NUCLEAR MEDICINE USES OF TRIUMF

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ABSTRACT

The operation of the TRIUMF Cyclotron affords those interested in using medically useful radioisotopes the possibility of producing neutron deficient radionuclides with the high energy proton beam and also permits the production of neutron rich radionuclides from the high neutron flux in the beam dump. The clinical use of radionuclides produced at the TRIUMF facility must be evaluated in terms of cost versus benefit.

The presence of a high energy particle accelerator at TRIUMF presents an excellent opportunity for potential medical users of radioisotopes to investigate a relatively little explored area of the rapidly growing field of diagnostic nuclear medicine. For the most part, reactor produced radionuclides are the only materials available to the medical user and in most cases the physical and biological properties of these have been well investigated. Iodine-131 for example has been available in abundance since just after World War II. In any event, the day to day operations of a nuclear medicine diagnostic facility requires only a few radionuclides; less than a half-dozen are used for over 95% of all procedures. Since the introduction of the Mo-99 - Tc-99m generator by Richard's group at the Brookhaven National laboratory, many institutions have been able to produce radiodiagnostic scanning agents at their own facility. In 1962, Harper, et al[1] reported their initial observations on the use of Tc-99m as a tracer in medicine and biology. During the last 10 years, extensive laboratory and clinical investigations have demonstrated the usefulness of this short-lived radionuclide. In fact, most departments doing scanning and organ imaging could operate very well with this nuclide alone. Little in the way of new radionuclides for organ imaging purposes has occurred since the introduction and widespread use of technetium 99m and in many ways the ideal characteristics of technetium have delayed investigation of the medical utility of other radionuclides especially the neutron deficient nuclides. For example, technetium as pertechnetate is the most widely used agent for brain tumor detection: as the sulfur colloid, the most widely used liver and spleen imaging agent; as macroaggregates of albumin or albumin micropheres it is probably the best lung perfusion scanning agent. Technetium promises to be extremely useful now in bone tumor detection and localization as the polyphosphate, since bone scanning has been one of the most underutilized diagnostic procedures because of the lack of a suitable inexpensive radioactive bone seeking element or compound. Technetium can be used to replace I-131 iodide for thyroid uptakes and thyroid scans. The aforementioned procedures represent perhaps 90% of the routine in vivo uses of radionuclides, and are summarized in Table I.

TABLE I CLINICAL CAPABILITIES OF TECHNETIUM-99m AND INDIUM-113m

RADIONUCLIDE FORM		ORGAN LOCALIZATION
^{99m}Tc	^{113m}In	
$^{99m}TcO_4^-$	^{113m}In-CHELATE	BRAIN(STOMACH-TcO_4^-)
^{99m}Tc-S COLLOID	^{113m}In-COLLOID,pH 7.5	LIVER, SPLEEN, BONE MARROW
^{99m}Tc-ALBUMIN	^{113m}In-STABILIZED,pH 3.5	HEART, PLACENTA
^{99m}Tc-MAA	^{113m}In-Fe $(OH)_3$	LUNGS
^{99m}Tc-Fe COMPLEX or ^{99m}Tc-DTPA	^{113m}In-CHELATES	KIDNEYS
^{99m}Tc-LABELED RBC (ALTERED)		SPLEEN
^{99m}Tc-POLYPHOSPHATE		BONE

It is not surprising that so much effort has gone into the testing and production of technetium compounds when one considers that generator produced Tc-99m from molybdenum-99 has a half-life of 5.9 hours, monoenergetic gamma photon of 140 KeV, no associated beta radiation (with resulting low patient absorbed doses), high information flux rates and a multiplicity of valence states. Instrumentation has, in many cases, been designed with this nuclide in mind; the gamma camera, for example, seems best suited for gamma radiation in the region of 100-300 KeV.

Neutron deficient radioisotopes tend to decay by positron emission. Casual inspection might suggest this rules out their medical utility. However by making use of the 180°, 511 KeV annihilation radiation the site of decay may be precisely determined and background noise markedly reduced by co-incidence circuitry.

The possibility of using the proton waste beam from a high energy accelerator for the production of predominantly neutron-deficient species opens up a new area for investigation for researchers interested in short-lived materials. By means of the high energy spallation reaction sizeable quantities (mCi) of neutron-deficient species can be made. This reaction is the most convenient for producing neutron-deficient isotopes. With the proton beam planned for TRIUMF, large quantities of almost any neutron-deficient species can be made and can be obtained carrier-free with very high specific activities. Some radionuclides of medical interest which may be produced at TRIUMF include ^{127}Xe, ^{123}I, ^{52}Fe, ^{67}Ca, ^{129}Cs, ^{111}In, ^{82}Br, ^{179}Ta, ^{128}Ba, ^{97m}Tc, ^{11}C, ^{13}N, ^{15}O, ^{18}F, ^{57}Co. In the case of the very short-lived ^{13}N and ^{15}O, some patient handling facilities at the production site would be justified if significant clinical utility could be shown for these isotopes.

