

## COVER PAGE

Title: Isotope Production R&D at Jefferson Lab's High-Power Electron Accelerators

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## COVER PAGE: SUPPLEMENT FOR COLLABORATIONS

The collaborating institutions are:

Thomas Jefferson National Accelerator Laboratory (Jefferson Lab, Jlab) PI: Dr. Andrew Hutton;  
Virginia Commonwealth University (VCU). PI: Dr. Jamal Zweit; and  
South Dakota School of Mines and Technology (SDSMT) PI: Dr. Douglas Wells

The three institutions bring together in-depth expertise to this research activity. Relevant to this R&D program are Jefferson Lab's expertise in SRF electron accelerators, radiation physics and controls and mechanical engineering; VCU's expertise in radio-chemistry, isotope separation and medical isotope research for therapy; and SDSMT's expertise in photo-nuclear reactions. Both VCU and SDSMT have extensive knowledge of medical isotope research and market needs.

Dr. Andrew Hutton of Jefferson Lab is the lead PI coordinating the overall research activity. The overall planning of each major aspect of this R&D, namely, the high power target system, irradiation of targets, measurement of yields at different energies, optimization of beam parameters, separation of the desired isotope, and evaluating radiochemical and chemical purity will be discussed and reviewed by all PIs and investigators. Once all PIs agree on a path for an activity, carrying out that activity is the responsibility of the PI of the expert institution. Each PI will communicate the progress and results to the collaborators at agreed upon intervals. Jefferson Lab will be responsible for providing the electron beam, designing the target system to handle 50kW of beam power, testing the target system and irradiating the targets at different energies. VCU will be responsible for quantitative gamma spectrometry and yield measurements, radio-chemical separation and analysis. SDSMT will be responsible for guiding the target irradiations. SDSMT, Jefferson Lab and VCU share the responsibility for measuring the yields and training a graduate student. Graduate student training will include simulations, participating in production runs and subsequent application experiments, including data analysis. All institutions will participate in establishing optimal beam parameters for  $^{67}\text{Cu}$  production.

Jefferson Lab's facilities include LERF and CEBAF, both of which are SRF continuous wave electron accelerators. Jefferson Lab has a well-equipped machine shop and radiological instrumentation. VCU's facilities include state-of-the art radio-chemistry lab, hot cells, and a radioisotope imaging facility for both SPECT/CT and PET/CT. SDSMT brings considerable experience with experiments in radioisotope production at accelerators.

	<b>Names</b>	<b>Institution</b>	<b>Year1 Budget</b>	<b>Year2 Budget</b>	<b>TOTAL Budget</b>
<b>Lead PI</b>	Dr. Andrew Hutton	Jefferson Lab	183,585	183,796	367,381
<b>Co-PI</b>	Dr. Jamal Zweit	VCU	134,226	146,517	280,743
<b>Co-PI</b>	Dr. Douglas Wells	SDSMT	73,800	77,186	150,986
<b>TOTAL</b>			391, 611	407,499	799,110

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## PROJECT NARRATIVE

### Background/Introduction

Addressing the demand and shortfall in supply of radioisotopes for nuclear medicine, national security, and many other applications in research and industry is enormously important because of its critical impact on each of these endeavors. Shortage of radioisotopes is the fundamental limiting factor in many biomedical research programs that attempt to exploit advances in molecular biology for targeted treatment with radioisotopes, as noted by both the National Academy of Sciences and the National Nuclear Science Advisory Committee [1, 2]. Applications of isotopes in research and medicine is a multi-billion dollar industry that serves nearly 20 million Americans each year in nuclear medical procedures, and serves an essential function in the nation's nuclear security and nuclear research. Despite this, the nation's supply of research radioisotopes is overly reliant on too few facilities and too few processes to provide adequate quantity and reliability of the supply [1, 3, 4, 5, 6, 7]. Moreover, the training of students and development of 'human capital' in nuclear sciences relevant to isotope production and nuclear medicine is lagging well behind the nation's need [1]. The infrastructure, science and technology and human capital associated with radioisotope production and research are closely connected to national needs in nuclear security, safeguards, non-proliferation, nuclear forensics, and radioisotope applications in the physical and biological sciences and engineering.

