Radiolytic Production of Gadolinium Nanoparticles for Cancer Therapy

Hypothesis: The average particle size of the gadolinium will decrease as total absorbed dose increases within a nuclear reactor.

Background and Introduction: In the United States, cancer is the second leading cause of death and is a major public health problem worldwide [1], [2]. There were estimated to be 1,685,210 new cancer cases and 595,690 cancer deaths in the U.S. alone in 2016 [2]. Current treatment for various cancers include chemotherapy, radiation therapy, hormone therapy, and surgery. Although survival rates have improved from these treatments, each one has its drawbacks and limitations. Chemotherapy, for example, distributes the toxic therapeutic agents throughout the entire body, thus, damaging both cancerous and normal cells. This limits the amount of dose to the cancer cells while causing adverse side effects to the patient including weakness, hair-loss, and organ dysfunction [1].

An interest in nanoparticles (NPs) has increased over the last decade for researchers because of their ability to carry both drugs and imaging probes throughout the body [1]. Additionally, they can be uniquely designed to target the molecules of diseased tissues, thus, having the potential to increase the dose to cancerous cells while decreasing the dose to healthy tissues and organs [3].

Gadolinium neutron capture therapy (GdNCT) is another potential method for the treatment of cancer [4]. GdNCT takes advantage of the energy released when stable gadolinium-157 (^{157}Gd) is bombarded by a neutron, producing an excited ^{158*}Gd that decays by gamma emission, conversion electrons, and Auger electrons (Figure 1) [4] [5]. ^{157}Gd is appealing in NCT for its extremely high neutron absorption cross section (255000 barn) and short path length in tissue, restricting cell death to the gadolinium-containing regions only [5].

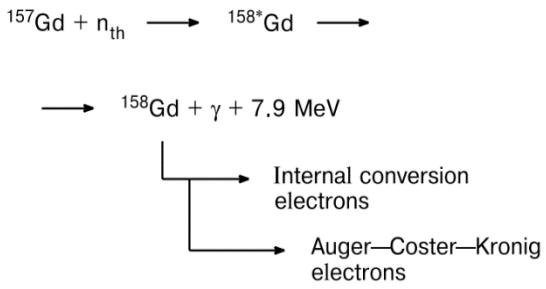

Figure 1: Gd decay scheme

The objective of this research proposal is to fabricate gadolinium nanoparticles for GdNCT applications by irradiation in a nuclear reactor. Average particle sizes of less than 100 nm are desired so that they can pass through the body and localize around tumors. Once the NPs have gathered around the tumor, neutron irradiation can occur using either a nuclear reactor or a neutron accelerator, destroying the tumor with minimal damage to the surrounding healthy tissues and organs.

Research Plan: The first step for this research project will be to determine the likely material components. A form of the gadolinium precursor, a reducing agent, a particle capping agent, and a solvent to prevent excess agglomeration will need to be used to create the gadolinium solution [6]. The solution will be distributed into 8 labelled vials, with Sample 1 being used as the un-irradiated reference sample. Samples 2-8 will be irradiated in the High Flux Isotope Reactor at a constant power (200kW) for times ranging from 30 to 1200 seconds (Table 1.)

Table 1 – Irradiation Times

Sample	2	3	4	5	6	7	8
Irradiation Time (s)	30	60	180	300	600	900	1200

I will complete dose calculations in order to determine the total absorbed dose for each sample irradiated in the reactor. The samples will be subject to both incident neutrons and gammas radiation. Therefore, the dose rate D_t is given by Equation (1)

$$D_t = K_n + D_\gamma \quad (1)$$

Where K_n is the neutron kerma rate and $D\gamma$ is the gamma dose rate. These dose rates will be determined using a Monte Carlo N-Particle (MCNP) code simulation of the reactor.

The samples will then be distributed onto a silicon wafer and left to dry. It is important that the radiation levels of the samples are safe and within NRC/reactor limits before removing them from the reactor for analysis. I will then image each sample under a scanning electron microscope (SEM) to determine the particle size distribution. An Energy Dispersive X-ray Spectroscopy (EDS) analysis will also be performed to verify the elemental composition of the particles.

Intellectual Merit: My background as a nuclear engineer is essential for the fulfillment of this project. It will combine my understanding of radiochemistry, reactor physics, and electron imaging with an engineering perspective. I completed a similar process for the production of boron nanoparticles in my Reactor Laboratory II class at Missouri University of Science and Technology, so I have first-hand experience in the process that needs to unfold. A much more comprehensive and in-depth analysis will need to be taken, however. I plan to collaborate with members of Oakridge National Laboratory to complete the irradiation procedure and use my knowledge of MCNP and scanning electron microscopy to determine the total absorbed dose for each irradiated sample.

Broader Impact: GdNCT is becoming a safe and effective way to destroy cancer cells with minimal damage to surrounding healthy cells. If the results are successful, my research will provide an efficient and valuable mean for creating gadolinium nanoparticles. This will make GdNCT cheaper and more accessible for cancer patients, resulting in the potential savior of countless future lives.

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