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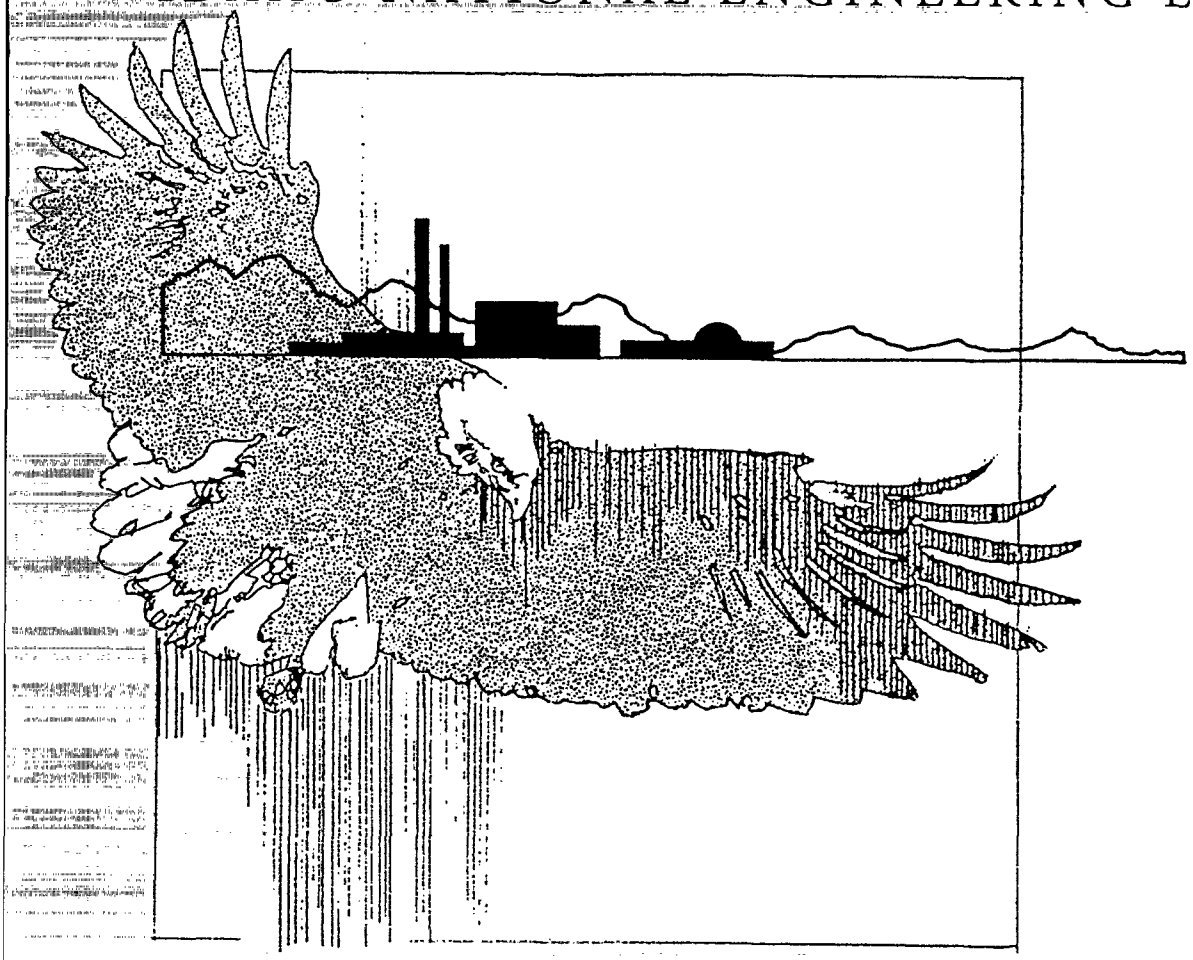

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Markets for Reactor-Produced Non-Fission Radioisotopes

Idaho National Engineering Laboratory

Lockheed Idaho Technologies Company

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Abstract

Current market segments for reactor produced radioisotopes are developed and reported from a review of current literature. Specific radioisotopes studied in this report are primarily selected from those with major medical or industrial markets, or those expected to have strongly emerging markets. Relative market sizes are indicated. Special emphasis is given to those radioisotopes that are best matched to production in high flux reactors such as the Advanced Test Reactor (ATR) at the Idaho National Engineering Laboratory or the High Flux Isotope Reactor (HFIR) at the Oak Ridge National Laboratory. A general bibliography of medical and industrial radioisotope applications, trends, and historical notes is included.

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Markets for Reactor-Produced Non-Fission Radioisotopes

Overview

This report presents the current status of applications and markets relevant to production of radioisotopes, other than fission products, in high flux nuclear reactors. Some two dozen isotopes were studied in detail and are discussed here. The criteria for their inclusion were generally that the radioisotope:

- Possess, or be predicted to grow into, a fairly large market in the U.S.
- Be a reasonably good fit for production in a high flux reactor such as the Advanced Test Reactor (ATR) or High Flux Isotope Reactor (HFIR)
- Not already have a domestic source sufficient to supply the demand.