Numerous reports document extensively the national need for research radioisotopes, especially for beta/gamma emitters such as  $^{67}\text{Cu}$  that enable synchronous imaging and therapy, and alpha-emitters such as  $^{225}\text{Ac}$  that enable research on cellular-level, targeted molecular treatment of a variety of diseases. Given these needs, no robust sources exist today in the United States for these, and many other, research radioisotopes. Nuclear medicine and bio-medical research are perhaps the most critically-sensitive users of radioisotopes because of the large number of patients involved and the short half-lives of most medical isotopes. Nuclear medicine in the U.S. continues to be an important part of non-invasive disease diagnosis and treatment and has had enormous positive impact on improving patient care. Further major gains are not only possible, but thought to be highly probable, if adequate radioisotope supplies are available. In response to a congressional request, the National Academy of Sciences (NAS) issued a major report and recommendations on "Advancing Nuclear Medicine through Innovation" [1] where they point out that the age of "personalized medicine" is emerging where new advances in molecular biology and pharmaceutical sciences can be wed to nuclear techniques and radio-nuclides to specifically target unique individual medical profiles. The creation of new isotopes for medical research would enable further advances in these biomedical sciences.

We propose to conduct research and development on new methods of isotope production and processing technologies that will have major payoffs for making more isotopes available for research and applications and, importantly, contribute to the training of next-generation young scientists/engineers in relevant nuclear/radiological sciences. This project will address the pressing national need for high-priority research radioisotopes, specifically  $^{67}\text{Cu}$ , by photo-production using bremsstrahlung photons from a high-power electron linac. We propose to investigate the production of useful quantities of  $^{67}\text{Cu}$  using the  $^{71}\text{Ga}(\gamma, \alpha)^{67}\text{Cu}$  reaction, to measure the bremsstrahlung yield curves of this mechanism of production, to assess and develop effective separation technology, and to develop and test high-power, high-temperature targetry that will have broader applications for all photo-nuclear production techniques. We are not aware of this particular production method for  $^{67}\text{Cu}$ . In parallel, we will evaluate the  $^{68}\text{Zn}(\gamma, p)^{67}\text{Cu}$  reaction to enable a direct comparison of the two techniques for producing  $^{67}\text{Cu}$ .

### Present Situation

In order to get a full picture, we will describe the present situation regarding mostly commercial isotopes and turn our attention to research isotopes. Currently, technetium-99m ( $^{99\text{m}}\text{Tc}$ ) is the worldwide workhorse of nuclear medicine. In the next few decades there will be a steady increase in the demand for cyclotron-

and accelerator-produced research isotopes and radiopharmaceuticals (other than  $^{99m}\text{Tc}$ ). Globally, over 10,000 hospitals use radioisotopes in medicine. The vast majority of these isotopes are produced by research reactors. And there are, currently, 232 operational research reactors in 56 International Atomic Energy Agency (IAEA) member states [8]. Most of these reactors are used for nuclear research, including the ones involved in isotope production. Only 78 out of these 232 research reactors are used for isotope production [9]. Twelve research reactors, distributed over 11 member states, are temporarily shut down [10], of which three are involved in isotope production [9]. The IAEA database also indicates that seven research reactors are under construction or planned in 6 member states [11]. It is not clear how many of these reactors will be involved in isotope production. More than half of the research reactors involved in isotope production (43 out of 78) are 40 years old or older [12].

Novel ways of producing research isotopes for medical or other purposes are necessary to address the issues of: (i) the production of isotopes that reactors cannot produce (generally proton-rich isotopes), (ii) the production of isotopes in short supply and (iii) the looming shortage of isotopes as aging reactors are shut down. New isotope production strategies are needed, for not only the current generation of research isotopes and radiopharmaceuticals, but for future products as well. This proposal is for a two-year research program to develop a technology platform which will enable production of relevant radioisotopes for medical and industrial research and applications. The project is a collaboration of Thomas Jefferson National Accelerator Facility (Jefferson Lab, JLab), [led by Dr. Andrew Hutton], Virginia Commonwealth University (VCU), [led by Dr. Jamal Zweit] and South Dakota School of Mines (USDMS), [led by Prof. Douglas Wells]. The three institutions collectively bring extensive expertise in all the critical areas required to develop electron accelerator-based techniques for production of radioisotopes, namely i) high power electron accelerators and targetry (Jefferson Lab), ii) separation and evaluation of the produced isotopes by radiochemical and chemical analysis (VCU) and iii) electron- & photo-nuclear reaction physics (SDSMT). The ample infrastructure at these institutions makes this collaboration well suited for the proposed R&D. The emphasis is on the generation of data leading to new methods of production. The DOE isotope program is already investing in radioisotope production research; and the R&D program proposed here will introduce new opportunities to the portfolio. We will conduct research on new isotope production and processing technologies that will ultimately lead to the steady availability of isotopes for essential research and applications. The proposed research will provide an opportunity to train the next generation of nuclear scientists in areas related to isotope production, separations and radiochemistry.

