The Feasibility of Domestic Medical Isotope Production for Clincal Imaging

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WPI

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Abstract

The purpose of this IQP was to investigate the feasibility of using MIT's Nuclear Reactor to domestically produce radioisotopes for medical imaging procedures at local area hospitals, namely Massachusetts General Hospital. The two most prevalent isotopes in nuclear medical imaging were focused on, Technetium-99m and Iodine-131. It was determined that due to irradiation rates and the necessity of using a Mo-99/Tc-99m generator, domestic production of Tc-99m is prohibitively expensive. Iodine-131, however, was found to have a more optimistic outlook as it can be eluted without the use of a radioisotope generator.

Contents

Introduction

Nuclear medicine, a branch of medicine that involves the application of radioactive substances to diagnose and treat disease, has become an essential aspect of dozens of medical procedures. On any given day, countless patients are administered trace amounts of radioactive materials for the purpose of gaining physiological or anatomical information from the isotope's radioactive decay products. Annually, more than 40 million people undergo some form of nuclear medicine procedures [8]. The two most common radioisotopes used in the medical industry are Technetium-99m (Tc-99m) and Iodine-131 (I-131); procedures using Tc-99m accounting for 80% of all nuclear medicine procedures yearly [11]. Both Tc-99m and I-131 are reactor produced isotopes meaning they are produced by irradiating a parent material with a neutron beam to induce radioactivity.

The production of Tc-99m is centralized to six reactors worldwide, all of which are international. These reactors are NRU Chalk River Laboratories in Canada (40 %), HFR Petten in the Netherlands (30 %), BR-2 Fleurus in Belgium (9%), OSIRIS Saclay in France (5 %), SAFARI-1 Pelindaba in South Africa (10 %), and OPAL Sydney in Austrailia (6%)[11] [7]. All of these reactors, excluding OPAL , are more than 40 years old and thus require extensive maintenance to stay online[7]. Since the production is centralized to a small number of reactors, when these reactors have to go offline for maintenance the world supply of Tc-99m is drastically cut which recently has lead to price spikes. The increasing prevalence of radioisotope shortages has caused doctors to either decide who does or does not get their scheduled procedure or they must switch to a different radioisotope that will expose the patient to unnecessary risk from the radiation [6].

The reason that the U.S. has relied on foreign reactors is primarily due to cost. The reactors listed above have substantial capacity and are mostly government subsidized [2]. This leads to, as will be shown, production costs that are substantially cheaper than domestic production. However, an annual increase of over 10% of radiopharmaceutical use in medical procedures has further strained global supplies [11]. Coupled with the scheduled closing of NRU Chalk River in 2016 and the closing of OSIRIS, BR-2, and HFR within five years, the necessity of alternative production means is becoming ever more immediate [7].

To address these concerns, several alternatives have been considered to provide a supply of radioisotopes for U.S. facilities. These alternatives include nuclear new build, alternative production processes besides neutron irradiation, and using domestic reactors [10]. The purpose of this paper is to investigate the feasibility of using the nuclear reactor at the Massachusetts Institute of Technology (MIT) to produce the two most commonly used radioisotopes, Tc-99m and I-131, for Massachusetts General Hospital (MGH).

Medical Imaging Modalities [1]

Medical imaging modalities can be divided into two different classes based on their resultant obtainable information, Anatomical imaging and functional imaging.

Anatomical Imaging Modalities

Anatomical imaging modalities are those that only provide information regarding the structure of the material being imaged and provide no information about the function of the material. In terms of biological systems, anatomical imaging provides information regarding anatomy and nothing (or in the case of MRI, limited functional information) about physiology. These modalities tend to be focused on the transmission of radiation through the body and observing the intensity of radiation exiting the body.

