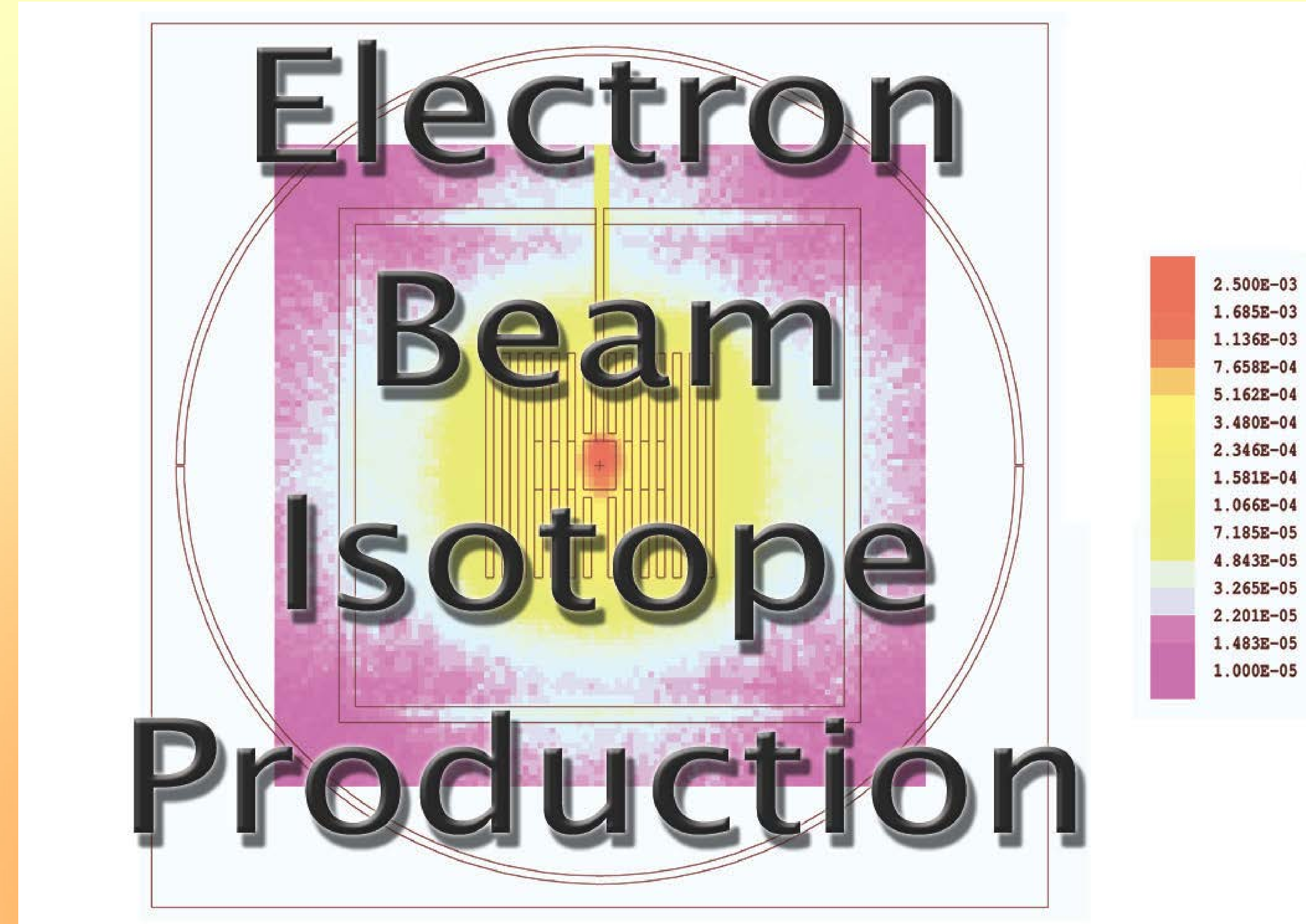
Electron Beam Isotope Production



Compact Neutron Generator Production of Medical Isotopes

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OVERVIEW

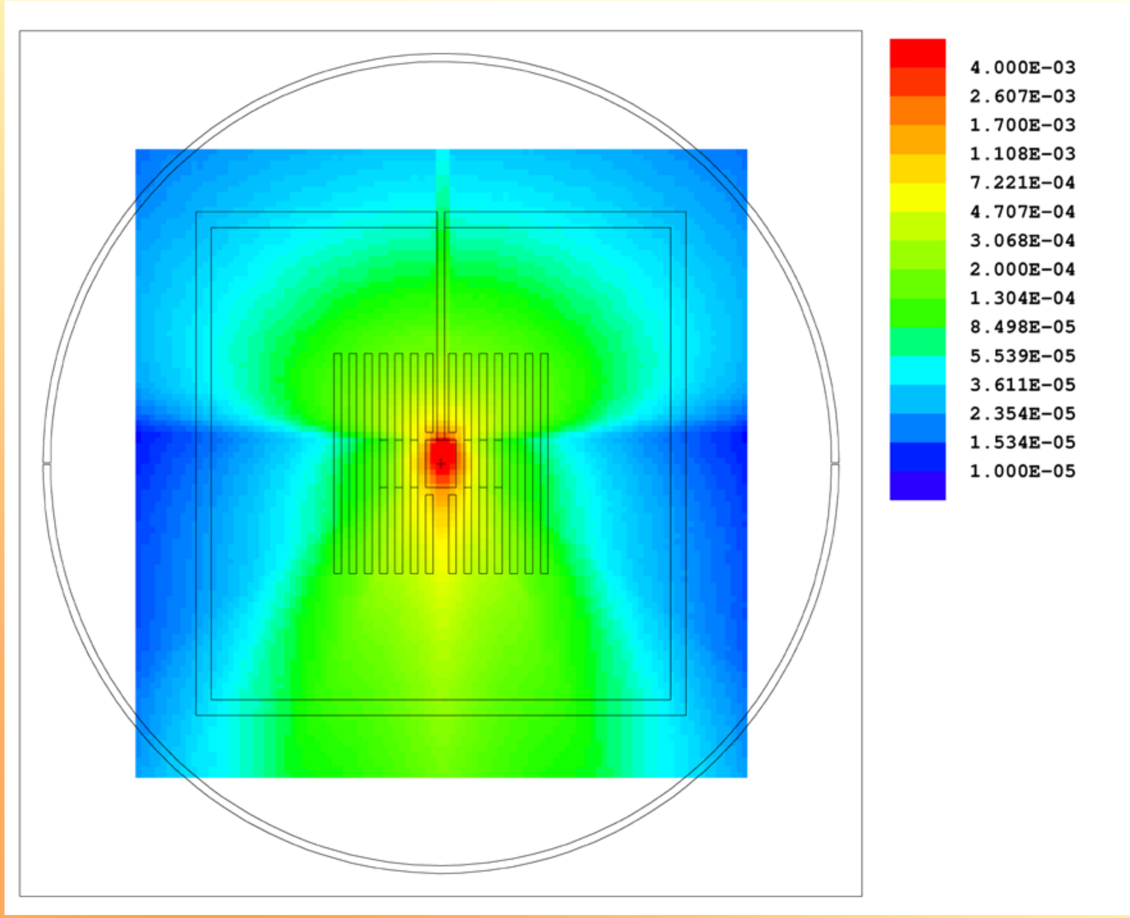
Each Isotope Type requires its own target, hard x-rays at the right energy to maximize desired reactions in target materials

Liquid lead bismuth eutectic is used to cool the target and as the liquid converter material to control beam heat in the beam window region