#### *Electron Accelerators as instruments for radioisotope production*

High power (~100 kW) electron accelerators are well suited for the production of some important isotopes for medical and industrial applications. Two of the methods to produce isotopes at electron accelerators are: i) directly irradiate the isotope target with the electron beam and ii) generate bremsstrahlung photons, using a radiator, which in turn irradiates the target. There are additional methods, such as fast-neutron secondary reactions and slow neutron capture, which electron accelerators are well-positioned to support, especially with the use of depleted uranium or enriched uranium and sub-critical assemblies. The latter would allow electron-driven isotope production systems to produce both neutron-rich and proton-rich isotopes.

The first method, direct irradiation with electrons deposits a great deal of energy in the target and photon conversion takes place in the isotope target. A large fraction of the electron energy goes into energy loss mechanisms in the target that do not contribute to the production of photons.

The second method, using a radiator, generates photons in a material that is physically isolated from the isotope target and makes heat management simpler. For sufficiently high Z targets, a large fraction of the electron energy is converted into bremsstrahlung photons. While the photo-nuclear peak cross-sections are generally lower than for proton induced reactions, photo-nuclear resonant cross sections have large widths. This feature, in conjunction with the large flux of photons that can be produced at high power electron

accelerators, enables substantial yields of desired isotopes by photo-production because the yields are proportional to the integral of the flux and the cross section.

In addition, the high penetrating power of photons enables much thicker targets than can be used with proton beams, which further boosts photo-nuclear yields, and alleviates some of the heating and corrosion issues encountered when using high power density proton beams. Jefferson Lab houses two Superconducting Radio Frequency electron accelerators well suited for this R&D. One is the Low-energy Electron Recirculator Facility (LERF) and the Continuous-wave Electron Beam Accelerator Facility (CEBAF). The capabilities of these accelerators will be described in the Proposed Research and Methods section.

### Photonuclear Reactions as a Source of Radioisotopes

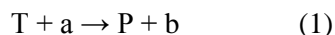
The fundamental production mechanism that we propose to explore is photo-nuclear reactions at giant dipole resonance energies (nuclear excitation energies in the 10-50 MeV region). Note that, historically, this production mechanism has been discounted because of the difficulties in separating chemically-identical species that are produced from ( $\gamma$ , n) reactions in the original target, which results in a low specific activity of the final product. We propose to focus on production of species that differ chemically from the target, which are produced from ( $\gamma$ , charged-particle) reactions. These photo-nuclear reactions create daughter species with a different atomic number from the target. In these cases, chemical separation is often feasible for separation and high specific activity can be achieved. First, though, we discuss the photo-production principles.

### Photo-production Principles

Radioactive nuclides can be produced through radio-activation using any radiation (particle or quantum) that carries energy sufficiently high to induce emissions. The principle is as follows:

- High energy radiation is directed onto a material (Target).
- Either the total energy or part of it is transferred to the nucleus of an atom of the target.
- The nucleus is 'excited' to a higher energy level, and thus unstable.
- Energy is removed from the nucleus by emission of a particle (neutron, proton,  $\alpha$ ,  $\beta$ ,  $\gamma$ ...).
- Thus a daughter nuclide is produced that may or may not be unstable. If it is unstable, it is a radio-nuclide.
- By delayed emission of another particle (usually a beta-particle, followed by prompt gamma emission(s)) the nuclear energy is brought to a more stable or ground state level (Radioactive decay).