X-ray Radiography

X-ray Radiography is a method of transmission imaging, meaning that an image is generated by detecting radiation that originates from a source, transmits through a material, and is subsequently detected. X-ray's are produced using an X-ray tube that focuses a beam of thermionic electrons onto, typically, a Tungsten anode. As the electrons approach the anode, the electrons decelerate and emit Bremsstrahlung radiation (braking radiation) as well as characteristic X-rays (photons which are emitted via the de-excitation of an atomic electron). These photons of a known intensity are then incident on the material to be imaged. The photons then either interact with the target or pass through the target unimpeded. Inside of the target material, the photons interact with materials via a variety of processes including photoelectric absorption, Compton scattering, Rayleigh scattering, and Pair production; photoelectric absorption is the dominant interaction for photons in the diagnostic energy range and is highly dependent on the Z-number of the material. Each of these processes has an associated probability of occurence that is dependent on energy and the target material. The attenuation of photons by these processes can be expressed mathematically as:

$$I(x) = I_0 exp(-\mu x) \tag{1}$$

where μ is the mass attenuation coefficient which quantifies the probability of interaction. I(x) is the intensity of photons of a given energy at a depth, x, and I_0 is the incident intensity of the photon beam. Every material has a different mass attenuation coefficient. The mass attenuation coefficient for photons generally increases as the density of the material increases. Therefore in the human body, bone has a higher

[1] All relevant information regarding imaging modalities can be found in Bushberg 2012

attenuation coefficient than tissue does; thus more photons are attenuated by bone. This simple fact is the basis of radiography.

An X-ray image is generated by having a beam of photons incident on a material and subsequently measuring the transmitted photons on the opposite side of the X-ray tube. Depending on what material the photons interact with, every point opposite the X-ray tube will have a different measurable intensity. Since every point contains the combined information of materials along the line of the photon beam, radiography is called projection imaging since it projects a 3-dimensional object onto a 2-dimensional plane.

X-ray radiography is advantageous in that it provides a high spatial resolution, there is high contrast between dissimilar material types such as tissue and bone, it is inexpensive, and it has a very fast acquisition time. Since photoelectric absorption is a highly density dependent process, X-ray radiography provides poor differentiation between tissue types. Also, since X-ray Radiography is a form of projection imaging, there is a fair amount of information compression as all of the information along the photons path is compressed to a single point.

- **Fluoroscopy**

  Fluoroscopy is a method where a series of X-ray images are obtained in less than a half of a second. A contrast agent can be introduced into the body that preferentially attenuates X-ray's such that a "movie" can be generated that tracks the movement of the contrast agent.

- **Mammography**

  Mammography is a specialized subset of X-ray radiography which is used to assist in the diagnosis of breast cancer that uses lower energy photons than standard radiography. Lower energy photons are used to differentiate between slightly different breast tissues and calcifications that are present.

Computed Tomography (CT)

Computed Tomography (CT) is effectively a 3-dimensional X-ray image. It uses computer processing techniques and reconstructive algorithms to generate tomographic images (slices) of a non-uniform material from a series of X-ray images. This is done by having an X-ray source on one side of the material and a detector on the other side, both of which are connected to a rotating grid. At a series of different angular positions, an X-ray image is taken. From the measured transmission at each position, a system of equations can be generated, each in the form of equation 1 above. The length, x, is equivalent to the system resolution (pixel width) and μ is the mass attenuation coefficient of the material that constitutes that pixel. Thus, enough images need to be taken such that there are enough equations to solve for each μ. Solving the system of equations yields information regarding what constitutes each pixel and an image can be reconstructed

based on this data. A substantial advantage of using CT over traditional X-ray imaging is the increase in contrast, defined as the ability to differentiate between different materials. The most significant downside to this modality is there is a large radiation dose that is administered to the patient. Instead of compressing the information along the beam path into a single point, CT works on a pixel-by-pixel basis. A typical chest X-ray will deliver roughly .01-.15 mGy to the patient (1 Gray is equivalent to 1 Joule of energy being absorbed per kilogram of material). A CT scan, being a series of X-ray images, will deliver around 13 mGy of absorbed dose. Therefore, while more information is being gained, the patient receives more radiation exposure. Also, since photoelectric absorption is highly dependent on the Z of a material, images cannot be created when a metallic implant is present since most of the photons along that path will not transmit through the patient.

