Feasibility of a Locally Shielded Brachytherapy Source

A Major Qualifying Project Report

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By

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Abstract

The feasibility of using Ytterbium 169 as a high dose rate brachytherapy source with local catheter shielding was investigated using Monte Carlo simulation software MCNP5. The spectra of Yb-169 and Iridium 192 point sources were simulated through gold, platinum, and stainless steel 304 shields of varying thicknesses from .5-10 mm. The simulation geometry was set up to conform to narrow beam detection geometry so the simulation results could be verified theoretically. The Yb-169 spectrum was also simulated through a phantom of gold nanoparticle infused tissue to determine the feasibility of using infused tissue as a shield out of catheter. The Yb-169 spectrum was effectively shielded by gold and platinum at .5 mm compared to Ir-192, while the gold nanoparticle infused tissue was ineffective as a shield.

Introduction

The American Cancer Society estimates that there were over 1.6 million new cases of cancer occurred in 2013, and that the cost of cancer diagnosis and treatment reached $201.5 billion in 2008 [1]. The 5 year relative survival rate for cancer patients diagnosed between 2002 and 2008 is only 68%, although survival statistics vary greatly by cancer type and stage at diagnosis [2]. Treating cancer effectively is usually an invasive and costly process, often involving chemotherapy and/or surgery, but other treatment types are available.

One effective method of cancer treatment is using radiation to destroy cancerous tissue. In radiation therapy, there are two ways of treating a patient, through external beam therapy or through brachytherapy. In external beam therapy, a high energy x-ray beam is used externally to deliver precise and uniform radiation doses to the patient's cancerous tissue while attempting to minimize radiation exposure to normal tissue. In brachytherapy, radiation is delivered to the cancerous tissue by using small radioactive sources that are permanently implanted in the tumor, called low dose rate brachytherapy, or temporarily exposed to the tumor using a catheter, which is called high-dose rate brachytherapy. The advantage of brachytherapy over external beam radiation is that it provides a more localized radiation exposure which minimizes the quantity of normal tissue that is irradiated. Brachytherapy sources (called seeds) can be implanted for a range of times and dose rates to deliver the appropriate dose for the patient being treated.

Treating cancer with radiation will invariably lead to the irradiation of healthy tissue. Radiation to healthy tissue can cause a number of negative side effects, including peeling

and blistering of the skin, fatigue, and other side effects based on the location of the treatment [3]. Because the side effects of radiation are so severe, it is essential during treatment planning to minimize the dose to healthy tissue while still delivering the proper dose to the cancerous tissue. However, many commonly used brachytherapy sources, such as Iridium 192 or Cobalt 60, are too energetic to shield locally. Finding a source useable for brachytherapy that can be effectively shielded locally would significantly increase the versatility of this treatment method.

The goal of this Major Qualifying Project was to examine the effects of localized shielding on the emission spectrums of Ytterbium-169 and Iridium-192 through computer simulations and theoretical calculations. The software used to simulate the shielding was Monte Carlo N-Particle 5 (MCNP5) created at Los Alamos National Laboratories and licensed through the U.S. Department of Energy.

Background

Radiation

Radiation, in general, is the release of energetic particles or waves by a source. These particles and waves vary greatly depending on the sources they come from, and each type of radiation interacts with matter in ways we seek to understand. Radiation can simply be understood as a means of energy transfer; it can provide electricity, cause harmful biological effects, and have other noticeable effects.

Types of Radiation

There are a few ways to classify radiation, and not all types of radiation come from nuclear decay. Gamma ray radiation comes from atomic nuclides, while x-ray radiation typically

comes from a non-decaying source, such as a linear accelerator. Gamma radiation and X-ray radiation are both emissions of light, and the range of energies that gamma and x ray photons can have is quite large. Most linear accelerators can produce x-rays in the 6-20 MeV range, while gamma rays from nuclear decay can range from a few keV up to many MeV.

Atomic radiation that emits more than just a photon is called alpha or beta radiation. Alpha radiation occurs when a nuclide emits a Helium 4 nucleus, or two protons and two neutrons. The nuclide loses 4 nucleons and two protons, so the end result is that the mass number is decreased by 4 and the atomic number is decreased by 2, changing the element of the decaying nuclide. Beta decay occurs when the decaying nuclide emits either an electron or positron, resulting in beta minus or beta plus decay, respectively. Beta minus decay causes the atomic number to increase by one, while beta plus decay causes the atomic number to decrease by one. Beta decay in either form does not cause a change in the mass number of a nucleon.