Short-lived medically useful radionuclides have been available to a large number of users only in the form of parent-daughter generator systems. These are summarized in Table II.

It is relatively easy to look at a chart of the nuclides and decide, based on physical properties alone, which nuclides might be diagnostically useful. The following characteristics should be considered:

a. An appropriate half-life, not so short that the manufacture of labelled compounds is too difficult but not so long that patient radiation doses or contamination are a problem. A half-life of somewhere between 2 hours and 2 days might be reasonable for local use only.

b. Gamma radiation of an energy greater than 100 KeV (because tissue attenuation is too great below that value) but less than 350 KeV because shielding and collimation are a problem beyond 350KeV. There should be a high yield of externally detectable radiations per disintegration but there should not be any associated alpha or beta radiation because of the resulting high patient radiation doses.

c. The radioactive element should be able to exist in a variety of valence states making possible a multitude of labelled compounds each with different biological properties for different diagnostic purposes.

d. Readily and cheaply available in the required specific activities and radiochemical purity.

Chemical toxicity may be of little or no significance since patient doses may be of the order of 10^{-12}gms, amounts undetectable by

TABLE II COMMERCIALLY AVAILABLE RADIONUCLIDE GENERATORS

PARENT/DAUGHTER	$T_{\frac{1}{2}}$	GAMMA ENERGY MeV	ABSORBANT	RADIOCHEMICAL PURITY	PRODUCTION
$^{68}Ge/^{68}Ga$	280da/68 min	0.510	ALUMINA (70%)	99.99 + %	CYCLOTRON
$^{132}Te/^{132}I$	77hr/2.3hr	0.53–2.3	ALUMINA (70%)	99 + % (up to 0.3% I-131)	REACTOR
$^{87}Y/^{87m}Sr$	80hr/2.8hr	0.390	DOWEX 1 (70%)	99.9 + %	CYCLOTRON
$^{99}Mo/^{99m}Tc$	67hr/6 hr	0.140	ALUMINA (75–85%)	99.99 %	REACTOR
$^{113}Sn/^{113m}In$	118da/1.7hr	0.390	ZIRCONIUM OXIDE (80–95%)	99.9 + %	REACTOR

usual chemical means. With short physical half-lives, biologic half-lives may be of slight importance in considering patient radiation dose.

The cardinal point to consider in all of the foregoing is that not enough biological research has been done with short-lived neutron deficient species and the existence of a high energy waste beam at TRIUMF offers the possibility of a greater choice of medically useful radionuclides to local users, at least. We believe that significant advances in nuclear medicine must come in the form of improved radio-pharmaceuticals. These will take the form of improvements in the physical and biological properties of new labelled compounds. We do not yet have labelled compounds which are suitable for imaging of organ systems such as the parathyroid glands, the adrenals, the pancreas, ovaries etc. nor do we have tumor specific tumor localizing agents. It is in this area we believe that significant advances will occur, permitting detection of malignant changes earlier and more accurately than by currently available non-isotopic methods. Compounds with known biochemical properties for organ or tumor specificity may have certain constituent elements activated by protons or neutrons and administered without further processing.

The thermal neutron flux of 10^{13}n/cm^2/sec in the beam dump may be used for production of radionuclides or for activation analysis of biomedical materials. Little utility is anticipated for the former considering the low cost of the few useful reactor produced nuclides now available commercially. Activation analysis, however, may have sufficient value to be considered as a part of the total nuclear medicine diagnostic capability in this locality. The medical applications of this non-destructive analytical technique have not been fully explored but activation analysis of human tissue and fluids may reveal concentrations of trace elements which are different in health and disease[2]. While it is true that atomic absorption spectrometry may be more sensitive for some elements than activation analysis (given fixed flux of 10^{13}), several elements may be simultaneously determined in the latter technique.

In summary then, it would appear that TRIUMF would offer a Nuclear Medicine facility the following possibilities.

a. A proton beam of sufficient microamperage and energy for neutron deficient radioisotope production on a relatively large scale.

b. A high fast neutron and thermal neutron flux in the beam dump for production of neutron rich radionuclide production and for activation analysis of biomedical materials.

In the final analysis, however, any routine application of TRIUMF produced radionuclides must offer a significant benefit to patient or clinician in terms of reduced patient radiation dose, enhanced diagnostic capability or more efficient methodology. The health care decision makers of this province must weigh marginal diagnostic improvements against cost and our nuclear medicine group must, as other groups, be aware of cost versus benefit in considering new medical radionuclides.

REFERENCES

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