Magnetic Resonance Imaging (MRI)

Magnetic Resonance Imaging is based on a nuclear property known as the Magnetic Moment characterizing the magnetic field generated by movement of constituent quarks of particles. The magnetic moments of Protons and Neutrons are effectively equal and opposite, with an almost negligible difference in magnitude. In an atom with an equal number of protons and neutrons, the magnetic moments effectively sum to zero. However, in an atom where there are more protons than neutrons, there is a net magnetic moment. Therefore, many of the constituent elements that make up the body have a zero net magnetic moment. One crucial molecule does have a net magnetic moment however, and this is water. Water is made of an Oxygen atom (zero magnetic moment) and two Hydrogen-1 atoms (A proton and an electron).

In a multi-atom material without an external magnetic field, thermal fluctuations cause the magnetic moments of the constituent atoms to point in random directions and effectively sum to zero. When an external magnetic field is introduced, the magnetic moments align themselves parallel and anti-parallel to the magnetic field. The anti-parallel states are at a higher-energy level than the parallel states and are thus at an unstable equilibrium in the system. At room temperature and a relatively low magnetic field, there is a very small number of net parallel spins. Quantitatively, there are approximately three excess protons in a parallel spin state for every million protons.

Along with the parallel and anti-parallel alignment, the protons also experience a torque from the magnetic field causing the magnetic moment vector to precess about the magnetic field vector. The precession

occurs with angular frequency:

$$\omega_0 = 2\pi f_0 = \gamma_n |\vec{B_0}|$$
$$\therefore f_0 = \frac{\gamma_n}{2\pi} |\vec{B_0}|$$

f_0 is known as the Larmor frequency, γ_n is the gyromagnetic ratio and is equivalent to the magnitude of the magnetic moment, and $|\vec{B_0}|$ is the magnitude of the magnetic field. The Larmor frequency is the frequency corresponding to the energy needed to flip the magnetic moment vector 90 degrees from $\vec{B_0}$.

In MRI, a material is placed in a magnetic field and radio-frequency photons are emitted from an antenna and are incident on a material. When the frequency is adjusted to the Larmor frequency of the protons for the given magnetic field strength, a drop in signal will be registered as the photons are absorbed by the protons. In order to use magnetic resonance to form an image, a field gradient needs to be present in the well-characterized magnetic field. The magnetic field gradient will lead to materials at different points in the field to have different Larmor frequencies. These points in the field will have a well-characterized position and when the frequency of incident RF photons hits the Larmor frequency, a decrease in signal will be registered as the photons are absorbed by the material. The difference in density between separate areas of the material will be registered as a spike of unequal magnitude. The gradient of spike magnitude can form an image since the ratio of densities to a reference density is known at each point in the magnetic field where each density corresponds to a unique material.

Since MRI is sensitive to varying hydrogen concentration there is great differentiation between similar tissue types, unlike X-ray and CT. The patient is only exposed to RF photons, therefore there is no absorbed dose. Unlike X-ray's quick acquisition time, MRI can take upwards of 20 minutes to obtain a usable image. MRI can also not be used on patients with metallic implants since they are placed inside of a large magnet.

Ultrasound Imaging (UI)

Ultrasound imaging uses high-frequency sound waves to generate an image. This is done by placing a Transducer against the body to generate a short-duration sound pulse. Once the sound-pulse is generated, the transducer is kept in place and detects reflected sound-waves. Sound waves are reflected because when an ultrasonic wave strikes an interface between two different materials (density change), part of the wave is reflected backwards towards the transducer. The intensity of the reflected wave depends on the density difference between the two materials. Also, the time it takes for the reflected wave to reach the transducer is a function of the depth in the tissue the interface exists.

Functional Imaging and Nuclear Medicine

Nuclear Medicine is a methodology that uses radioisotope-tagged tracer agents that are preferentially uptaken by an organ of interest. Instead of providing anatomical information like X-ray and CT provide, Nuclear Medicine scans provide physiological information about a tissue based on the rate of uptake of the radiopharmaceutical. There are two main types of Nuclear Medicine Scans, Positron Emission Tomography (PET) and Single Photon Emission Computed Tomography (SPECT). The focus of this paper will be on the production of nuclear medicine radioisotopes.

