-Rad Chelex-100 resin. The purified potassium is found in the eluent. The overall chemical yield for potassium is 91 ± 3% (5).

Bromine-77 --- is formed in high yield in Mo targets, and efforts are in progress to modify the current processing procedures to permit quantitative radiobromine isolation in addition to strontium, yttrium, and zirconium recoveries. Efforts to convert radiobromine to Br_2 followed by distillation have largely been unsuccessful to date. If other possible chemical recovery schemes prove unsatisfactory, we plan to investigate spallation yields of ^{77}Br from Y, Sr, and Rb target materials.

Table 1. 590- and 800-MeV Proton Spallation Cross Sections

Target	Nuclide	σ_{800}(mb)	σ_{590}(mb)
V	^{43}K	5.4 ± 0.3	3.8 ± 0.8
	^{42}K	11.8 ± 0.5	8.9 ± 3.6
Ni	^{52}Fe	(1.3)	---
	^{59}Fe	(0.12)	---
	^{61}Cu	(6.1)	---
	^{64}Cu	(14)	---
	^{67}Cu	(1.3)	---
As	^{66}Ga	(10)	---
	^{67}Ga	(25)	---
	^{72}Ga	(2.8)	---
	^{82}Sr	24.5 ± 0.8	15 ± 3
Mo	^{85}Sr	50 ± 2	---
	^{123}I	51 ± 3	57 ± 9
La	^{123}Xe	---	36 ± 5
	^{127}Xe	51 ± 7	53 ± 11
	^{172}Hf	---	42 ± 15
Ta	^{175}Hf	---	67 ± 12

Table 2. Projected Yields of Selected Radionuclides From LAMPF
(Assume: I = 500 uA; Target Thickness = 2.5 cm)

Nuclide	EOB Yield at 0.5 Sat'n Factor	Comments
^{43}K	41 Ci	460 mCi at EOB + 6D; $^{42}K/^{43}K$ (%) = 8.5
^{52}Fe	2.6 Ci	325 mCi at EOB + 1D; $^{59}Fe/^{52}Fe$ (%) = 0.8
^{67}Cu	1.3 Ci	160 mCi at EOB + 7.7D; $^{64}Cu/^{67}Cu$ (%) = 0.6
^{82}Sr	252 Ci	Parent of 75 sec ^{82}Rb
^{123}I	6.0 Ci †	Assume 2-H BBT, + 2-H Proc., + 2-H Decay
^{127}Xe	228 Ci	209 Ci at EOB + 4.6 D for ^{125}I Recovery

†Yield based on 590 MeV data.

Strontium-82 --- is produced by spallation processes in molybdenum targets and can be recovered with a 94% chemical yield (6). To date, four thick targets have been remotely processed, and more than 50 mCi of ^{82}Sr has been distributed to collaborating medical teams for pre-clinical testing.

Iodine-123 --- High-purity ^{123}I is recovered from the decay of 2.1-h ^{123}Xe, which is formed by spallation reactions in lanthanum targets. Following irradiation, the target is placed in a vacuum furnace coupled to a 100-kw motor generator, brought to 1400°C in about 30 seconds, and the radioxenon removed by cryopumping. Greater than 98% of the xenon is recovered in about 15 minutes (7,8).

Xenon-127 --- is also made by bombarding La targets with medium-energy protons and recovered as an extension of the ^{123}I procedure described above (7,8). After decay of ^{123}Xe for ^{123}I recovery, the radioxenon is cryopumped to a second cold trap for subsequent decay of 17-h ^{125}Xe and recovery of 60-d ^{125}I. Following this, the xenon is transferred to a third trap and ^{127}Xe recovered.

Hafnium-172 --- The long-lived (1.87 y) parent of a Hf-Lu generator system, ^{172}Hf is produced in a Ta target and subsequently recovered with a 93% radiochemical yield. Other heavy rare earth elements (such as ^{169}Yb and ^{167}Tm) have demonstrated clinical value in nuclear medicine, but are costly to prepare. We are of the opinion that the availability of 6.7-d ^{172}Lu via a long lived generator would stimulate more extensive compound labeling research and preclinical testing of heavy rare earths. ^{172}Lu is not suitable for clinical applications.

Radionuclide Generator Development

For several years now, we have been collaborating principally with Y. Yano of the Donner Laboratory and B. Hoop of Massachusetts General Hospital in Sr-Rb generator research, investigating separations based on the Bio-Rex 70 cation exchanger and Chelex-100 chelating resin (9,10,11). Difficulties have been experienced with both systems, but we believe that deficiencies can largely be overcome with further study. Yano has recently shown excellent Sr-Rb separations with the Bio-Rex 70/2% saline system (11), although Hoop had experienced significant Sr breakthrough with a similar system (10). Recent studies at our laboratory indicate that the Chelex 100/0.1 M NH_4OH-0.1 M NH_4Cl (pH = 9.2) system requires the addition of a small amount of

stable Sr for a maximum Sr-Rb separation factor, and present studies are aimed at determining the optimum loading.

In addition, we have noted small but significant Sr leakage during initial column loading operations. However, the leakage is minimized following washing the column with several hundred milliliters of the eluant.

At this point we can only say that not all of the answers are in hand to permit a definitive decision as to which system is superior.

