

CARDIOVASCULAR RADIATION THERAPY

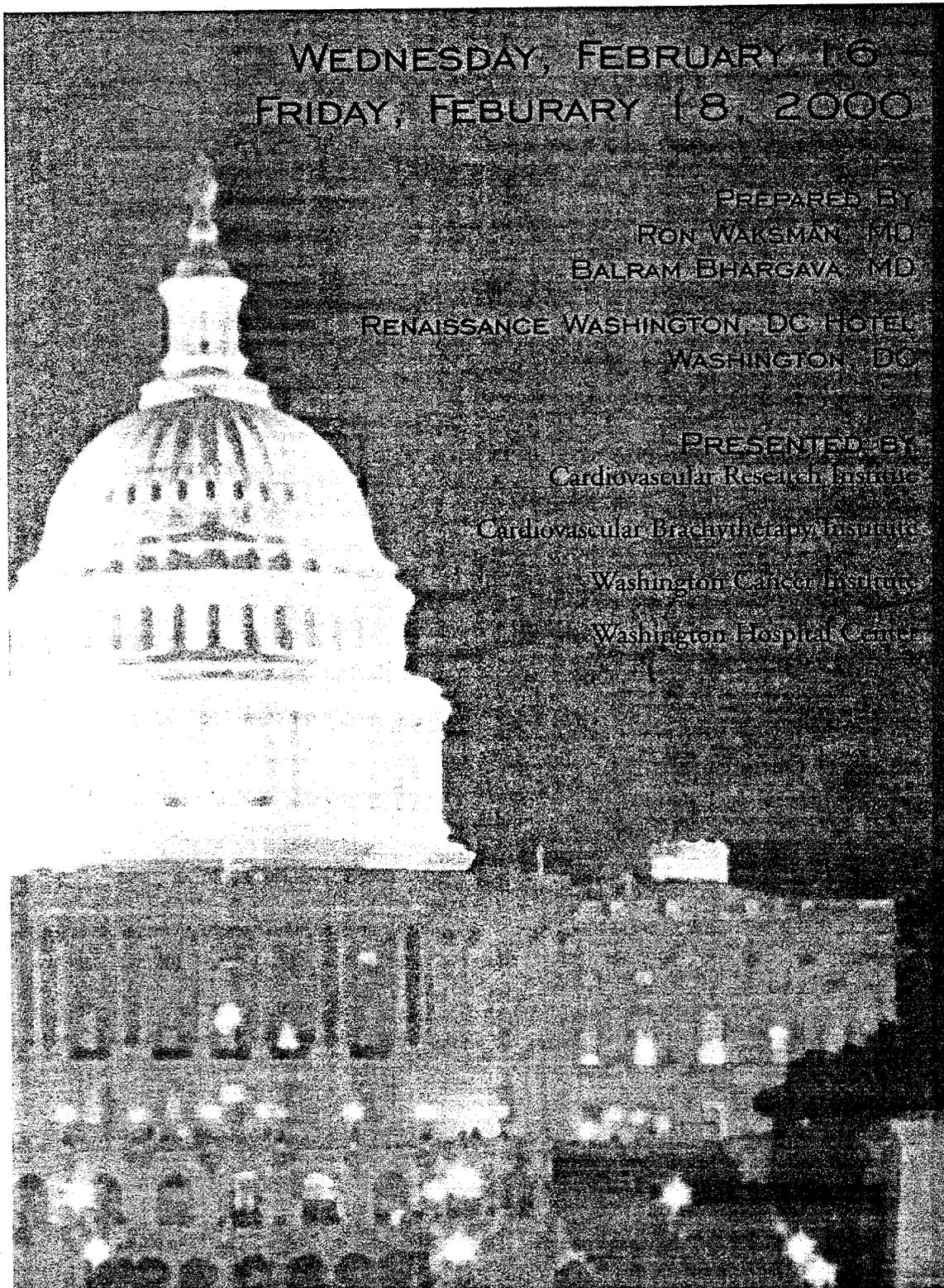
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PRODUCTION AND AVAILABILITY OF BETA-EMITTING RADIOISOTOPES FOR RESTENOSIS THERAPY

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Introduction

The reliable availability of beta-emitting radioisotopes at reasonable costs is an important issue for the expected widespread application of intravascular radiation therapy for the prevention of arterial restenosis. This paper briefly summarizes the issues associated with the reactor-production of beta-emitting radioisotopes of interest for vascular radiation therapy.

Production of Beta-Emitting Radioisotopes

Radioisotopes are produced by essentially three routes, involving irradiation of target materials in an accelerator or nuclear reactor, or via fission of uranium in a nuclear reactor. Generally, most simple production pathways in an accelerator involve the production of "proton-rich" radioactive nuclei, which decay by positron emission and/or electron capture, which decreases the proton/neutron ratio. Since production of radioisotopes in a nuclear reactor generally involves neutron irradiation of target materials with subsequent capture of a neutron by the target nucleus, reactor-produced radioisotopes are thus usually "neutron-rich," and the unstable radioactive nucleus decays so as to increase the proton/neutron ratio. Very often, this decay process involves beta-decay, with the emission of a beta-particle. Thus, most beta-emitting radioisotopes are reactor-produced (Table 1).