This process can be expressed thus:



Or, more concisely as:



where:

T = target nucleus

a = incident radiation particle or quantum

b = nuclear particle/quantum promptly emitted

P = product nuclide (activation product; normally radioactive)

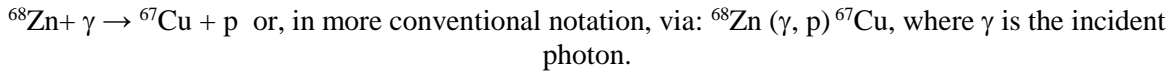
**T** basically might be any nucleus, **a** can be a neutron, proton, triton, a heavier ion, or in our case a photon. **b** most likely is an uncharged nucleon (neutron) but can be a proton or other particle. Which one is emitted depends upon the nuclear properties of the target atom as well as the type of and, in particular, the incident energy of the activating radiation.

This process is applied frequently for analytical purposes (activation analysis) whereby reactor neutron irradiation is used for radio-activation in most cases. However, the radio-nuclides that are produced can be

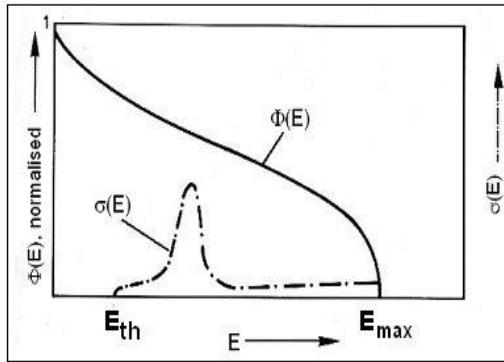
used for other purposes, e.g. medical applications, either for diagnostics or for radiotherapy. Radio-nuclides can be applied as radio-indicators (“tracers”), e.g. for monitoring of industrial or natural processes as well. One fundamental difference between neutron activation and photon activation is that neutron activation generally produces neutron-rich (proton-poor) nuclear species, whereas photon activation generally produces proton-rich (neutron poor) nuclear species. Thus, for the most part, the photon activation methods of this proposal should be viewed as complementary to neutron activation, rather than in direct competition.

For the production of radio-nuclides by photo-reactions a strong source of high energy photons is required, most favourably from a bremsstrahlung source powered by an electron linear accelerator. To obtain appreciably high activity yields, the average current of the photon-producing electron beam should be as high as achievable, and the maximum energy of the bremsstrahlung continuum (equal to the incident electron kinetic energy) should be not less than  $\approx 30$  MeV to  $\approx 50$  MeV or higher (see below, quantitative considerations). For this proposal, bremsstrahlung beams from electron linacs at  $\geq 100$  MeV and  $>1$  mA are available.

Estimation of the radioactivity yield, i.e., the number of active nuclides produced per time unit, is determined by three physical parameters, namely i) the total number of target atoms to be activated, ii) the energy distribution of the incident photon radiation and iii) the activation cross-section of the respective photo-nuclear reaction (see Figure 1; Eq. (2)). As one example:  $^{67}\text{Cu}$  can be produced through bremsstrahlung irradiation of  $^{68}\text{Zn}$  as a target. According to Eq. (1) the photo-nuclear reaction is:



Similarly,  $^{67}\text{Cu}$  can be produced via the  $^{71}\text{Ga} (\gamma, \alpha) ^{67}\text{Cu}$  reaction, as in this proposal.



**Figure 1: Bremsstrahlung continuum and photonuclear cross section**

$E$ : Incident bremsstrahlung energy.

$\Phi(E)$ : Energy-differential bremsstrahlung photon flux density.

$\sigma(E)$ : Energy-differential cross-section of the photo-reaction.

$E_{th}$ : Threshold energy of the photo-nuclear reaction.

$E_{max}$ : Maximum energy of the bremsstrahlung continuum.