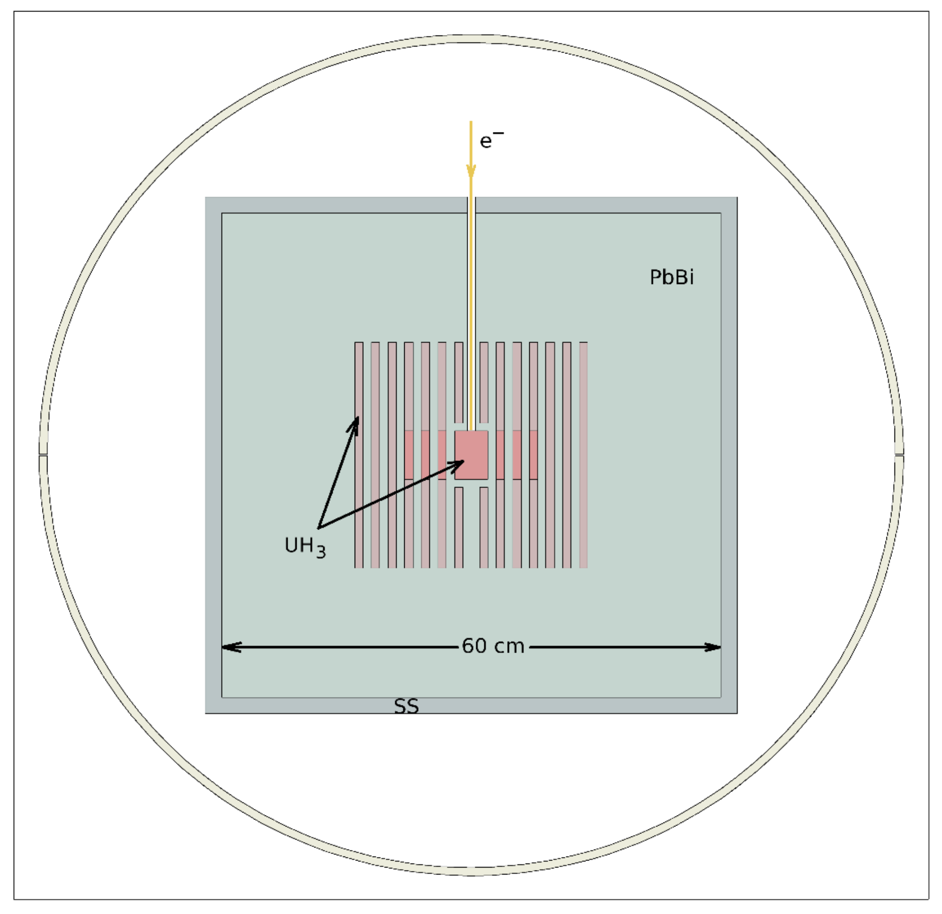
LEU is used to provide neutrons and is hydrided to moderate neutrons in fuel and hydrides are used to shape the “in-target” neutron spectrum.

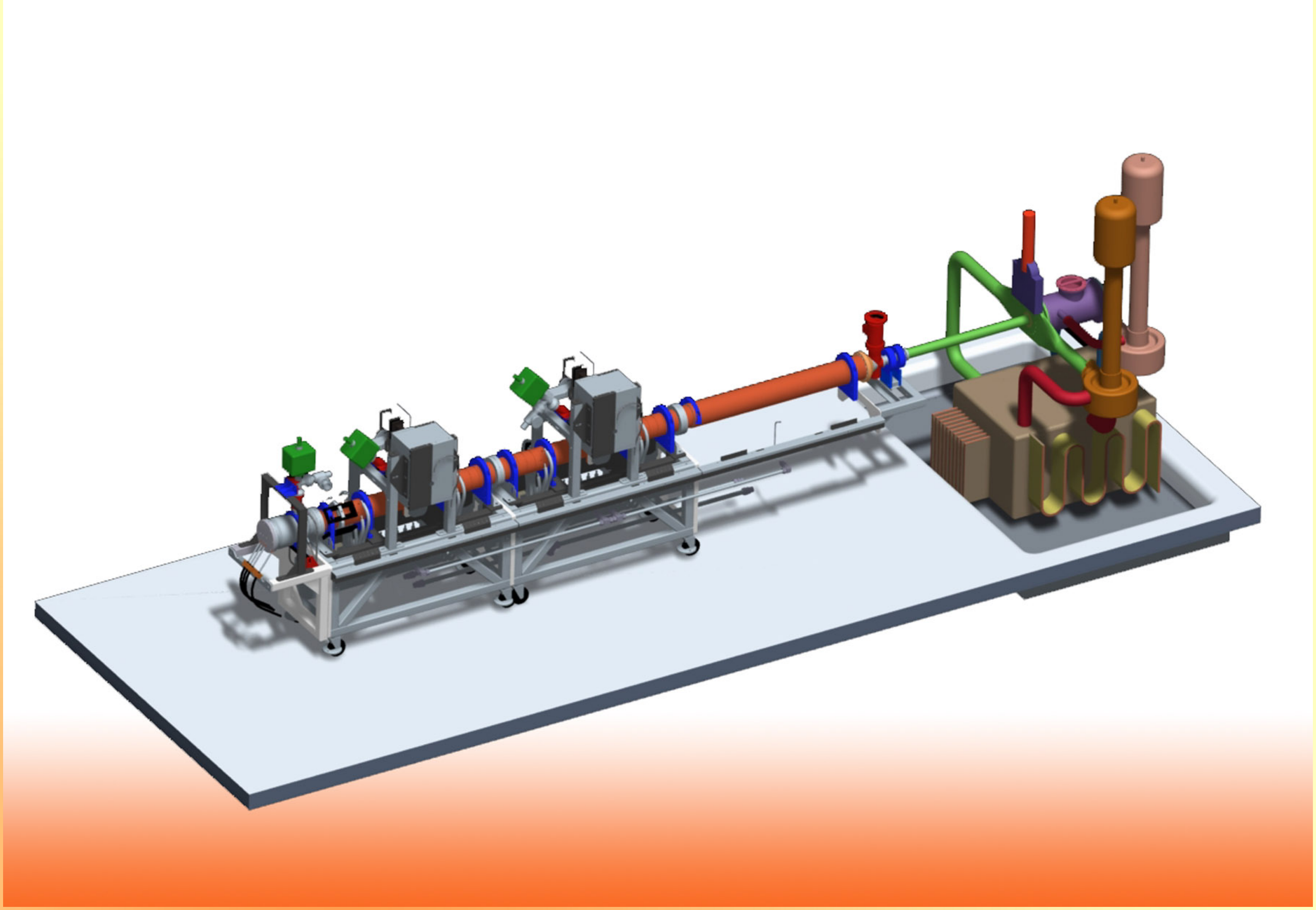
In the fueled configuration, the device is a compact neutron Generator - In the Unfueled configuration, the device is a beam target cooled by liquid metal