Single Photon Emission Computed Tomography (SPECT)

SPECT uses radioisotope-tagged pharmacological agents that decay via gamma-ray emission. Gamma emission is a form of radioactive decay whereby the nucleus of an atom emits a photon to reach a lower, more stable energy state. The radioisotope preferably only emits a gamma-ray because the decay products of other emitters (be it β^- or α emitters) will not be able to leave the body due to electromagnetic interactions and therefore will not contribute to the image, adding only to the absorbed dose to the patient. These radioisotopes are chemically combined with a pharmacological agent that is preferentially uptaken by an organ of interest. Once these enter the body, they concentrate in the organ of interest and subsequently decay via gamma emission. The gamma rays are then collimated and detected by a (most commonly) Sodium Iodide (NaI) crystal that is positioned in a lattice configuration. A Photomultiplier Tube (PMT) is then used to amplify the gamma-ray to a detectable intensity. The channel that the gamma-rays collimate into have a spike in signal and thus can provide information about the origin of the gamma rays.

Positron Emission Tomography (PET)

PET scans use radioisotopes that emit positrons (β^+) to generate an image. The positron then, due to Coulombic interactions, interacts with an atomic electron and the pair annihilate each other, creating two .511 MeV photons that are emitted 180 degrees away from each other. These two photons are then subsequently measured. This coincident measurement can localize the origin of decay to much higher precision than SPECT leading to a better spatial resolution. A disadvantage of PET is that the positron-emitting isotopes tend to have drastically shorter half-lives than gamma-emitters. PET isotope generation generally requires on-site cyclotrons, thus making PET the much more expensive option.

The overall advantages of Nuclear Medicine scans is that they are the only modalities that provide all types of functional imaging. Whereas diseased tissue may not show up on an anatomical scan such as X-ray or CT, Nuclear Medicine would provide high-contrast between them. A disadvantage of Nuclear Medicine

scans is there is an associated high patient radiation exposure. They also provide no anatomical information so the specialist conducting the test needs to know in advance what it is they are looking at. There is also a very limited availability of the isotopes needed to perform these procedures. PET isotopes require on-site cyclotrons and SPECT isotopes are produced at a minimal number of foreign reactors that are steadily aging.

Combined Image Modalities

In order to overcome the limits of a given imaging modality, it has become common practice to merge anatomical imaging modalities with functional ones. For example, CT scans may be overlayed with SPECT scans to provide clearer information about where the tissue of interest resides.

Tc-99m production [2]

Technetium-99m (Tc-99m)is a meta-stable isotope of Technetium, the first synthetic element created in 1937 in Italy by Carlo Perrier and Emilio Segre [7]. As was noted earlier, it is the most widely used radioisotope in nuclear medicine and is used for a variety of SPECT-based scans. The breadth of scans that utilize Tc-99m include scans of the brain, thyroid, lungs, liver, spleen, kidney, gall bladder, salivary and lacrimal glands, heart, and skeleton [11]. With such wide-reaching clinical applications, Tc-99m is the most important isotope to consider for domestic production.

The production of Technetium-99m is a multi-step process that begins with Molybdenum-98 (Mo-98), a radioactively stable isotope of Molybdenum. Mo-98 is irradiated with thermal neutrons, neutrons that are in equilibrium with their surrounding environment at room temperature, which are absorbed by the Mo-98, turning it into Molybdenum-99 (Mo-99). The probability that a particle will absorb incident radiation is referred to as the microscopic absorption cross-section, σ, and is dependent on both the target material as well as the energy of the impinging neutrons. Mo-98, for instance, has a microscopic absorption cross section for thermal neutrons of .130 barns, where 1 barn is equivalent to $10^{-24}\ cm^2$. Mo-99 has a half-life of 2.75 days and emits a beta particle (β^-), which transforms the isotope into a metastable isotope of Technetium-99 (Tc-99). Metastable isotopes are isotopes in an energetically excited state that subsequently emit a gamma particle (γ) to bring it down to an energetically stable state. In this case, Tc-99m has a half-life of 6.0058 hours and emits a 140-keV γ particle transforming it to stable Tc-99. The 140-keV γ particle is the clinically relevant product of this process as this can be easily picked up with radiation detectors outside the body using a gamma camera.