The discussion emphasis is weighted much more strongly to those radioisotopes that are considered good candidates for production. The four radioisotopes currently produced in significant quantities at the ATR and/or HFIR (Ir-192, Co-60, Cf-252, and Ni-63) were not extensively studied since their supply and market need are already familiar. Market entry of Mo-99 or other fission product radioisotopes would present unique problems in the U.S.; these radioisotopes are omitted from this report for brevity.

The radioisotopes studied included the following:

Au-198	Cd-109	Co-58
Cu-67	Fe-55	Fe-59
Gd-153	Ho-166	I-125
Os-191	P-32	P-33
Pd-103	Po-210	Re-186
Se-75	Sm-145	Sm-153
Sn-117m	Sr-89	Tl-204
Tm-170	W-188	Yb-169

Other radioisotopes, including some fission products, appear in this report mainly for comparison or as background information

It should be noted that market conditions can change rapidly, especially for newly emerging radioisotopes, so that the relative rankings provided in this report could change markedly with time. This report provides current information in a format that may serve as a useful framework for continued study.

A useful compilation of radioisotope data is presented in Table 1 for groupings of alpha-particle, positron, and beta-particle emitters. The beta emitters are arranged in ascending order of the energy of their beta particle. Compilations of x-ray, conversion

electron (e-), and gamma-ray emitters is presented in Table 2. They are arranged in ascending order of the energy of the photon or conversion electron emitted, whichever is deemed to be the primary attribute of interest for the radioisotope in question.

Table 1. Principal Radiation of Selected α, β+, and β- Emitters.

Nuclide Parent/Daughter	Half-Life (days)	Principal Radiation	Energy* (keV)	Abundance (%)
Po-210	138.4	α	5304	100
Co-58	70.9	β+	30	15
		γ	810.8	100
Na-22	951.5	β+	195	89
Ni-63	36,562	β–	17.1	100
P-33	25.34	β–	76	100
Cu-67	2.580	β–	142	100
		γ	184.6	49
		γ	93	23
I-131	8.040	β–	182	100
		γ	364.5	81
Sm-153	1.95	β–	225	100
		γ	103.2	28
		x-ray	42	32
Tl-204	1380	β–	238	98
Tm-170	128.6	β–	315	100
Re-186	3.777	β–	323	100
		γ	137	9
Au-198	2.694	β–	406	100
		γ	411.8	96
Dy-165	0.0973	β–	442	100
		γ	95	4
Sr-89	50.55	β–	583	100
P-32	14.28	β–	695	100
Ho-166	1.117	β–	711	100
		γ	80.6	6
W-188/Re-188	69.4/17 h	β–	765 (D)	100
		γ	155 (D)	15
		β–	99	100

* Average beta decay energies are given. Symbol (D) signifies daughter radiation.

Table 2. Principal Radiation of Selected *x*-ray, *e*-, and γ-ray Emitters.

Nuclide Parent/Daughter	Half-Life (days)	Principal Radiation	Energy* (keV)	Abundance (%)
Fe-55	997.1	*x-ray*	6	16
Pd-103/Rh-103m	16.97/56 m	*x-ray*	21 (D)	42
		γ	39.8 (D)	0.07
Cd-109/Ag-109m	462/40 s	*x-ray*	22	55
		conversion e-	81 (D)	40
		γ	88 (D)	4
I-125	60.14	*conversion e-*	4	158
		conversion e-	31	11
		x-ray	27	76
		γ	35	7
Sn-117m	13.61	*conversion e-*	127	66
		γ	158.6	86
Sm-145	340	γ	61	12
		x-ray	38.7	74
		x-ray	44	21
Gd-153	241.6	*x-ray*	42	62
		γ	97.4	28
		γ	103.2	20
Yb-169	32.02	γ	63.1	44
		γ	198	35
		x-ray	51	94
Os-191/Ir-191m	15.4/5 s	γ	129.4 (D)	26
		x-ray	65 (D)	28
		β–	37.5	100
I-123	0.5504	γ	159	83
		x-ray	27.5	47
Se-75	119.8	γ	265	59
		γ	136	59
		x-ray	10	32
Ir-192	73.83	γ	468	48
		γ	316.5	83
		β–	171	95
Cs-137	10,968	γ	662	85
		β–	188	100
Fe-59	44.5	γ	1100	57
		γ	1300	43
		β–	118	100
Co-60	1,925	γ	1333	100
		γ	1173	100
		β–	96	100

* Average beta decay energies are given. Symbol (D) signifies daughter radiation.

Industrial Markets

Gauging

Industrial radioisotope gauging comprises a broad set of methods for determining the thickness, concentration, density, or weight of a product undergoing continuous production. Gauging methods can measure the total product thickness, as for sheets of film or paper, or the coating thickness on a workpiece, as in spray painting, etc. Special methods include the measurement of moisture content with neutron scattering or the simultaneous measurement of both the impurity levels and thickness of cigarette paper. Special geometries have been treated, for example, in down-hole well logging where the region measured is not planar, and in tube thickness gauging.

The radiation employed very generally includes beta particles, gamma rays, and to a lesser extent, alpha particles and neutrons. A summary of the major radioisotopes is shown in Table 3, where the entries are categorized by the type of radiation. Generally, the beta-particle emitters are the most commonly used because the range of beta particles in solids is comparable to typical sheet thicknesses. The gamma emitters are the next most commonly used.