Importance of Reactor Neutron Flux for Radioisotope Production - While power reactors are categorized by the total power (Megawatts), the neutron flux, which is defined as the neutrons per unit area per unit time (neutrons/cm²/sec), is usually used to categorize research reactors. Since the neutron flux is the determining factor affecting the reactor production of a radioisotope, higher production specific activity yields (Ci/mg, or μ Ci/mg) are generally obtained at higher fluxes. In general, beta-emitting radioisotopes are "neutron-rich" and are thus produced in a nuclear reactor by neutron irradiation of targets placed in the reactor for specified time intervals. The production of beta-emitting radioisotopes thus requires the availability of target materials, which are often specific stable isotopes enriched from naturally-occurring isotopic mixtures. While holmium-165 is the only stable isotope of holmium in nature which is required for production of holmium-166, rhenium-185 is required for the production of rhenium-186, but occurs in only 37.4% natural abundance in nature, thus requiring enrichment to levels exceeding 97%.

While the production of rhenium-186 and holmium-166, for example, involves a simple neutron capture process on rhenium-185 and holmium-165, respectively, the production of some other beta-emitting radioisotopes of current interest is more complex. While strontium-90, the parent of yttrium-90, is isolated from multiple radioactive products produced from uranium fission, tungsten-188, the parent from which carrier-free rhenium-188 is obtained, is reactor-produced (1-2). Since the tungsten-188 is reactor-produced by a double neutron

TABLE 1.

Examples of Reactor-Produced Beta-Emitting Radioisotopes Under Evaluation for Vascular Radiation Therapy *

Half-Life/Maximum Energy	Target Material	Nuclear Reaction	Comment
Holmium-166 26.8 Hours/1.85 MeV	Natural Ho-165	Ho-165(n, γ)Ho-166	High production yields - half-life permits distribution
Phosphorus-32 14.3 Days/1.71 MeV	P-31 or S-32	P-31(n, γ)P-32 S-32(n,p)P-32	Good half-life and beta energy for linear sources
Rhenium-186 90 Hours/1.08McV	Enriched Re-185	Re-185(n, γ)Re-186	High production yields and good half-life for distribution
Rhenium-188 16.9 Hours-2.12 MeV	Enriched Re-187 or decay of W-188	Re-187(n, γ)Re-188	High production yields but short half-life for distribution
Strontium-90 52 years/2.3 MeV (i.e. Decays to Y-90 Daughter)	Uranium	U-235(Fission) Sr-90 γ -90	Isolated from multiple fission products
Tungsten-188 69 Days-2.12 MeV (i.e. Decays to Re-188 Daughter)	Enriched W-186	W-186(n, γ)W-187 (n, γ)W-188 Re-188	W-188 solid source or Re-188 liquid source from W-188/Re-188 generator
Yttrium-90 72 Hours-2.3 MeV	Enriched Y-89	Y-89(n, γ)Y-90	Y-90 wire source

* Nuclear Data taken from "Radioactive Decay Tables," D. C. Kacner, 1981 (DOE-TIC-11026), Technical Information Center, U.S. Department of Energy.

capture using enriched tungsten-186 targets, the production yield is a function of the square of the reactor flux. Thus, doubling of the flux increases the yield by a factor of four. For this reason, very high neutron fluxes are required to produce tungsten-188 (vide infra).

Reactors Available for Production of Beta-emitting Radioisotopes

There are about 295 operating research reactors operating in the world, many of which are used for medical radioisotope production. Generally, power reactors are not designed and do not have the neutron flux or facilities required for production of radioisotopes for medical applications, but in some cases where high thermal neutron flux is not required and irradiation facilities are available, radioactive sources can be produced in some of these reactors. An important distinction between nuclear reactors and accelerators is that accelerators are often operated commercially or by universities. In contrast, because of the extremely high capital and operating costs, regulatory requirements and possible use of highly enriched uranium, principle research reactors in the U.S. which are used for medical radioisotope production are owned and operated by the U.S. government at the national laboratories, or operated at universities. The principal reactors currently used for medical radioisotope production in the U.S. are located at two sites operated by the U.S. Department of Energy at Oak Ridge, Tennessee (High Flux Isotope Reactor, *HFIR*) and in Utah (Advanced Test Reactor, *ATR*), and by a university in Columbia, Missouri (Missouri University Research Reactor, *MURR*). While no privately owned reactors are operating for radioisotope production in the U.S., a commercial reactor is operated by MDS Nordion in Chalk River, Canada.

Use of Radionuclide Generators to Provide Beta-Emitting Radioisotopes

In some cases, the radioisotope of interest can also be obtained by use of a radionuclide generator system, where the daughter radioisotope of interest is formed by radioactive decay of the reactor- or accelerator-produced parent. Radioactive generator systems represent convenient in-house production systems, since the generators can be installed in a radiopharmacy and the daughter eluted as required. Two generator systems of current interest for vascular radiation therapy are the strontium-90/yttrium-90 pair and the tungsten-188/rhenium-188 generator system, which provide carrier-free rhenium-188 (1-3). The strontium-90/yttrium-90 system can be used as a "in vivo" generator where the long-lived strontium-90 parent is encapsulated. The equilibrium strontium-90/yttrium-90 pair is thus used as a continuous source of yttrium-90. In the case of the tungsten-188/rhenium-188 generator system, the reactor-produced tungsten-188 can also be used as a solid source for an "in vivo" generator. An attractive alternative, however, is to use tungsten-188 for fabrication of a chromatographic-type generator system very similar to the well known molybdenum-99/technetium-99m generator system. In this case the rhenium-188 is removed from the generator by elution with saline, concentrated, and then used for the liquid-filled balloon approach (1-3).

Summary and Conclusions

Beta-emitting radioisotopes offer many advantages for vascular radiation therapy, and with the increasing interest in the use of these radioisotopes, the availability of the required reactor production and processing facilities is important.

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