Attenuation and Shielding

When radiation interacts with matter, there are many possible outcomes. Gamma radiation in particular can interact with matter in numerous ways. *Absorption* occurs when a gamma ray interacts with an atomic electron, imparting some of its energy to the electron. The electron, now in an excited state, could possibly then leave its atom and become a free electron, a process known as the *photoelectric effect*. If the electron does not leave the atom, it remains in an excited state and can release a new photon, called *coherent scattering*. Gamma radiation can also interact with particles in such a way as to change its wavelength and direction, which is called *Compton scattering*.

Because gamma radiation can interact with matter in a variety of ways, there are materials that can be used to block, or shield, radiation from targets that radiation could damage. The loss of intensity of radiation by interacting with matter is called *attenuation*. Attenuation is dependent on the type of radiation, the material and its properties, and the intensity of the radiation. These quantities are combined into the *mass attenuation coefficient*, μ, which is a measure of how effectively a substance absorbs or scatters light of a given wavelength, per unit mass. Based on the thickness of the material d, and its density ρ, the probability that a photon will not interact in the material is

$$P = e^{-\mu\rho d}$$

The mass attenuation coefficient of elemental gold with respect to photon energy is shown in figure 1.

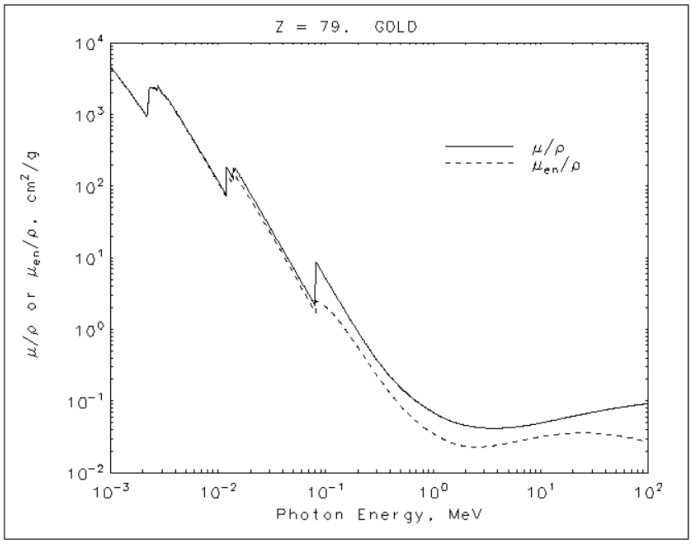

Figure 1 – The mass attenuation coefficient of elemental gold[F1].

Shielding Properties of Gold and Platinum

Due to the restrictions on shield placement for a brachytherapy geometry, we needed to find volume efficient shielding materials to test for the simulations. Gold, platinum and stainless steel 304 make for excellent radiation shields under these volume restrictions. They are biocompatible, or non-toxic when placed in the body in metallic form. Gold and platinum are very dense; gold's density is 19.3 g/cm^3 and platinum's density is 21.45 g/cm^3. Stainless steel is not as dense, at 8 g/cm^3, but the

cost difference of stainless steel from gold or platinum makes it worth investigating as well. Coupled with their relatively high mass-energy attenuation coefficients, these materials make very effective radiation shields. Although gold and platinum are expensive, they are the best options for investigating implanted radiation shielding.

Biological Effects Of Radiation

Through proof of evidence in a variety of experiments, it has been shown that the de facto best way to kill a cell clonogenically (preventing it from reproducing) is to damage its DNA. DNA stores genetic information and is the blueprint for the types of proteins that get synthesized by the cell. When powerful enough radiation interacts with DNA, it can ionize an atom or molecule in it, causing strand breaks that interfere with the DNA's ability to do its job.

Ionizing radiation can interact with DNA in two ways. When ionizing radiation imparts energy directly to the DNA molecule it is called a direct action. Ionizing radiation can also interact with the matter around DNA, creating ions and free radicals that can interact with DNA and cause damage as well. This is called an indirect action. Water is one of the main channels of indirect action, with numerous interactions of ionized and excited molecules creating free radicals to interact with DNA.