Detection methods vary widely in industrial gauging. The most popular methods are beta transmission (for thin samples) and beta backscatter (for measuring from one side). Similar techniques are used for gamma rays, and special geometries have been developed, for example, in providing a wide beam to 'weigh' (i.e., measure the net mass flow of) the contents of a moving belt of ore or other product. Sometimes gauging detection methods are combined with analytical methods to provide simultaneous measurements of both geometry and composition, especially for laminated structures of differing atomic numbers.

In general, radioisotope gauging provides a very rapid on-line, non-destructive and non-contacting measurement. The sources can usually be chosen to give a long lifetime between changeout. Radioisotope gauging is a steady market for radioisotopes.

Table 3. Major Radioisotopes in Industrial Gauging.

Radioisotope	Relative Use	Comments
		Alpha emitters
Am-241	Moderate	Alpha particle source. Long 433 year half-life.
Po-210	Very Low	Alpha particle source. Short 4.5 month half-life.
		Beta emitters
Kr-85	High	Beta particle source with 0.67 MeV maximum energy. Moderate 10.6 year half-life. Power reactor waste by-product.
Sr-90	Moderate	Beta particle source with 2.27 MeV maximum energy of daughter, Y-90. Moderate 28 year half-life. Power reactor waste by-product.
Ni-63	Moderate	Beta particle source with very low 0.067 MeV maximum energy and no gamma rays. Long 100 year half-life.
Tl-204	Moderate	Beta particle source with 0.77 MeV maximum energy. Short 3.8 year half-life.
C-14	Low	Beta particle source with 0.159 MeV maximum energy. Long 5730 year half-life. Power reactor waste by-product.
Pm-147	Low	Beta particle source with 0.23 MeV maximum energy. Short 2.6 year half-life. Power reactor waste by-product.
Ru-106	Low	Beta particle source with 3.6 MeV maximum energy of daughter, Rh-106. Short 1.0 year half-life.
		Low energy photon emitters
Cd-109	High	Photon source with 22 keV energy. Acceptably long 1.2 year half-life.
Fe-55	High	Photon source with 6 keV energy. Moderate 2.6 year half-life.
Sr-90/Al	Moderate	Photon source with 60-150 keV bremsstrahlung energy. Long 28 year half-life.
Am-241	Moderate	Photon source with 60 keV energy. Very long 433 year half-life. Useful for steel thickness measurements to 10 mm.
H-3/Zr	Moderate	Photon source with 5-9 keV bremsstrahlung energy. Long 12.3 year half-life.
Pu-238	Low	Photon source with 12-17 keV energy. Long 86 year half-life.
Pb-210	Low	Photon source with 47 keV energy. Long 22 year half-life.
Tm-170	Low	Photon source with 84 keV energy. Short 0.35 year half-life.
Pm-147/Al	Low	Photon source with 12-45 keV bremsstrahlung energy. Moderate 2.6 year half-life.
		High energy photon emitters
Co-60	Moderate	Photon source with 1200-1300 keV energy. Long 5.3 year half-life. Useful for steel thickness measurements to 150 mm.
Cs-137	Low	Photon source with 660 keV energy. Long 30 year half-life. Useful for steel thickness measurements to 100 mm.

Radiography

Industrial radiography plays a very central role in assuring public safety by non-destructively examining welds and searching for flaws in pressure vessels, piping, bridges, airplanes, ships, etc. The major radioisotopes in radiography are summarized in Table 4. Two radioisotopes, Ir-192 and Co-60, are the leaders in gamma radiography. While Co-60 has more penetrating radiation that permits radiography of thicker sections, the sources need shielding that makes them larger and bulkier. In contrast, the lower energy gamma rays and very high specific activity of Ir-192 have allowed much more portable gamma radiography equipment to become widespread. A very significant (3:1) premium is paid per curie for Ir-192 over Co-60. Some inroads are being made into the use of these radioisotopes by compact, field deployable accelerator sources.

Table 4. Major Radioisotopes in Radiography.

Radioisotope	Relative Use	Comments
Co-60	High	High energy spectrum. Optimum thickness of steel sections is 50-150 mm, or 150-450 mm for light alloys. Source sizes up to 2,000 curies.
Ir-192	High	Moderate energy spectrum. Optimum thickness of steel sections is 12-62 mm, or 40-190 mm for light alloys. Source sizes up to 200 curies. Sources more portable than Co-60.
Yb-169	Moderate-Low	Alternative to Tm-170. Relatively short half life means sensitivity to supply, and use for one-time projects only.
Tm-170	Low	Lower energy spectrum better suited to thin sections of light alloys. Optimum thickness of steel sections is 3-13 mm, or 8-37 mm for light alloys. Source sizes up to 35,000 curies. Relatively low specific activity means very large source size.
Cs-137	Low	Alternate to Co-60 sources.
Sb-124	Very Low	Alternate to Ir-192 sources. Less favorable specific activity than Ir-192 due to lower cross sections and natural abundance.
Cf-252	Low	Source for neutron radiography used in aircraft industry. Sources are typically 1 microcurie to 1 millicurie.
Co-58	Emerging	Positron source with reasonably long half-life and specific activity. Used in positron microscope studies to examine structure and flaws in semiconductors, crystals, etc., and bonding of coatings or thin laminates.