The activity value of the product nuclide ( $^{67}\text{Cu}$ ) is obtained from Eq. (2), which is valid for all nuclear activation processes, is:

$$A(t_i) = N \cdot \int_{E_{th}}^{E_{max}} \phi(E) \cdot \sigma(E) dE \cdot (1 - e^{-\lambda \cdot t_i}) \quad (2)$$

where:

$A$  = Activity induced ( $\text{s}^{-1}$ )

$t_i$  = Exposure period (s)

$N$  = Number of target nuclides to be activated

$E_{th}$  = Threshold energy of the nuclear reaction (MeV)

$E_{max}$  = Maximum of the bremsstrahlung continuum (MeV)

$\phi(E)$  = Energy-differential bremsstrahlung flux density ( $\text{cm}^{-2}\text{s}^{-1}$ )

$\sigma(E)$  = Energy-differential reaction cross section ( $\text{cm}^2$ )

$\lambda$  = Decay constant of the reaction product ( $\text{s}^{-1}$ ) =  $\ln(2)/\text{half-life}$

Note that for “large” targets (by volume or mass), to estimate the yield one may have to sum over individual target sub-volumes to properly account for spatial variations on flux-density. Among the quantities in Eq. (2), the following can be optimized to meet the requirements for radio-nuclide production:

- N The total mass of the target should be optimized for the application to provide the activity of interest and, simultaneously, to avoid undesirable handling of excessively large amounts of radioactive matter.
- $E_{\max}$  The output energy of the accelerator-produced electron radiation should be optimized in a way to set it sufficiently high to produce appreciably high desirable activities, but low enough to minimise contamination by production of undesired radio-nuclides through higher-order reactions.
- $\phi$  The photon flux density should be selected as high as practical through an appropriate setting of the electron beam current (or the total output power of the accelerator, respectively).
- $t_i$  Longer exposure periods yield higher activities. However, other factors that might limit the exposure time have to be accounted for, too; see below.

Note that for many photo-nuclear reactions the relevant cross sections are unknown or poorly known, and may need to be measured. Equally useful to cross sections, for isotope production, are yield curves as a function of electron beam energy:

$$Y(E_{\max}) = \int_{E_{th}}^{E_{\max}} \phi(E) \cdot \sigma(E) dE$$

To find the optimal experimental parameters, other facts have to be considered as well. Among these are the behaviour and induced radioactivity of all materials involved that are subject to extremely high energy/high particle flux bombardment, over a possibly long exposure period. Also, one has to account for radiolytically induced corrosion reactions that might lead to problematic effects on the target. Note that as one changes the electron beam energy, and therefore the bremsstrahlung end-point energy, new photo-production reaction channels may open, and the ratio of different photo-production yields will change. Thus, a careful experimental and calculational program is important to assess optimal end-point energies for particular targets and particular desired radioisotopes.

Electron beam energies over the range of 20 to 100 MeV are ideal for photonuclear production of isotopes such as  $^{67}\text{Cu}$ . In this energy range, in thick targets, the isotopic yield/unit power is considerably higher with gamma rays than for protons and neutrons [13].

### Opportunity

Historically,  $(\gamma, x)$  reactions have not been exploited for isotope production because of the difficulty of achieving useful specific activity, although the technique is well-known to be capable of production of large quantities of total activity, and to be practical for many other applications [see Ref. 13 and references therein]. However, all photo-nuclear reactions with charged-particle exit-channel products enable, in principle, relatively simple post-irradiation chemical separations and subsequent high specific-activity products because of the fact that the reaction products are chemically different than the original target material.

In addition, there are important advantages to adding electron accelerators to the U.S. portfolio of isotope production facilities. Electron beam accelerators are substantially simpler to operate, much cheaper to construct, and carry far less of a regulatory, safety and environmental burden than do nuclear reactors. Development of isotope production capability using electron accelerators would open a straightforward path to ensuring better access to isotopes throughout the U.S. and a more reliable domestic supply of short-



lived isotopes that are amenable to production using this technique. Furthermore, electron accelerators, when coupled to sub-critical assemblies, are capable of producing large quantities of neutron-rich radio-isotopes as well as proton-rich radio-isotopes.

We examined radionuclides that are favourable for photo-production and that have been identified by NSAC, DOE, or NIH as of interest [1, 3, 4, 6, 7]. Nuclides that are of particular interest are those produced in reactions such as,  $(\gamma, p)$ , or  $(\gamma, \alpha)$ . The production of no carrier added species is achievable when an element, different from the produced isotope, is used as a target material. Some  $(\gamma, n)$  reactions however, namely those where the radioactive chain enables no carrier added separation, such as  $^{226}\text{Ra}(\gamma, n)^{225}\text{Ac}$ , are of interest as well.