Ionizing radiation's ability to cause clonogenic cell death has many applications in medicine. Ionizing radiation can be used in this way to treat cancer, or cells that divide uncontrollably. Cancerous cells are abnormal in that they have no restrictions on how many times they divide and can cause adverse effects to people when there is a large enough mass of them. Ionizing radiation, however, can clonogenically kill these immortal cells, preventing them

from multiplying to the eventual death of the host. Killing these tumors is a very effective way of treating this disease.

Radiation therapy is usually administered over an extended period of time, from a week to several months. This happens because of the radioresistivity of hypoxic tumor cells. When a tumor forms and grows it does not create capillaries and blood vessels. As the tumor increases in size, blood will eventually be unable to reach the central cells of the tumor, causing them to become hypoxic, or oxygen deprived. Because of the lack of oxygen, the number of indirect actions are reduced as the materials to form free radicals namely oxygen) is less abundant. This noticeably increases the radioresistivity of the tumor cells, and thus makes treatment less effective. Treating tumors over a series of irradiations will kill the outer, aerated cells and allow blood to flow the next layer of the tumor, aerating inner cells. This process is repeated until the tumor eventually shrinks into nonexistence.

One method of radiation therapy is Brachytherapy, which will be discussed in detail.

Brachytherapy

Brachytherapy is an advanced and cutting edge method of treating cancer. In brachytherapy, short range radioactive sources (seeds) are placed into or near a tumor to give it a high dose of radiation while minimizing radiation to the surrounding healthy tissue. Brachytherapy seeds may be left in place for a variety of times, from minutes to the life of the source. Brachytherapy seeds are encapsulated in a protective material to let the radiation escape and prevent any harmful chemical reactions that may happen between tissue and source. There are currently two commonly used methods of brachytherapy: Low Dose Rate (LDR) and High Dose Rate (HDR) brachytherapy.

LDR brachytherapy uses low activity sources to treat cancer at early stages of progression. In LDR brachytherapy, seeds the size of rice grains are implanted into the tumor using ultrasound guidance and insertion needles [1a]. These seeds are left in the tumor to irradiate the tumor over the following month or more, depending on the half-life and activity of the source used. Once the seeds burn out they are usually left in the patient as they pose no health risk to the patient chemically or radiologically. LDR brachytherapy is commonly used to treat prostate cancer. Figure 2 shows a common LDR brachytherapy setup for prostate cancer treatment.

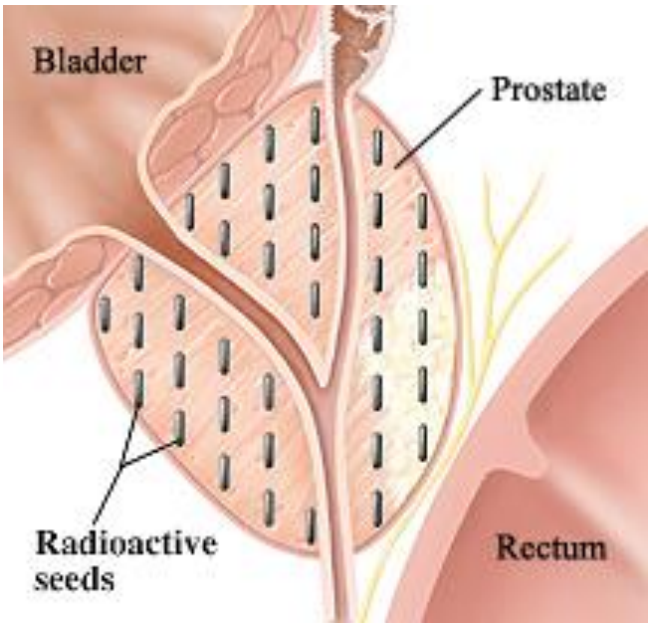

Figure 2 – LDR brachytherapy seeds inside a prostate[F2].

HDR brachytherapy uses high activity sources to rapidly irradiate the tumor for shorter periods of time. HDR sources are usually inserted into a tumor via one or more catheters and held in specific locations along the catheter(s) for specific amounts of time before being removed [2a]. Treatment is usually spread out over the course of 1-2 weeks, with the patient keeping the catheters imbedded until the treatment is complete. After treatment is complete, the catheter(s) are removed and the patient has nothing left in his or her body. HDR brachytherapy is a common and successful treatment for prostate, cervix, endometrium, breast, skin, bronchus, esophagus, and head and neck cancers as well as soft tissue sarcomas [3a].