Beyond these two major radioisotopes, a few others deserve mention. For imaging thinner sections and/or lower atomic weight materials, radioisotopes with lower energy spectra are better. These include Yb-169 and Tm-170. The market for these is small, however. The alternate radioisotopes to Co-60 and Ir-192, Cs-137 and Sb-124

respectively, do not seem to have made any inroads. For neutron radiography, Cf-252 is included in Table 4.

Product integrity and structure can also be studied with electrons and positrons. While very widespread, electron microscopy is outside the scope of this work. Positron microscopy offers a unique method that is especially sensitive to atomic defects for investigating a material, and several isotopes have been used. These are Na-22, an accelerator-produced radioisotope with a long half-life, and Co-58, a reactor-produced radioisotope with a fairly short 71 day half-life and four times less abundant positron emission. The supply and quality of Na-22 have been irregular, and research users of Na-22 are willing to make the modifications to their equipment in order to use Co-58. Overall, it is felt that Co-58 can compete with Na-22 if it can be shown that the supply is reliable.

Analytical Measurements

Radioisotope instruments have been developed for a number of chemical, elemental, or physical analyses of material samples. The major uses are x-ray fluorescence measurements, electron capture detectors, neutron activation analyses, and Mössbauer spectrometry. The first two employ reactor-produced radioisotopes. The last two employ either transuranic radioisotopes like Cf-252 or Am-241/Be, or accelerator-produced isotopes like Co-57, and are not discussed further.

X-ray fluorescence relies very generally on the ability to excite and detect characteristic x-rays of elements by exposing them to x-rays. Across the periodic table, the energies of the characteristic x-rays are very low for the light elements, and moderately high for the heavier elements. Accordingly, a range of photon sources are required, depending upon the elements one needs to detect. At the light end, Fe-55 is popular because it has a low-energy (6 keV) photon and can detect elements as light as aluminum with an atomic number of 13. In the middle range, Cd-109 is popular as a 22 keV source that detects elements with atomic numbers from 26 to 42 and from 60 to 90. These and other radioisotopes are presented in the summary in Table 5. Source sizes required range from 1 millicurie to 1 curie. Aside from the energy of the photon emitted, other considerations are important in instrument design, such as having a high specific activity to reduce the source size and self-shielding. Generally a specific activity of 2-5 curies per gram of Cd-109 is considered adequate for x-ray fluorescence equipment. This is considerably lower than the 100 curies per gram required for a medical Ag-109m generator, stemming from a limit on toxic cadmium breakthrough.

Electron capture detectors exploit the electron affinity of various compounds such as poisons, explosives, insecticides, and other hazards. The radioisotope is simply a constant source of electrons providing a steady leakage current. As the compound absorbs electrons and interrupts the current, it is detected. The sensitivity of electron capture detectors is enormous. The isotope of choice is Ni-63 with a source size of about 10 millicuries, with some usage of H-3, Fe-55 and others as well. Fe-55 can be produced in a relatively small cyclotron, while reactor production is dependent upon a scarce and expensive supply of Fe-54.

Table 5. Major Radioisotopes in Analytical Measurements.

Radioisotope	Relative Use	Comments
Fe-55	Moderate	Photon source with 6 keV energy. Moderate 2.6 year half-life. Excites K x-rays of Al-Cr and L x-rays of Br-Xe.
Pu-238	Low	Photon source with 12-17 keV energy. Long 86 year half-life. Excites K x-rays of Mn-Y and L x-rays of Eu-Bi.
Cd-109	Moderate	Photon source with 22 keV energy. Acceptable 1.2 year half-life. Excites K x-rays of Fe-Mo and L x-rays of Nd-Th.
Am-241	Moderate	Photon source with 60 keV energy. Very long 433 year half-life. Excites K x-rays of I-Lu. As a neutron source, typically 1 to 100 curies of Am-241 are combined with a Be converter.
Co-57	Low	Photon source with 122 and 136 keV energy. Short 0.7 year half-life. Accelerator produced radioisotope. Excites K x-rays of Hg-U. Important Mössbauer effect source.
Gd-153	Low-Moderate	Photon source with 42 keV x-ray spectrum and several 100 keV gamma rays. Relatively short 0.66 year half-life. Excites x-rays of heavier elements up to Fr.
Ni-63	Moderate	Pure beta emitter with 67 keV maximum energy and long 100 year half-life. Very desirable for electron capture detectors.
Tl-204	Moderate	Pure beta emitter with 770 keV maximum energy and moderate 3.8 year half-life.

Radiation Processing

Radiation processing applications are almost the exclusive domain of large Co-60 sources. Major radioisotopes in radiation processing are shown in Table 6. The two dominant applications are medical product sterilization and food irradiation. Inroads are being made on the dominance of Co-60 by electron accelerators. The use of Cs-137 sources is small in this application, probably because incidents with leakage from Cs-137 sources have led to their reputation as a risky technology.

A minor market in radiation processing exists for anti-static treatment. Typically, a large alpha-emitting source is plated on a long surface and placed next to a continuous rolling paper or plastic sheet to discharge the static electricity built up in processing.

Table 6. Major Radioisotopes in Radiation Processing.

Radioisotope	Relative Use	Comments
Co-60	Very High	High energy spectrum. Source sizes in the range of 0.1-4 million curies. Source replacement needed every 2-3 years due to 5.3 year half-life.
Cs-137	Low	Alternate to Co-60 sources. Source replacement only needed every 10-15 years due to 30 year half-life.
Po-210	Low	Alpha emitter used to control static electricity buildup in paper and plastics processing.