Reasonable yields of isotopes ( $\sim 10\text{s of } \mu\text{Ci/g.hr}$  or  $\sim \text{mCi/g.hr}$ ) require kW of beam power. Our analysis has indicated specific isotopes which could be optimally produced in a facility such as Low-energy Electron Recirculator Facility (LERF). This proposal focuses on  $^{67}\text{Cu}$  which is an attractive isotope for both therapy and imaging because it combines both beta and gamma emissions. It can be used to synthesize various compounds including small molecules and macromolecules. We propose producing  $^{67}\text{Cu}$  in gallium (Ga) via the  $^{71}\text{Ga}(\gamma, \alpha)^{67}\text{Cu}$  reaction, while not excluding the traditional  $^{68}\text{Zn}$  target.

#### Choice of $^{67}\text{Cu}$

We chose  $^{67}\text{Cu}$  because it is approved for human trials; it has been identified as a high priority research isotope by DOE; and among its useful attributes it emits both useful therapeutic radiation as well as imaging radiation. It emits both a beta particle of useful energy (mean energy 141 keV) for therapy and a gamma ray (93 keV and 185 keV) of energy that can be used with SPECT imaging systems; in this regard,  $^{67}\text{Cu}$  is a truly theranostic isotope. Initial research shows promise in the treatment of Non-Hodgkins Lymphoma, Ovarian, Bladder and Colorectal cancers. However,  $^{67}\text{Cu}$  has not been regularly available for several reasons. As noted in a recent review of the medicinal and research uses of copper isotopes, “This isotope ( $^{67}\text{Cu}$ ) of copper, owing to interesting decay properties, is potentially useful for radio immunotherapy, but due to limited availability, research that actually uses this isotope are few, compared to other Cu isotopes” [14]. In addition to macromolecules, such as antibodies and peptides, it can also be used to radiolabel small molecules for imaging and therapy. A comprehensive review of the production, separation and use of this isotope can be found in the referenced publication [15].

This R&D aims at a method for realizing a reliable and steady supply of  $^{67}\text{Cu}$  at a reasonable cost using beam from a high power electron linac hitting a new hither to unexplored target downstream of a radiator (high Z material such as tungsten). This target, namely gallium (Ga), has a high boiling point ( $2200^\circ\text{C}$ ) and a low melting point ( $30^\circ\text{C}$ ) and shows much promise in  $^{67}\text{Cu}$ . Since gallium does not boil nor tungsten melt at any reasonably achievable temperature, the target can be directly exposed to the electron beamline during irradiation, simplifying the design.

LERF at Jefferson Lab can deliver over 100kW of beam power. Since beam power is a very important parameter in isotope production, developing high power target technology ( $\sim 50\text{kW}$ ), as proposed here, will be a major step in providing an alternate and complementary method of isotope production. The techniques developed during this research program are expected to be applicable for production of other important isotopes as well, and would add novel production and processing technologies to the DOE's portfolio of essential isotopes. The proposed research will train students in areas related to isotope production and radiochemistry.

#### Expertise

The three collaborating institutions bring specialized core competencies to this research. In broad terms, Jefferson Lab's expertise is in high power Superconducting Radio Frequency (SRF) electron accelerators, high power beam dumps and targetry. VCU brings expertise in isotope separation, from the irradiated

target and other impurities (radioactive and stable), quantify isotope/s yields, characterize radiochemical properties and determine the quality of  $^{67}\text{Cu}$ . SDSMT brings expertise in photo-nuclear reactions specializing in isotope production. Jefferson Lab, VCU and SDSMT have been collaborating on isotope production for over two years and have an established relationship.

Dr. Andrew Hutton is the Associate Director for Accelerators at Jefferson Lab. He has contributed to accelerator science and technology at CERN and SLAC and holds patents for innovations in the field. Dr. Pavel Degtiarenko is a senior radiation physicist in the Jefferson Lab Radiation Control Department. He specializes in model calculations and evaluation of the radiation environment at Jefferson Lab, including effects of high power electron beam interactions with materials and structures. He holds several U.S. patents, three of which involve new methods of cooling high power particle accelerator targets. Dr. George Kharashvili is a radiation physicist in the Jefferson Lab Radiation Control Department. His research interests include applications of accelerators in research and technology, interaction of radiation with matter, and radiation metrology. Mr. Kevin Jordan is a senior engineer at Jefferson Lab. He is an expert in RF inductive heating. A number of his many patents include patents in Boron Nitride nanotube technology. He has also authored a paper titled, “BNNT-Mediated Irreversible Electroporation: Its Potential on Cancer Cells”. Mr. Joseph Gubeli is a diagnostics engineer whose skills include rigorous mechanical and thermal simulations and design.