Currently, HDR brachytherapy is unwieldy to use on tumors near vital organs because of the risk of side effects from irradiating the organ. This MQP tested the feasibility of using gold and platinum as a shield for HDR brachytherapy to increase its versatility.

Methods

Simulation Setup and Considerations

The simulations performed for this Major Qualifying Project used the Monte Carlo N-Particle 5 (MCNP5) radiation transport program created at Los Alamos National Labs and licensed through the Department of Energy. The two isotopes chosen were Yb-169 and Ir-192 for their use as brachytherapy sources. The shielding materials chosen were Gold, Platinum, and Stainless Steel 304, which were chosen due to their biocompatibility.

Simulations were run over a range of shield thicknesses to acquire transmission ratios for each shielding material and source combination geometry. For these simulations the range of shielding thicknesses were selected based on the space available in the brachytherapy delivery catheter to enable localized shielding. Sufficient particle histories were run to produce a convergence in the Monte Carlo code that is less than 5%. The isotopes were also simulated without shielding to acquire baseline flux values for each isotope.

Simulated Shielding Geometry

The setup of the simulation geometry focused on the attenuation the shield will have for a simple, narrow beam geometry, as shown in figure 2. The source used was an isotropic point

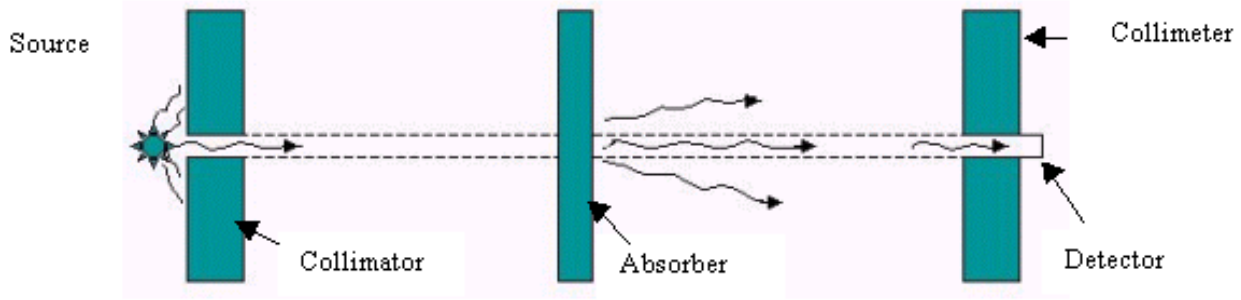

Figure 3 – Narrow beam geometry the simulations and calculations were based on[F3].

source, which is a good approximation of a small source far away. The shields used were cylinders of varying thickness (height), with the far plane 10 cm away from the source and the near plane varying distance between 9.95 cm and 9 cm from the source. The detector, a sphere of 1 cm radius, was placed 10 cm from the back of the shield, or 20 cm from the source, to ensure that photons that the shield deflected were not detected. To collimate the simulations, a cylinder of radius 1.1 cm extended the length of the geometry and discounted any photons that passed through its surface. The end result of the simulation was to obtain the number of photons that passed through the detector without regard to the photon's energy or location where it passed through the detector. This photon flux was tracked by an F4 tally coded into the MCNP5 distribution and called upon in the simulation code. Once unshielded flux values and shielded flux values were acquired, the transmission ratio was calculated as the ratio of the photon fluence for the shielded and unshielded geometries via:

$$Transmission = \frac{Flux\ Shielded}{Flux\ Unshielded}$$

An image of the geometry set up for these simulations is shown in figure 4.

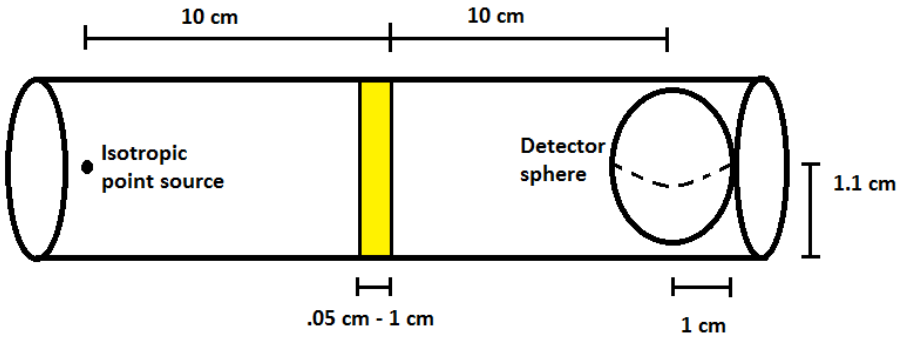

Figure 4 – The geometry developed for the MCNP5 simulations

Testing the Validity of the Monte Carlo Simulations

The Monte Carlo code that generated the simulation data was developed to mimic a well-studied narrow beam geometry. This geometry was used to validate the output data using its well behaved equations. The transmission of the Yb-169 spectrum through gold and platinum using a "narrow