In order to figure out how much Mo-98 is needed to generate a certain activity of Tc-99m, the amount of Mo-99 needed must first be determined. This is done using the equation:

$$A_2 = \frac{\lambda_1 N_1 \lambda_2}{\lambda_2 - \lambda_1} \left(e^{-\lambda_1 t} - e^{-\lambda_2 t}\right) \tag{2}$$

In the equation above, λ_1 and λ_2 are the decay constants for Mo-99 and Tc-99m, respectively. The decay constant for an isotope is defined as:

$$\lambda = \frac{ln(2)}{t_{1/2}} = \frac{.693}{t_{1/2}}$$

where $t_{1/2}$ is the half-life of the isotope of interest. The decay constants of Mo-99 and Tc-99m are $\lambda_1 = 2.9178338{\cdot}10^{-6}\ s^{-1}$ and $\lambda_2 = 3.205235{\cdot}10^{-4}\ s^{-1}$, respectively. The time, t, in equation 2 references the time

[2] All relevant information regarding equations and concepts can be found in Turner 2007.

that the Mo-99 is allowed to decay before retrieval for clinical use and A_2 is the activity of Tc-99m after a time,t, given in either Becquerels (Bq) or Curies (Ci). For computational purposes, the activity will be used in Becquerel. It should be noted that 1 Ci = $3.7{\cdot}10^{10} Bq$.

The real variable of interest here is N_1, the number of Mo-99 atoms needed to provide a certain activity of Tc-99m after the decay time, t. Therefore, equation 1 can be rearranged to solve for N_1:

$$N_1 = \frac{A_2(\lambda_2 - \lambda_1)}{\lambda_2\lambda_1\left(e^{-\lambda_1 t} - e^{\lambda_2 t}\right)} \tag{3}$$

As a base calculation, the amount of Mo-99 that needs to be produced by irradiation to provide for one nuclear cardiology treatment per day will be determined. Based on numbers provided by Mass General Hospital, a typical nuclear cardiology study uses approximately 25 mCi (.025 Ci) of Tc-99m, or $9.25{\cdot}10^{8} Bq$ [6]. Using the values above for the decay constants and taking t=1 day=86,400 seconds, equation 3 can be used to get $N_2 = 4.042 \cdot 10^{14}$ atoms of Mo-99. This can be converted to a mass using the formula:

$$m = \frac{N \cdot A}{N_0} \tag{4}$$

In this formula, N is the number of atoms of Mo-99 present, A is the molar mass of Mo-99, and N_0 is Avogadro's constant ($6.022 \cdot 10^{23}$ atoms/mole). The molar mass of Mo-99 is simply 99 g/mole. These numbers can be plugged into equation 4 to get m = 66.45 ng.

Now that a value is identified for the number of Mo-99 atoms needed to treat one nuclear cardiology patient per day, the mass of Mo-98 needed. can be determined. To do this, the formula for neutron activations is used:

$$A_1 = n_0\sigma\phi\left(1 - e^{-\lambda_1\tau}\right) \tag{5}$$

where n_0 is the number of Mo-98 atoms needed to irradiate, σ is the cross section described earlier, ϕ is the peak thermal neutron flux of MIT's Nuclear Reactor, and τ is the irradiation time (not to be confused with the irradiation time used earlier). A_1 can be mathematically described as:

$$A = \lambda \cdot N$$

Equation 5 can be rearranged to solve for the number of Mo-98 atoms needed as a function of time:

$$n_0 = \frac{\lambda_1 N}{\sigma\phi\left(1 - e^{-\lambda_1\tau}\right)} \tag{6}$$

Using the same equation for the mass given above, the number of Mo-98 atoms needed can also be converted to a mass. Using MATLAB, the mass of Mo-98 needed to provide 25 mCi of Tc-99m per day as a function of neutron irradiation time was plotted.