There are now about 150 gamma-ray irradiation facilities for radiation sterilization of medical products used in over 40 countries. Their collective source strength is about 125 million curies of Co-60. There are only about 20 electron accelerators employed in the same application. Electron accelerators with energies of about 5-10 MeV and throughput of 5-150 kW are used for sterilization. At 10 MeV, essentially 100% of all disposable medical products can potentially be sterilized, so there is no need to achieve higher energies, just higher throughput.

There are now about 30 commercial food irradiation plants in 25 countries. Projections are for growth to 80 plants in 40 countries by the late 1990s. Most plants are capable of handling both medical products and food. When applied to food irradiation, electron accelerators are usually only effective on thin layers of food; Co-60 sources are used for bulk food products packaged in boxes. Some accelerators use high atomic number converter plates to generate bremsstrahlung x-rays, but the conversion efficiency is not very favorable (being only about 5% for 5 MeV electrons). There is an upper 5 MeV limit to the energy of radiation permitted in food irradiation. This is due to the photoneutron threshold reactions in hydrogen, oxygen, and carbon which begin to appreciably activate the food above this energy.

Foods currently approved for irradiation in the U.S. include flour, fruit, potatoes, poultry, spices, vegetable seasonings, and wheat. The doses required for food irradiation are generally much less than those required for medical product sterilization.

Both Co-60 and electron beam sources have been applied in a number of large pilot projects for natural drinking water and wastewater sterilization. However, the cost has

not generally compared favorably to alternative chemical treatments. Electron beams are under investigation for treatment of flue gases to convert NO_x products radiolytically, and this application seems promising.

Heat and Lighting Sources

Radioisotope markets for isotopic heat or power sources have generally been on the decline for the past several decades. Initially boosted by major roles in the space nuclear (especially SNAP) and artificial heart programs, the use of radioisotopes has generally subsided to two uses: Power sources for deep space missions using Pu-238, and power sources for remote military intelligence sensors using Sr-90/Y-90. In general, radioisotope power sources have suffered from poor public acceptance; questions of launch safety for Pu-238 and potential environmental contamination with Sr-90 sources have continued to retard these two applications. A summary of these and other radioisotopes extensively studied by the federal government in the past is presented in Table 7. Most of the radioisotopes are fission products available from spent fuel reprocessing. A few heat source radioisotopes with desirable qualities are reactor-produced, but these are not likely to enjoy a great demand over the fission product isotopes.

Radioisotope markets for lighting sources have not grown as quickly as predicted, having suffered from a widely publicized incident in 1979 involving a chronic tritium release from an industrial manufacturer of lighting sources. A summary of the major radioisotopes for lighting is found in Table 7. The radioisotopes are divided into two major categories: Those emitting beta particles that directly activate phosphors, and those used in low voltage lamps. The first type are fully self-powered lights—a typical example is the tritium-powered runway safety lighting at airfields. The second type affords cheap, low-power lamps—a typical example is the ubiquitous krypton-excited 'power-on' lamp in consumer products. Undoubtedly the direct evidence of public safety and convenience have had much to do with continued public acceptance of radioisotopes in lighting applications. Although Kr-85 has been supplied in fairly large quantities from spent fuel operations at Hanford (1500 curies per year at $120 per curie), that supply was shut down several years ago. Sales of H-3 from DOE were stopped several years ago in response to growing sensitivity to the lack of a major tritium supply for the U.S. nuclear arsenal, although the sales amounted to only a fraction of the projected needs. Sales by the DOE prior to this were about 250,000 curies per year at $3 per curie.

Table 7. Major Radioisotopes for Isotopic Heat and Lighting Sources.

Radioisotope	Relative Use	Comments
		Heat and Power Sources
Pu-238	High	Transuranic isotope power source. Long half-life of 87.4 years, moderate specific power of 0.56 watts/g, and low shielding requirements (if kept free of impurities) are optimally suited for deep space missions. Difficult to produce.
Sr-90/Y-90	Moderate	Fission product isotope power source. High energy of beta particles requires massive shielding, especially hindering the design of smaller units. Long 28 year half-life, and has a high specific activity of 0.96 watts/g.
Pm-147	Low	Only fission product that can be a lightly shielded isotope power source. Good specific power of 0.333 watt/g. Moderate 2.6 year half-life.
Tm-170	Low	Non-fission product isotope power source. Short 4.3 month half-life, but high specific power of 3 watts/g.
Po-210	Very Low	Non-fission product isotope power source. Short 4.5 month half-life, but extremely high specific power of 144 watts/g. Difficult to produce due to low radiative capture cross section.
Tm-171	Very Low	Proposed isotope power source, especially for artificial hearts. Very difficult to produce due to need for double neutron capture. Moderate 1.9 year half-life, and reasonable specific activity of 0.2 watts/g. Very little shielding required.
		Lighting - Phosphor activation
Kr-85	High	Beta particle source with 670 keV maximum energy. Moderate 10.6 year half-life. Power reactor waste by-product. Specific power of 0.6 watts/g.
H-3	High	Beta particle source with 19 keV maximum energy. Long 12.3 year half-life. Specific power of 0.33 watts/g.
Pm-147	Low	Beta particle source with 230 keV maximum energy. Short 2.6 year half-life. Power reactor waste by-product. Specific power of 0.34 watts/g.
		Lighting - Gas ionization
Kr-85	High	Beta particle source with 670 keV maximum energy. Moderate 10.6 year half-life. Power reactor waste by-product. Specific power of 0.6 watts/g.
H-3	High	Beta particle source with 19 keV maximum energy. Long 12.3 year half-life. Specific power of 0.33 watts/g.
Am-241	Moderate	Alpha particle source with 5.5 MeV energy and very long 433 year half-life. Specific power of 0.1 watts/g. Photon source with 60 keV energy.