beam" geometry was calculated using equation 8.43 from *Atoms, Radiation and Radiation Protection* by James Turner and compared to the data obtained through our simulations under similar geometry to test the validity of the simulation geometry [8]. The equation for calculating photon transmission through a shield in this geometry is

$$Transmission = \sum_i C_i e^{-\mu_i * \rho * d}$$

Where μ (cm^2/g) is the mass-energy attenuation coefficient of the material for photons of energy E_i, ρ is the density of the material (in g/cm^3), d is the thickness of the material (in cm), and C_i is the yield of photons with energy E_i. A histogram showing photon energies and yields for both isotope spectra are listed in figure 5. This equation was used along with data from NIST on the mass-energy attenuation coefficients, to calculate the theoretical values that the MCNP5 data should conform to.

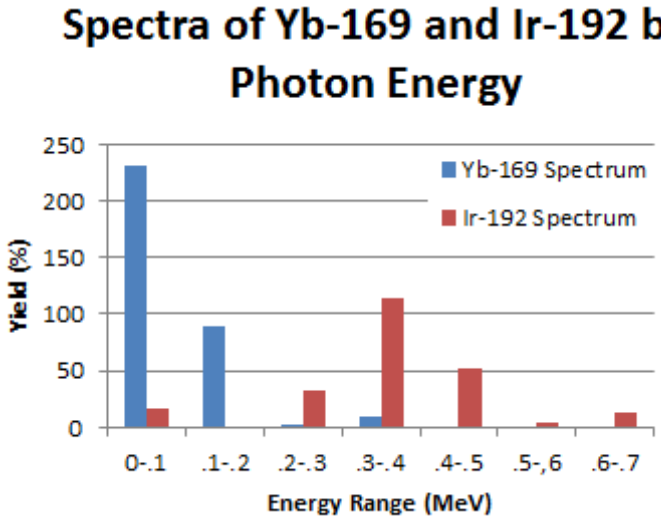

Figure 5 – The spectra of Yb-169 and Ir-192

Gold Nanoparticles

Since gold is a very good radiation shield, we also explored other ways of using gold to shield radiation from an HDR brachytherapy source. Gold nanoparticles (AuNP) were a possibility worth looking into, as functional nanoparticles are being researched for other medical purposes as well. We tested the shielding effectiveness of AuNP infused into tissue. To show a potential effect, we wanted to find the highest concentration of AuNP in tissue to make any

differences in photon fluence more pronounced. The highest concentration of AuNP found in the literature was 250 mM in vitro [7]. Thus, the mass of gold in 1 cm^3 of infused tissue is (with gold molar mass of 196.967 g/mol):

$$\frac{.25 \text{ mol Au}}{1000 \text{ cm}^3 \text{ tissue}} \times \frac{196.97 \text{ g}}{1 \text{ mol}} = \frac{.04924 \text{ g Au}}{1 \text{ cm}^3 \text{ tissue}}$$

With the amount of AuNP in the tissue found, we now solve for the mass ratio in tissue:

$$\frac{.04924 \ {}^{\text{g}}/_{\text{cm}^3}}{19.3 \ {}^{\text{g}}/_{\text{cm}^3}} = .00255 \text{ AuNP} : 1 \text{ Solution}$$

Which leads to a tissue to solution ratio of 0.99745 : 1, or .4936 g Au per g tissue. Using the NIST ICRU 4-component tissue, which has a density of 1.00 g/cm^3, we can solve for the density of the infused tissue:

$$\frac{.04924 \text{ g AuNP} + .99745 \times 1.00 \text{ g tissue}}{\text{cm}^3} = 1.04669 \ \frac{\text{g}}{\text{cm}^3}$$

These simulations were set up using the same narrow beam geometry as the previous simulations. The transmission ratio was obtained by simulating the AuNP tissue and normal tissue at various thicknesses and using normal tissue rather than vacuum as the baseline transmission values. The results from simulations of regular and infused tissue at the same thicknesses were compared to find the transmission reduction ratio that the infused gold nanoparticles caused:

$$\frac{\varphi_{\text{AuNP tissue}}}{\varphi_{\text{normal tissue}}} = \varphi_{\text{ratio}}$$

The Yb-169 spectrum was used for these AuNP simulations. Yb-169 has a lower energy spectrum than Ir-192, so the reduction in photon fluence caused by the AuNP in the tissue would be more easily noticed than if Ir-192 was used.