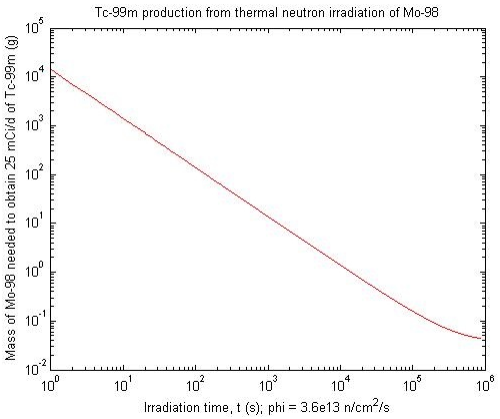

Figure 1: mass of Mo-98 needed to irradiate to treat 1 nuclear cardiology patient per day

It can be seen that the mass of Mo-98 needed decreases as irradiation time increases until a saturation value is reached after around 1 week of irradiation. Taking a one week irradiation value, roughly .04 g of Mo-98 would need to be irradiated for a week in order that one patient can be treated per day with 35-mCi of Tc-99m.

A more realistic approach is to consider how much can be feasibly irradiated at a given time and then calculate the irradiation time necessary to provide MGH with a one week supply of Tc-99m assuming isotope retrieval of once per week. MIT's website quotes the dimensions of the irradiation capsules used in their in-core facility on their website as a cylinder with an inner diameter of 2 inches and a length of 22 inches. In order to get a uniform irradiation and neglect edge effects, the cylinder will not be filled more than a third of the length. Therefore, the irradiation volume to be considered was decided to be a length of 6 inches with an inner diameter of 2 inches after consulting industry professionals. Therefore the volume can be easily calculated and the resultant mass of Molybdenum that fits into the capsule based on the density. It is also known that the relative isotopic abundance of Mo-98 in natural Molybdenum is 24.13 %, therefore the mass of Mo-98 that can fit into the capsule is:

$$\mathrm{m_{Mo-98}} = .2413 * (\pi \mathrm{r}^2 \mathrm{L}) * \rho$$

From this, the number of Mo-98 atoms that are present in the irradiation cylinder can be calculated:

$$n_0 = \frac{m_{Mo-98} * N_0}{A}$$

Next, the number of Mo-99 atoms needed to provide a one-week supply of Tc-99m, N, can be calculated. This is done using equation 2 and the variables defined in the prior calculations. Now the necessary irradiation time can be calculated to generate the necessary amount of Mo-99 atoms given the initial quantity of Mo-98 atoms in the irradiation cylinder by rearranging equation 5 to solve for t. This gives:

$$t = \frac{1}{\lambda_1} \ln \left(\frac{1}{1 - \left(\frac{N\lambda_1}{n_0 \sigma \phi} \right)} \right)$$

The irradiation time needed at MIT's nuclear reactor is thus equal to 12.1 hours. Due to contingency issues in terms of irradiation rates at MIT, a rate could not be provided at the time of this report. In lieu of MIT's rate, the rate that the University of Massachusetts at Lowell (UML) charges was used to provide a reasonable estimate. On an hourly basis, UML charges $350 per hour [5]. Multiplying the irradiation time by the hourly rate yields $ 4,235.70 for irradiation. Dr. Hu stated that in production of Tc-99m, irradiation only accounts for $\approx$ 10 % of the total cost. The rest of this cost goes into transportation and the Mo-99/Tc-99m generator which is a device used to store Tc-99m until it is needed for a procedure. It should also be noted the generators currently in use are made by foreign companies. Therefore if foreign reactor independence is to be sought, then either MGH or MIT would have to put the capital into acquiring the Technetium generator production means. Using the fact that irradiation is only $\approx$ 10 % of total cost as a scaling factor, the total cost of domestic Tc-99m production for a one-week supply at MGH is $42,357.