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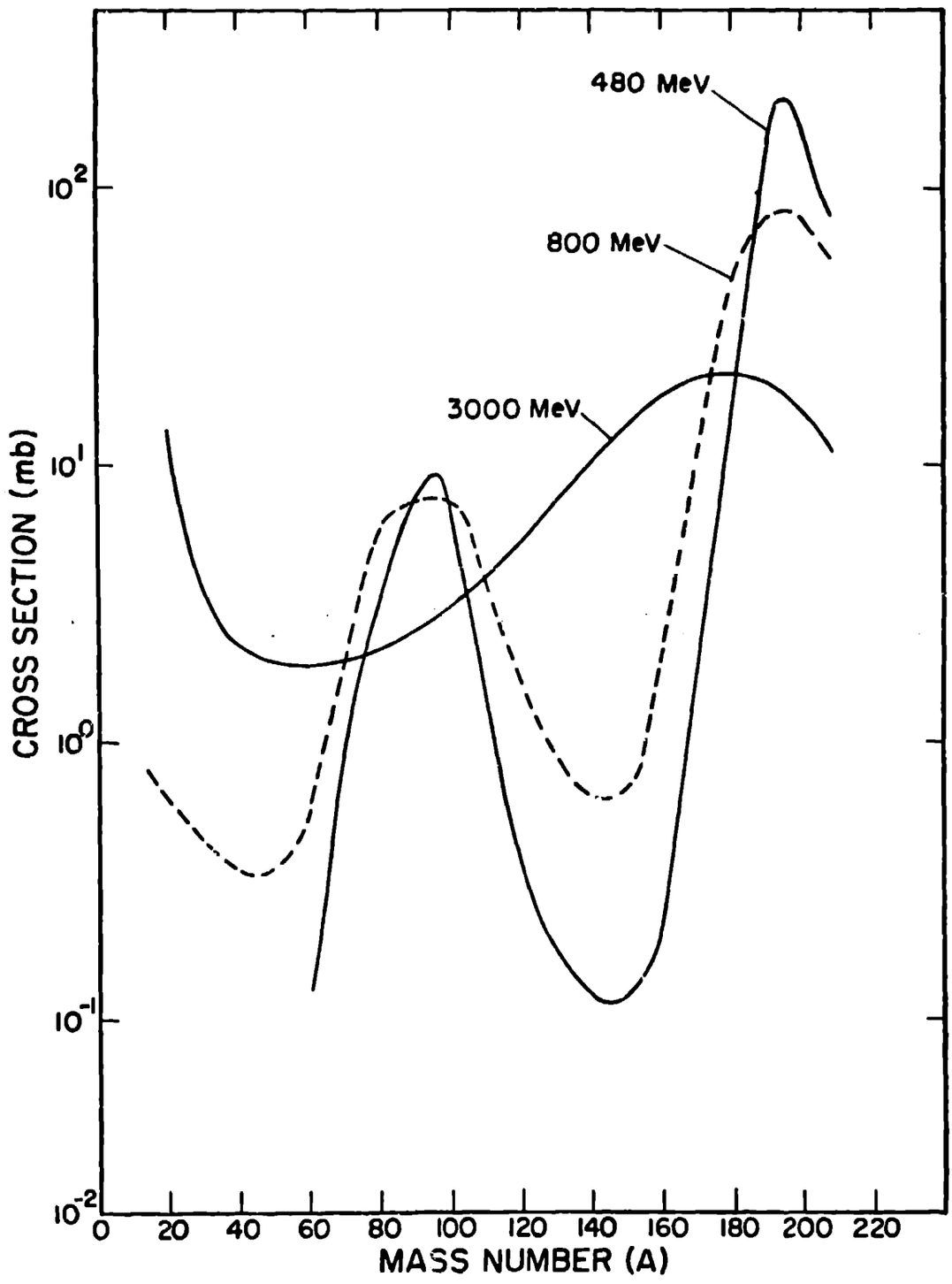
Figure Captions

Figure 1. Approximate Cross Sections for Formation of Product Mass Numbers from the Reactions of 480-, 800-, and 3000-MeV Protons with Bismuth.

Figure 2. Selected Radionuclide Product Yields from the Reaction of 590-MeV Protons with Vanadium.


480 MeV
800 MeV
3000 MeV
CROSS SECTION (mb)
10^2
10^1
10^0
10^{-1}
10^{-2}
0
20
40
60
80
100
120
140
160
180
200
220
MASS NUMBER (A)

Vanadium Thin Target Cross Sections for 590 MeV Protons

Nuclide		Cross Section (mb)	Yield
27.8d	^{51}Cr	2.0 ± 0.8	I
23h	^{48}Cr	0.55 ± 0.25	C
16.1d	^{48}V	12 ± 2	C
1.84d	^{48}Sc	4.4 ± 1.3	I
3.44d	^{47}Sc	14 ± 3	C
83.9d	^{46}Sc	21 ± 4	I
2.44d	^{44m}Sc	8.4 ± 2.5	I
3.92h	^{44}Sc	9.6 ± 3.0	I
3.92h	^{43}Sc	4.0 ± 2.0	C
22.4h	^{43}K	3.8 ± 0.8	C
12.4h	^{42}K	8.9 ± 2.7	I
1.83	^{41}Ar	1.9 ± 1.0	C
21.2h	^{28}Mg	0.17 ± 0.09	I
15h	^{24}Na	0.96 ± 0.3	C
2.602y	^{22}Na	0.62 ± 0.25	C
53.3d	^{7}Be	1.5 ± 0.3	C