Alarm Sensing

Alarm sensing has historically been a fairly straightforward application of radioisotopes and sensors to determine conditions such as high or low setpoint levels in fluid-filled tanks, etc. It is felt that this application is largely in decline, since radioisotopes offer little advantage over increasingly robust, inexpensive electromechanical sensors. Applications typically utilized gamma emitters that could penetrate steel-walled vessels.

One particular application in alarm sensing, ionization smoke detectors, has grown very fast in recent decades. Small units typically employ a few microcuries of Am-241 or other transuranic alpha-emitters, and have been sold in the hundreds of millions. Here again, their benefits to public safety have led to high public acceptance.

Radioisotope Tracers

Many stable and radioisotope tracers have been produced over the years, especially for environmental and plant biology studies. Literally hundreds of isotopes have been used, and dozens are still popular to some degree. Almost 30 radioisotopes were listed in a comprehensive 1984 monograph: Stable isotopes included B-10, N-14, N-15, Mg-26, K-41, Cu-65, and radioactive isotopes included N-13, Mg-28, P-32, P-33, S-35, Cl-36, K-40, K-42, K-43, Ca-45, Mn-54, Fe-59, Cu-64, Cu-67, Zn-65, Rb-86, Sr-85, Sr-89, Mo-99, Cs-134, and Cs-137. The 1984 prices for most of them were between $50 and $200 per millicurie. The only exception was Cl-36, quoted at $1000 per millicurie. While high flux reactors could produce virtually any of them, the quantities required are typically quite small. However, some of these such as P-32, P-33, Cu-67, Sr-89, and Cs-137 are required in much greater quantities for medical uses. Tracer uses of these radioisotopes could be supplied by small increases in production by medical radioisotope manufacturers.

Radioisotope tracers were explored extensively several decades ago for diverse industrial applications, including flow measurement with Na-24, Br-82, H-3, Ar-41, Kr-85, and Xe-133. Other related studies included leak detection, stirred reactor mixing, residence times in chemical processes, and line plugging detection. It is believed that these uses are also in decline, with the increasing performance offered by alternative flow metering and scale-model visualization techniques.

Medical Markets

Brachytherapy and External Beam Therapy

Brachytherapy is the practice of inserting small sealed sources of radioisotopes, typically called seeds, in or near a cancerous tumor for treatment. A summary of major radioisotopes for brachytherapy appears in Table 8. For a number of reasons discussed in the table, I-125 has become the most popular source for brachytherapy seeds.

Usually a number of seeds are implanted to achieve a relatively uniform dose to the tumor. The practice of surgically emplacing catheters or applicators near a tumor for source loading after the surgery is called "remote afterloading." Ir-192 has become a very popular radioisotope for remote afterloader systems, although Cs-137 and Co-60 are also used. High dose rate afterloaders utilize a 10 curie source, and low dose rate afterloaders utilize a 1 curie or smaller source. Remote afterloading represented a major improvement in brachytherapy because trial dosimetry can be established before treatment, and the occupational exposure to medical workers is almost completely eliminated. High dose rate afterloaders allow rapid treatment, often on an outpatient basis, yet cost upwards of $300,000 for the equipment. There is, however, some controversy that high dose rate afterloaders are not as effective as low dose rate afterloaders.

External beam therapy employs a variety of clinical radiation generators, including x-ray tubes, linear accelerators, heavy particle beams, and devices using radionuclide sources. It is beyond the scope of this report to describe the great variety of generators. Radionuclide gamma-ray sources have used Ra-226, Cs-137, and Co-60, with Co-60 being by far the most commonly used radioisotope. A specific activity greater than about 200 curies per gram is routinely needed for medical Co-60 sources.

Table 9. Major Radioisotopes in Brachytherapy.

Radioisotope	Relative Use	Comments
I-125	High	Very low energy spectrum. Good Ra-226 substitute for delivering a localized dose. Longer-lived than Au-198, and has lower shielding requirement. Relatively complex dosimetry required. Sources are fairly anisotropic.
Ir-192	High	Moderate energy spectrum. Good Ra-226 substitute for delivering a moderately localized dose. Lower average energy spectrum than Cs-137 or Co-60 reduces shielding required. Adequate half-life. Commonly used in remote afterloader systems.
Cs-137	High	High energy spectrum. Good Ra-226 substitute for delivering a non-localized dose. Clinical source life of about 7 years.
Au-198	Moderate	Was a good Ra-226 substitute. Largely replaced by longer-lived I-125 sources.
Pd-103	Moderate	Low energy spectrum. High dose rate alternative to I-125. Less anisotropy of sources than I-125.
Co-60	Rarely used	Was a good Ra-226 substitute. Available with higher specific activity, but more expensive than Cs-137.
Ra-226	Rarely used	Great historical significance because it occurs in nature and was the first brachytherapy agent. Constant low-level emissions of daughters were found to be themselves carcinogenic. Radon hazard. Use largely discontinued.
Sm-145	Proposed	Photon Activation Therapy (PAT) agent. Also suggested as a replacement for I-125.