Beam Interacting with Converter



Beam and Nested Cylinder Array Immersed in Lead Bismuth Eutectic





Low cost, low power,
Electron Beam Driven
Isotope Production

- Diagnostic and Therapeutic Isotopes
- Three Production Methods:
- Gamma, n
- N, gamma
- N, f

Gamma, n

Energetic x-rays (Bremsstrahlung Radiation) are produced by accelerated electrons slowing down in liquid or solid high Z converter

Some X-rays whose energies are in the Giant Dipole Resonance range are absorbed by target nuclei Causing neutrons to be expelled from excited nuclei in the target

Examples: tin-112 to indium-111, radium-226 to actinium-225

N, Gamma

Hard x-rays from the converter produce photonuclear reactions in low enriched uranium providing neutrons

Flux of neutrons is generated in low enriched uranium fuel surrounding the converter region

Neutron energies are tailored to approximate neutron capture cross section of target isotope in and near the target

Examples cobalt-59 to cobalt-60; radium-226 to actinium-227

N, fission

Neutrons induce fission in the low enriched uranium target

Fission product isotopes are produced

Examples: Moly-99, Iodine-131 and Xenon-133

Fission Products Moly-99

MCNPX is used to model productivity of proposed designs for isotopes in short supply

Fission product isotopes can be produced in a cylindrical target placed between fueled cylinders of a subcritical array

6.5 day irradiation anticipated to produce 500 or so 6-day curies of moly-99 per irradiation.

Results would be promising were there available separations facilities to process the low enriched uranium foil post irradiation

Moly-99 is a commodity isotope used for scores of diagnostic procedures but its producer price is estimated to be $20-$25 per diagnosis with over 10 million annual U.S. diagnoses

Gamma, n Indium-111

Indium-111 can be produced by irradiating tin-112 with gamma

Giant Dipole Resonance peaks at around 16 MeV

One day irradiation yields about .15 curie of indium-111 when average beam power is 3 milliamps

This is a mid-priced isotope estimated price is about $500 per scan.