The price that MGH pays for their weekly supplies is drastically cheaper. In a tyical week, MGH purchases two Tc-99m generators to provide a week supply at a price of $\approx$ $3,000 per generator [6]. Therefore in a week, MGH spends around $6,000 for their Tc-99m supply. Domestic production is about 7 times more expensive than the current price MGH pays. The reason for this cost differential is primarily due to government subsidization of foreign reactors. Another factor that drives down cost is the size and therefore increased capacity of foreign reactors. As Dr. Hu stated, if domestic production of Tc-99m is to be considered a feasible option, some government intervention will be a necessity [2].

Iodine-131 production

Iodine-131 (I-131) is a radioisotope of Iodine that is used in nuclear medicine for treating thyroid cancer and imaging the thyroid, liver, kidney, and for detecting urinary tract obstruction [11]. With a half-life of 8 days, it decays to Xe-131, a stable isotope of Xenon, by means of β^--emission and a concurrent γ. The energy's of the gamma emission, 364-keV and 637-keV [11], make I-131 a prime SPECT radioisotope. At MGH, on a typical day between 1-11 people will be administered I-131 treatments [6]. This range makes the amount of I-131 used much more variable than Tc-99m. In a week, MGH will use somewhere between 200-800 mCi resulting in $\approx$ 350 treatments annually [6]. For calculation purposes, the maximum amount of I-131 will be considered as an upper limit to what MIT can do. Anything less

The production of I-131 is nearly identical to that of Tc-99m except with different isotopes. A target of natural Tellurium powder is irradiated with thermal neutrons. In natural Tellurium, 33.799% by mass is Tellurium-130. When Te-130 absorbs a neutron, it transforms into Tellurium-131. Tellurium-131 is a β^- emitter with a half life of 25 minutes that decays into I-131 [3]. The calculation of irradiation time necessary given an initial mass of natural Tellurium powder is identical to that of irradiating Molybdenum-98. The calculation that was performed can be found in Appendix B. The time necessary for irradiation was 11.47 hours which, when multiplied by UML's hourly rate, gives an irradiation charge of $4,016.50. However, I-131 does not require a generator to separate out the usable products as Tc-99m does [2] and only production costs as well as transportation and storage costs would need to be considered. The price that MGH pays for I-131 is $118 for the first 5 mCi and then $6.32 for each additional mCi [6]. For 800 mCi, the total cost would be $118 + (795 mCi * $ 6.32 * mCi^{-1}) = $5,024.40. Therefore based on the values provided, domestic production of I-131 may actually be cheaper than outsourcing to a foreign reactor. It should be noted that these are preliminary results and further research needs to be conducted to get a total costs.

Conclusion

As the demand for medical isotopes increases in coming years and the age of foreign reactors necessitates their closure, new supply lines will become increasingly necessary. The domestic production of radioisotopes is an alluring prospect due to the accompanying independence and convenience of having a production facility "in your backyard". As is shown, however, Tc-99m, with a production cost of over $40,000 on a weekly basis is prohibitively expensive, and as Dr. Hu stated, "If domestic production of Tc-99m is to be considered as a feasible option, some form of government subsidization will be a necessity." [2]. The domestic production of I-131 has a much more optimistic outlook as is does not require a generator to single out I-131 from the irradiated Tellurium powder. As was stated however, this is only preliminary research and if domestic reactors are to be considered as an alternative, more research will be necessary to determine a definitive cost. However, given that radioisotope demand is ever-increasing and foreign reactors are becoming a more unstable supply, it would be invaluable for MGH to consider switching supply lines.

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Appendix A: Technetium-99m Production Calculations

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%Calculating the number of Mo-98 atoms available
r = 1 * 2.54;          %radius of in-core dummy fuel element (cm)
L =6 * 2.54;         %length of in-core dummy fuel element (cm)
N_0 = 6.022e23;        %Avogadro's constant (atoms/mole)
A = 98;                %Molar mass of Mo-98 (g/mole)
V = (pi * r^2) * L;    %Volume of in-core dummy fuel element (cm^3)
rho = 10.28;           %density of Molybdenum (g/cm^3)
m = V * rho;           %mass of Molybdenum (g)
m_Mo = m * .2413;      %portion of m that is Mo-98 (g)
n = (m_Mo * N_0)/A;    %number of Mo-98 atoms that can fit capsule