Results and Discussion

Figure 6 shows the results of the Iridium 192 simulations through gold, platinum, and stainless steel shields of varying thicknesses. Gold and platinum effectively shielded 30% of the photons from the Iridium spectrum at .5 mm thickness, while stainless steel was found to be fairly ineffective at thicknesses appropriate for brachytherapy catheter shielding (on the order of .5 mm)[9]. Iridium is one of the more commonly used brachytherapy sources, and the ability to shield 60% of photons at 1.5 mm could possibly be useful for Ir-192 brachytherapy.

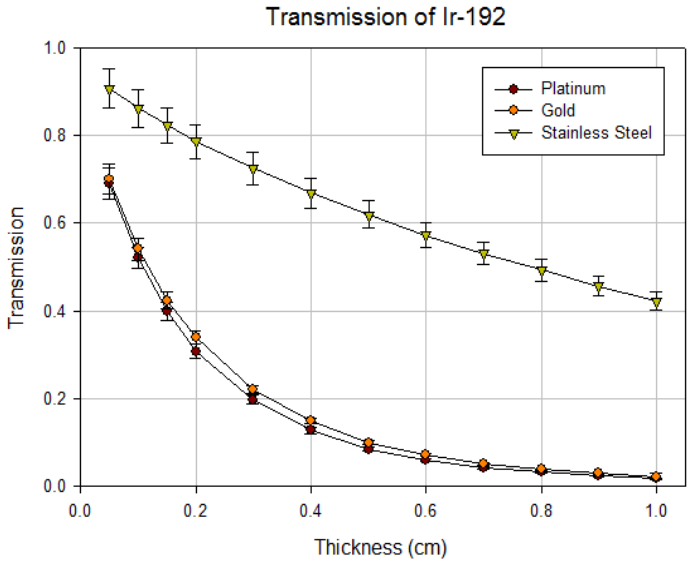

Figure 6 – Transmission of Ir-192 through Gold, Platinum, and Stainless Steel

Figure 7 shows the results of the Ytterbium 169 simulations through gold, platinum, and stainless steel shields of varying thicknesses. Unlike Ir-192, Yb-169 has a less energetic spectrum, so it is more effectively shielded by these materials, as shown in the graph. At .5 mm, both gold and platinum shields reduced fluence by approximately 90%, which is very encouraging for using Yb-169 as a