Diagnostic Imaging

Medical diagnostic imaging is certainly the paramount application of medical radioisotopes in terms of prestige and revenues. In the U.S. alone, over 36,000 nuclear medicine diagnostic procedures are performed each day. Of course, the dominant radioisotope is Tc-99m produced from Mo-99 in commercial radioisotope generators, with yearly domestic revenues of $35M for the bulk Mo-99 itself. The other big revenue isotopes are largely cyclotron-produced, consisting of Tl-201 and I-123, and F-18 for positron emission tomography.

Other radioisotopes in diagnostic imaging are relatively minor and are summarized in Table 9. The emerging isotopes, both Cd-109 and Os-191, are difficult to produce. Cd-109 for medical applications needs to be much higher specific activity (100 curies per gram) than can be produced in high flux thermal reactors; it is typically produced in a large accelerator at great expense. Os-191 is essentially just a research isotope at this time.

Table 9. Selected Radioisotopes in Diagnostic Imaging.

Radioisotope	Relative Use	Comments
Tc-99m	Dominant	Extremely popular radioisotope. Low patient dose, optimum gamma energy, ease of preparation with radioisotope generators, and acceptably short half-life have all contributed to its success. Despite its less than ideal chemistry, many ligands have been developed with specificity for a variety of imaging modalities.
Tl-201	Very High	Popular cardiac imaging isotope produced in cyclotrons.
I-123	Very High	Popular imaging isotope produced in cyclotrons. Iodination chemistry is very well established and flexible. Has replaced I-131 for imaging due to its extremely low patient dose relative to other iodine isotopes.
F-18	High	Popular positron emission tomography (PET) imaging isotope produced in cyclotrons. Has emerged as a result of chronic shortages of enriched stable isotopes used to produce other PET radioisotopes.
Se-75	Low	Largely replaced by Tc-99m. Chemistry is very favorable (can covalently bond to ligands). Still useful in some studies of the pancreas and brain, among others.
Yb-169	Low	Useful for cisternography (imaging of the cerebrospinal fluid volumes).
Cd-109/Ag-109m	Emerging	Ultrashort half-life (40 s) useful for studies of physiologic functions with a short time scale. Also used in pediatric imaging.
Os-191/Ir-191m	Proposed	Ultrashort half-life (5 s) useful for studies of physiologic functions with a short time scale.
Gd-153	Obsolete	Briefly the radioisotope of choice for bone densitometry measurements using dual photon absorptiometry (DPA), needed for studies of osteoporosis.
Sm-153	Obsolete	Alternate radioisotope for DPA—has same daughter x-rays as Gd-153, but has a beta decay in addition. Short half-life required weekly changeout of densitometer sources.

In-vitro Studies

Radiolabeled immunoassays are among the most commonly applied medical analytical techniques and are central to many medical diagnoses. Radioisotopes that have been used in radioimmunoassays include H-3, C-14, Co-57, Se-75, I-125, and I-131. Of these, the most commonly used ones today are I-125, Co-57, and H-3; more than 90% of all such laboratory tests utilize I-125, however. Beside medical use, these techniques can also be applied to the determination of environmental pollutants such as herbicides and pesticides to concentrations as low as 10^{-14} molar in some cases. While other alternative

labeling schemes exist, and in some cases are more sensitive, the radiolabeled assays are generally the most robust and free of interfering effects.

Unsealed Source Therapies

Unsealed source therapies are divided into three broad categories. First are radioisotopes used in arthritis therapy. Some six million Americans suffer from rheumatoid arthritis. Of these, about 50% involve the knee joint and 80% involve the hand, with smaller involvement of the hip, shoulder, wrist, etc. Chronic inflammation of the synovial tissues (i.e., lining) of the joint can lead to eventual destruction of the cartilage. Aside from treatment with ethical drugs which are not always effective, two forms of excising the synovial tissues exist—surgical and radiation synovectomy. The currently preferred radionuclide for radiation synovectomy is Dy-165, which has surpassed the use of Er-169, Re-186, P-32, Au-198, and Y-90 for this treatment. Ho-166 offers potential advantages over Dy-165 in (1) the energies of radiation emitted, (2) the improved properties of the colloid preparation, and (3) the longer half-life. Of these, the half-life is especially important, since Dy-165 therapy involves travel to special facilities near its point of origin because of its 2.3 hour half-life, versus 27 hours for Ho-166. A summary is presented in Table 10.

Table 10. Major Radioisotopes in Arthritis Therapy.