%
activity = (3.7e10)*1.3;       %activity of Tc-99m needed (Bq)
%MGH reportedly goes through roughly 1.3 Ci of Tc-99m in a week's time
lambda_1 = .693/(2.7489*86400);    %decay constant of Mo-99 (s^-1)
lambda_2 = .693/(6.0058*360);     %decay constant of Tc-99m (s^-1)
t_milk = 7 * 86400;              %number of seconds in a week
N = (activity*(lambda_2 - lambda_1))/((lambda_2*lambda_1)*(exp(-lambda_1*t_milk) - exp(-lambda_2*t_milk
%N_1 provides the number of Mo-99 atoms needed to provide a weekly supply
%of Tc-99m for MGH nuclear cardiology
m_Mo_99 = (N * A)/N_0;



%calculating the time and cost of irradiation
sigma = .130e-24; %radiative capture cross section of Mo-98 (cm^2/atom)
phi = 3.6e13; %maximum thermal neutron flux of MIT reactor (n/cm^2/s)
t_1 = (1/lambda_1)*log(1/(1 - ((N*lambda_1)/(n * sigma * phi))));
t_1
%Atom Percent
%http://atom.kaeri.re.kr/ton/
```

```
hour_rate = 350;       %hourly irradiation rate of UMASS Lowell

irrad_cost = (t_1/360)*hour_rate;       %irradiation cost in dollars
irrad_cost



%MIT's reactor dimensions
%http://web.mit.edu/nrl/www/facilities/In-core%20Characteristic%20and%20constraints.html
t_1 =
   4.3567e+03

irrad_cost =
   4.2357e+03
```

Appendix B: Iodine-131 Production Calculations

```
%Calculating the number of Te-130 atoms available
r = 1 * 2.54;          %radius of in-core dummy fuel element (cm)
L =6 * 2.54;         %length of in-core dummy fuel element (cm)
N_0 = 6.022e23;        %Avogadro's constant (atoms/mole)
A = 130;                %Molar mass of Te-130 (g/mole)
V = (pi * r^2) * L;    %Volume of in-core dummy fuel element (cm^3)
rho = 6.24;           %density of Tellurium (g/cm^3)
m = V * rho;           %mass of Tellurium (g)
m_Mo = m * .33799;      %portion of m that is Te-130 (g)
n = (m_Mo * N_0)/A;    %number of Te-130 atoms that can fit capsule
activity = (3.7e10)*.8;       %activity of I-131 needed (Bq)
%MGH reportedly goes through roughly 800 mCi of I-131 in a weeks time
lambda_1 = .693/(25*60);    %decay constant of Te-131 (s^-1)
lambda_2 = .693/(8.02070 * 86400);     %decay constant of I-131 (s^-1)
t_milk = 7 * 86400;              %number of seconds in a week
N = (activity*(lambda_2 - lambda_1))/((lambda_2*lambda_1)*(exp(-lambda_1*t_milk)-exp(-lambda_2*t_milk))
%N_1 provides the number of Te-131 atoms needed to provide a weekly supply
%of I-131 for MGH nuclear cardiology
m_Te_131 = (N * A)/N_0

%calculating the time and cost of irradiation
sigma = .270 * (10 ^(-24)); %radiative capture cross section of Te-130 (cm^2/atom)
phi = 3.6e13; %maximum thermal neutron flux of MIT reactor (n/cm^2/s)
t_1 = (1/lambda_1)*log(1/(1 - ((N*lambda_1)/(n * sigma * phi))));
t_1
%Atom Percent
%http://atom.kaeri.re.kr/ton/

hour_rate = 350;       %hourly irradiation rate of UMASS Lowell

irrad_cost = (t_1/360)*hour_rate;       %irradiation cost in dollars
```

```
irrad_cost


%MIT's reactor dimensions
%http://web.mit.edu/nrl/www/facilities/In-core%20Characteristic%20and%20constraints.html


t_1 =
   4.1313e+03


irrad_cost =
   4.0165e+03
```