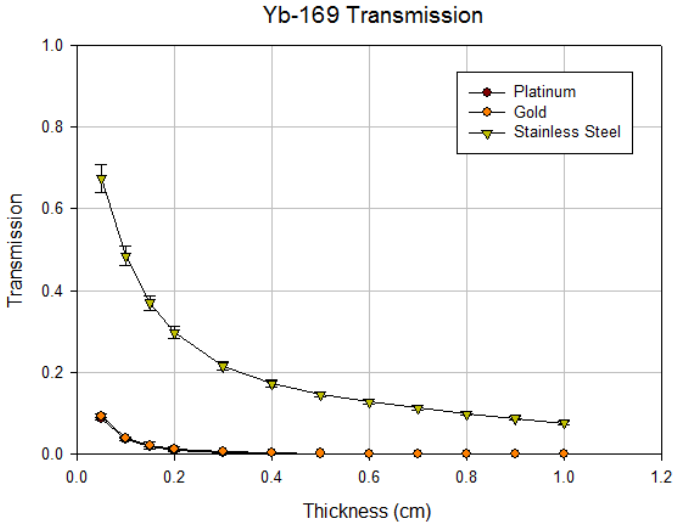

Figure 7 – Transmission of Yb-169 through Gold, Platinum, and Stainless Steel

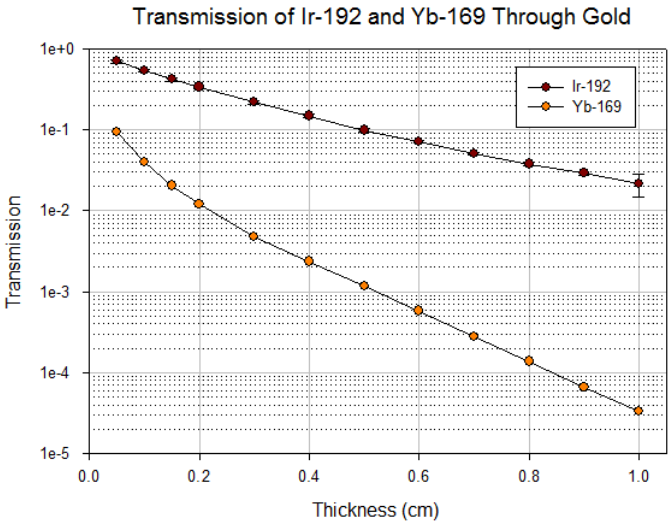

Figure 8 – Transmission of Ir-192 and Yb-169 through Gold on a seimlog scale

brachytherapy source with shielding. Figure 8 shows a comparison between the Ir-192 and Yb-169 fluence through gold shielding on a semilog scale. The tenth value (10% transmission, or .1) for Yb-169 occurs at .5 mm, while for Ir-192 it occurs at 5 mm, demonstrating how much more easily we can shield the Yb-169 spectrum than the Ir-192 spectrum. Stainless steel also shielded 50% of the photons at 1 mm thickness, which is enough of a result to encourage experimental trials, given how inexpensive this material is with respect to gold and platinum.

Figure 9 shows the results of the gold nanoparticle infused tissue simulations. At thicknesses of 1-10 mm, there was no significant difference between the regular ICRU 4-component tissue and the tissue infused with gold nanoparticles. The simulations were done out to one inch (25.4 mm) of thickness of infused tissue, and at that thickness there was only a 5% reduction in the photon fluence of the Yb-169 spectrum, which from our prior

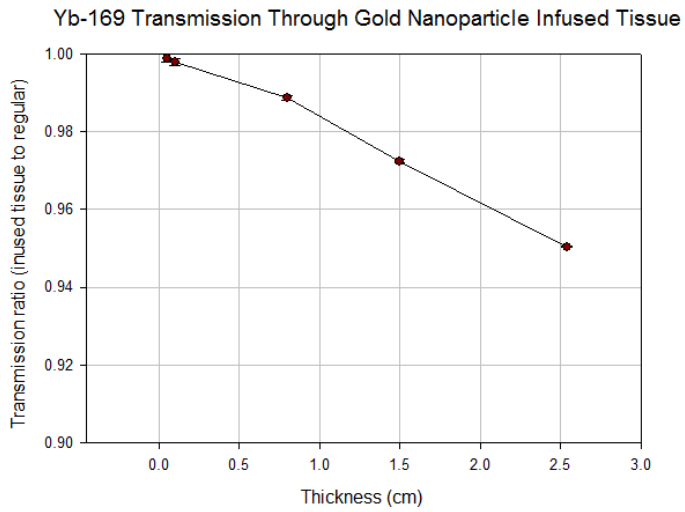

Figure 9 – Yb-169 transmission through gold nanoparticle infused tissue

simulations is more easily shielded than the Ir-192 spectrum. The conclusion from this series of simulations is that tissue infused with gold nanoparticles is not an effective shield for HDR brachytherapy purposes.

Future Work

The Yb-169 results lead to a need for experimental verification. If gold and platinum catheter platings reduce fluence by 90% in experimental trials, then using gold and platinum shielding in HDR brachytherapy could make this form of cancer treatment much more versatile and useful for treating tumors closer to vital organs. The adaptation of Yb-169 as a commonly used brachytherapy source could also increase treatment versatility. For the Master's thesis portion of this project, a realistic geometry for Yb-169 in a shielded catheter will be developed for MCNP5 use, and dose distributions will be found using these simulations. Measurements of Yb-169 via Gafchromic film may also be acquired.

References

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[4] http://www.varian.com/us/oncology/brachytherapy/permanent_seed_prostate.html

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[8] *Atoms, Radiation and Radiation Protection* by James Turner

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[F2] http://cancer.uc.edu/cancerinfo/TypesOfCancer/ProstateCancer/InterstitialBrachyther.aspx

[F3] http://www.nucleonica.net/Application/Help/Helpfiles/AttenuationGammaRadiation.htm