Radioisotope	Relative Use	Comments
Au-198	Declining	Prepared as colloidal suspension for radiation synovectomy.
Dy-165	Growing	Best choice radioisotope for radiation synovectomy, but difficult to produce. More efficacious than Au-198.
Ho-166	Growing	Alternate for Dy-165 therapy. More effective than Au-198.
Re-188	Proposed	
Sm-153	Proposed	

Second in the category are radioimmunotherapies, where a therapeutic dose is delivered to a cancerous tumor by labeling a cell-killing radioisotope onto a monoclonal antibody whose uptake is very strong in the tumor. A summary of currently used radioisotopes is presented in Table 11. Ideally, the half-life of the radioisotope should be roughly equal to the uptake and residence time of the monoclonal antibody. It should be noted that this therapy is relatively new and in many cases unproved. Considerable research effort is being undertaken to bring this therapy to real clinical use.

Table 11. Major Radioisotopes in Radioimmunotherapy.

Radioisotope	Relative Use	Comments
P-32	Declining	Still popular radioisotope, with many old-line advocates. No useful gamma ray for imaging.
Cu-67	Growing	Radiation cascade is known to be highly lethal to cells. Has a useful gamma ray for imaging. Cu-64 has similar properties, but has a shorter half life.
Re-186	Growing	Chemical analog of technetium that can take advantage of ligands developed for Tc-99m. In a sense, if you can image the tumor with Tc-99m, then you can treat it with Re-186 (or Re-188). Has a useful gamma ray for imaging.
W-188/Re-188	Proposed	Alternate to Re-186 with a shorter half life and more energetic beta. Has a useful gamma ray for imaging.
P-33	Proposed	Alternate to P-32 with much lower energy beta for more localized dose distribution. No useful gamma ray for imaging.
Ho-166	Proposed	
Sm-153	Proposed	
Sm-145	Proposed	

The third major area of unsealed source therapy is for bone cancer pain relief, and ultimately, bone cancer therapy. Bone metastases develop in more than 50% of patients with lung, breast, or prostate cancer, and often lead to progressive bone pain. There are about 1 million new cases of cancer each year, and about 50% of all patients dying of cancer have skeletal metastases at the time of death, making the demand for this therapy very high. Relatively new radiotherapies include Sr-89, Re-186, and Sm-153. The latter two have theoretical advantages over Sr-89. The first treatment of bone pain began over 40 years ago with P-32, which is still widely used. Other radioisotopes either tested or proposed for bone pain palliation include As-76, Ho-166, I-131, P-33, Re-188, Sn-117m, and Y-90. A summary of radioisotopes is shown in Table 12.

Beyond the goal of palliation, Sn-117m has been proposed as a therapy for bone cancer. Its conversion electrons, with a range of approximately 0.2 mm in water, can impart a highly localized radiation dose. When delivered to bone mineral, the short range of the conversion electrons should be much more sparing of sensitive marrow than high energy beta emission from isotopes such as P-32, Sr-89, and others with ranges on the order of 1 cm. The radiopharmaceutical $^{117m}(Sn^{4+})$DTPA is the preparation of choice. Preliminary studies in patients have proven efficacy of pain relief. The limiting toxicity will be associated with the DTPA and not the radioisotope; this may very well be sufficient to deliver a therapeutic dose to the bone metastases.

Table 12. Major Radioisotopes in Bone Cancer Pain Relief.

Radioisotope	Relative Use	Comments
Sr-89	Growing Rapidly	Metastron (Amersham) approved as a new drug in the U.S. in June, 1993. Has been approved in Europe for several years. Has no gamma ray for imaging—imaging studies typically need to use Sr-85. Biological half-life three times longer in bone metastases than in normal bone.
Re-186	Growing	Prepared as ^{186}Re-HEDP (Mallinckrodt). Phase II clinical trials nearing completion. Provides a high-dose rate alternative to Sr-89, which may be found more efficacious. Has a gamma ray quite suitable for imaging. Rhenium chemistry very similar to technetium—should enjoy wide choice of ligands developed for Tc-99m delivery. Biological half-life only about two times longer in bone metastases than in normal bone.
Sm-153	Growing	Prepared as ^{153}Sm-EDTMP. Phase II clinical trials nearing completion. Has a gamma ray quite suitable for imaging. Similar dose rate to Re-186, but permits treatment on an outpatient basis.
Sn-117m	Proposed	Prepared as ^{117m}Sn-DTPA. Dose (mainly derived from conversion electrons) is very highly localized, which may spare the bone marrow. Difficult to produce this radioisotope with high specific activity. Has a gamma ray quite suitable for imaging.
P-32	Declining	Prepared as sodium orthophosphonate (Mallinckrodt). Prevalent use since the 1940s. Considerable side effects. Many problems with dosimetry over the years due to carryover into other organs—dose discrepancies have been as high as five-fold.
W-188/Re-188	Proposed	Very high dose rate alternative to Sr-89 and Re-186.
Ho-166	Proposed	High dose rate alternative to Sr-89.

In-vivo Studies

Studies involving direct introduction of radioisotopes into patients other than for therapy or imaging are classed as in-vivo studies. These include examples such as lung ventilation studies using Xe-133, blood pool volume determinations using Cr-51 or Fe-59, renal clearance and function studies, and so on. The most important factor in the choice of radioisotope is its physical and chemical compatibility: inert gases for ventilation studies, chemicals that bind to red blood cells such as iron or chromium, etc. Of course, the radioisotope delivering the lowest dose is highly preferred.

The market for in-vivo study radioisotopes is considered to be fairly small and to have a number of fission product isotopes that are already the well-established choices.

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