It is used to locate hidden infections in patients.
Interesting because gamma, p and gamma, n yield same product

Pure tin-112 scarce, only two grams available at Oak Ridge

Premium Isotopes

Premium value isotopes are alpha emitters, the scarcest (of course!) and the most challenging to make

Premium isotopes are not diagnostic isotopes they rather are therapeutic drugs; either experimental drugs in the pharmaceutical companies' product pipelines or newly approved drugs in the U.S. and E.U

All of the premium isotopes are alpha emitters that are self targeting or can be targeted by labeling molecular targeting agent with the alpha emitter

All are derived from the irradiation of radium-226

Alpha Emitters

Alphas have high linear energy transport

Approximately 5 MeV is deposited in the length of 2 to 10 cell diameter the length of an alpha's track in human tissue, severing both DNA strands of the targeted cells.

Out of range tissue is spared in contrast to side effects caused by chemo therapies and beta and gamma radiation therapies.

Ideal therapeutic agents have short half-lives, lodge securely in cancerous tissue pending decay and emit several alphas for some applications and a single alpha for other applications

Roster of Alpha Emitters

Prized alpha emitters have short half lives (hours or days) and can be delivered to the cancer cells with a targeting agent or best of all will self target

All prized alpha emitters are made from Radium-226

They include radium-223, thorium-227, actinium-225 and bismuth-213 and could include radium-224 and lead-212 to deliver bismuth-212.

Radium-226 is scarce and as it decays, it generates radon-222 an inert gas that causes harm if inhaled in small quantities

Radium-226 to Actinium-227

Radium-226 can be irradiated with neutrons to produce actinium-227 parent of thorium-227 and radium-223

Irradiation is for 10 weeks or so

Produced are: actinium-227 and thorium-228 parent of radium-224 and bismuth-212

Target contains radium-226 and, for best results, target is placed in a flux of neutrons that constituted by epi thermal energy groups above 50 eV and below 1 KeV.

Radium-223

This isotope is an approved drug, sold by Bayer as Xofigo

It is approved today by FDA and EMA to treat prostate cancer that has spread to bone

Being a calcium mimic, it is self targeting, that is it is taken up by cancerous metastatic cells in bone

Over its 11.4 day half life it generates a cascade of alphas in bone where the cancer cells are active

It is being studied to treat breast cancer which also spreads to bone
Bayer sells it as Xofigo for $69,000 for a treatment of six injections given over a six month period

Each dose is 1.35 micro curies per Kg of patient weight

Thorium-227

This isotope labels molecular targeting agents, monoclonal antibodies, for example, that have affinities for unique surface attributes of some types of cancer cells

Experimental drugs using thorium-227 are being developed by firms in drug development agreements with Bayer

Thorium-227 has a 18 day half life and decays to radium-223
It like radium-223 is separated from actinium-227

Many new drugs will be developed using thorium-227 because there are numerous molecular targeting agents on the market or in development pipelines that can be bound to this isotope

Radium-224 and Lead-212

These isotopes are decay products of thorium-228 inevitably co-produced with actinium-227

Radium-224 has a shorter half-life than radium-223 (3.6 days vs. 11.4 days) but the half life of is first decay daughter, radon-220 is 58 seconds much longer than the 4 second half-life of radon-219 radium-223's first decay daughter

Lead-212 has a half-life of 10 hours and decays to bismuth-212 that has an hour half-life. Lead-212 is combined with a targeting agent, a fast acting peptide, injected and delivers the alpha emitting bismuth to the cancerous cells decaying to bismuth-212 which has a one hour half life and emits one alpha

Actinium-225

One way to make actinium-225 is by gamma, n on radium-226 With a two milliamp beam set between 33 and 36 MeV to produce gammas between 11 and 12 MeV, 1.2 curies of actinium-225 can be produced during a 40 day irradiation.

The dose will be approximately 1.4 microcuries per Kg. of patient weight averaging 100 microcuries per patient (70 Kg) delivered and 100 microcuries to account for one half life of decay loss, this production will be adequate to provide 5,000 + doses.

Actinium-225 has a half life of 10 days emitting a cascade of alpha particles

Conclusion

The compact neutron generator is being developed to produce premium medical isotopes that prolong life, reduce pain and improve the quality of life.

This is a growing area that will take advantage of advances in medicine dealing with peptides, monoclonal antibodies, targeting agents that can be combined with alpha emitters for an important new class of cancer drugs.

The object is to commercialize the device adapting it for alpha emitter production.