Professor Jamal Zweit is a Professor of Radiology and affiliate Professor of Biochemistry and Molecular Biology, Radiation Oncology and Molecular Pathology at VCU. Dr. Zweit is the founding director of CMI, the Center for Molecular Imaging at VCU. He is internationally recognized for his expertise in multi-modality molecular imaging, radiopharmaceuticals, radiation & medical physics, and nanotechnology, predominantly in cancer biology and therapy. He has over 25 years of experience in radioisotope production, radiopharmaceuticals for imaging and therapy, with emphasis on radio-metal-based PET imaging, and targeted therapy. Professor Sundaresan Gobalakrishnan is the head of the Multi-modality Imaging Laboratory and scientist manager of the Center for Molecular Imaging. His research focus is on the *in vivo* evaluation and validation of multi-modal imaging approaches, including studies of targeted hybrid probes.

Prof. Douglas Wells was the head of Idaho Accelerator Center at Idaho prior to becoming the Dean of Graduate Education at South Dakota School of Mines and Technology. His extensive research interests include Photon Activation Analysis and production Medical Isotopes with electron accelerators. His background lies primarily in photonuclear physics ( $\gamma$ ,  $x$ ) reactions and the inverse capture ( $x$ ,  $\gamma$ ) reactions, and applications thereof. Prof. Frank Strieder has specialized in low-energy nuclear physics, especially nuclear astrophysics, including capture reactions ( $x$ ,  $\gamma$ ) and their inverse ( $\gamma$ ,  $x$ ). Prof. Stanley Howard is an internationally recognized expert in metallurgical science and engineering, including high-purity separations, corrosion and thermodynamic properties of liquid and solid metal systems.

## **Proposed Research and Methods**

### *Jefferson Lab's electron accelerator capabilities*

Jefferson Lab houses two SRF accelerators. Both will be used during this R&D period. CEBAF is a high-energy accelerator, up to 12 GeV for Nuclear Physics research. The beam current at CEBAF is limited by the 1 MW beam dumps in the experimental halls and rarely exceeds  $\sim 100\ \mu\text{A}$ . CEBAF's injector can deliver beam energies up to 123 MeV and is limited in current to a few microA. LERF's beam energy is over 150 MeV with beam currents up to 1 mA. LERF's injector beam energy is up to 10 MeV with currents up to 6 mA.

In this R&D proposal we aim to demonstrate the feasibility of production of  $^{67}\text{Cu}$  at high energy (up to 100 MeV) and high power (10s of kW) electron accelerators. We have the following objectives:

- i) Demonstrate a target system that can handle ~50kW of beam power (Jefferson Lab);
- ii) Quantify isotope/s yields and separation efficiency of  $^{67}\text{Cu}$  from the irradiated target (VCU);
- iii) Measure impurities (radioactive and stable), and characterize the radiochemical properties and quality of  $^{67}\text{Cu}$  (VCU)

While doing so, we will experimentally investigate optimal beam parameters for production and provide training opportunities for students. (VCU, SDSMT, Jefferson Lab).

In order to carry out our objectives, we have to make choices regarding target materials and the types of tests to conduct.

High power electron beam can activate the experimental area when the beam energy exceeds neutron production thresholds of the materials it traverses. One of the optimizations for this R&D is to limit neutron production to the level that the existing shielding around the beam dump can contain. Our strategy is to use LERF's capability of very high current ( $\leq 6$  mA) at low energy ( $\leq 10$  MeV) for high power tests of components and to use CEBAF for high energy ( $\geq 18.5$  MeV), low current ( $\sim$ few microAmps) for isotope irradiation tests. The beam time at LERF is dedicated to these tests only and there is a beam time cost for each test. Since beam time at LERF comes at a minimum of an 8-hour shift, it is essential to keep the tests at LERF to a minimum in order to keep within the budget for this R&D. At CEBAF's injector beamline, we can conduct high energy, low current tests parasitically at opportune times such as beam studies or when experimental halls cannot take beam.

It should be noted that for this R&D all the tests are at the injectors of LERF and CEBAF. Tests at LERF injector are at low energy but at high beam current, hence high beam power. The tests at CEBAF injector are at higher beam energies but at low beam current, hence at low beam power. The two tests are parallel and are independent of each other. Together they provide a path to isotope production at higher energies and higher powers, where LERF is the ideal place for production.

#### Bremsstrahlung Converter and Target

As can be ascertained from the section on Photo-Production Principles, very high power densities may be induced into both the bremsstrahlung converter and the material to be converted. In general, a converter will be of material such as Tungsten or Tantalum which has the necessary properties of a high conversion rate of electrons to photons and the material properties to withstand high power densities and accompanying temperature excursions. The optimization of such a converter is far from a trivial matter however and is also a part of this R&D. There are necessary trade-offs in the dissipation of the incident electron energy, the cooling of the converter, the distance of the converter from the target of interest and the resulting attenuation of the appropriate energy photons intended for the target. A similar set of difficult optimizations are necessary for the target to be converted. A target is subject to not only irradiation from gamma rays of sufficient energy to cause nuclear conversions, but, also irradiation from gamma and electrons of insufficient energy to cause conversions. In all cases, almost all of the incident energy must be dealt with by the target. Such power densities can easily boil target material and induce chemical or radiolytic reactions between different materials.

We chose gallium for target material because of its interesting properties. It has a high boiling point (2200  $^{\circ}\text{C}$ ) and a low melting point (30  $^{\circ}\text{C}$ ). In addition, we will use chemically pure, natural Ga due to cost considerations also because the objective is to investigate the power handling capability of the target. Naturally occurring Ga and Zn, even when highly chemically pure, have other isotopes or contaminants ( $^{71}\text{Ga}$  is  $\sim 40\%$  of naturally occurring Ga and  $^{68}\text{Zn}$  is  $\sim 20\%$  of naturally occurring Zn) and when irradiated in a photo-production process, yield unwanted or contaminating species, some of which are radioactive.

The use of a target enriched in the isotope of interest, (in other words the isotope that is converted through the production process to the wanted radio-isotope), increases the yield of the photo-production process and

reduces contaminating species. But, isotopically enriched targets can be very expensive and since only a very small portion of the target is converted, a necessary optimization is in the method to recover the unconverted enriched target material. For this R&D, we will use chemically pure targets whose composition is known. (See Table 1 for contaminants in gallium at various levels of chemical purity). The choice of chemical purity as opposed to isotopical enrichment is driven by cost and recognizing that the objectives are to investigate the target for power handling capability and isolate  $^{67}\text{Cu}$  post-irradiation.

Purity Levels				
4N	6N	7N	MBE Grade - 8N	
99.99%	99.9999%	99.99999%	99.999999% Plus	

Total Impurities			
<50ppm	<500ppb	<50ppb	<10ppb

Critical Elements				
Cu	<10ppm	<0.5ppb	<0.5ppb	<0.5ppb
Zn	<5ppm	<3.0ppb	<1.0ppb	<1.0ppb
Cd	<5ppm	<0.5ppb	<0.5ppb	<0.5ppb
Si	<2ppm	<1.0ppb	<0.5ppb	<0.5ppb
Fe	<5ppm	<0.1ppb	<0.1ppb	<0.1ppb
Al	<5ppm	<0.2ppb	<0.2ppb	<0.2ppb
Ca	<5ppm	<5ppb	<5.0ppb	<5.0ppb
Na	<5ppm	<0.2ppb	<0.2ppb	<0.2ppb
Pb	<10ppm	<0.5ppb	<0.5ppb	<0.5ppb
In	<10ppm	<1.0ppb	<0.5ppb	<0.5ppb

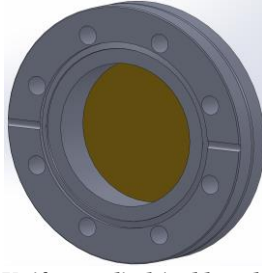
Analysis Method: Glow Discharge Mass Spectroscopy (GDMS)

*Table 1 Impurities in gallium at different chemical enrichment levels [16]*

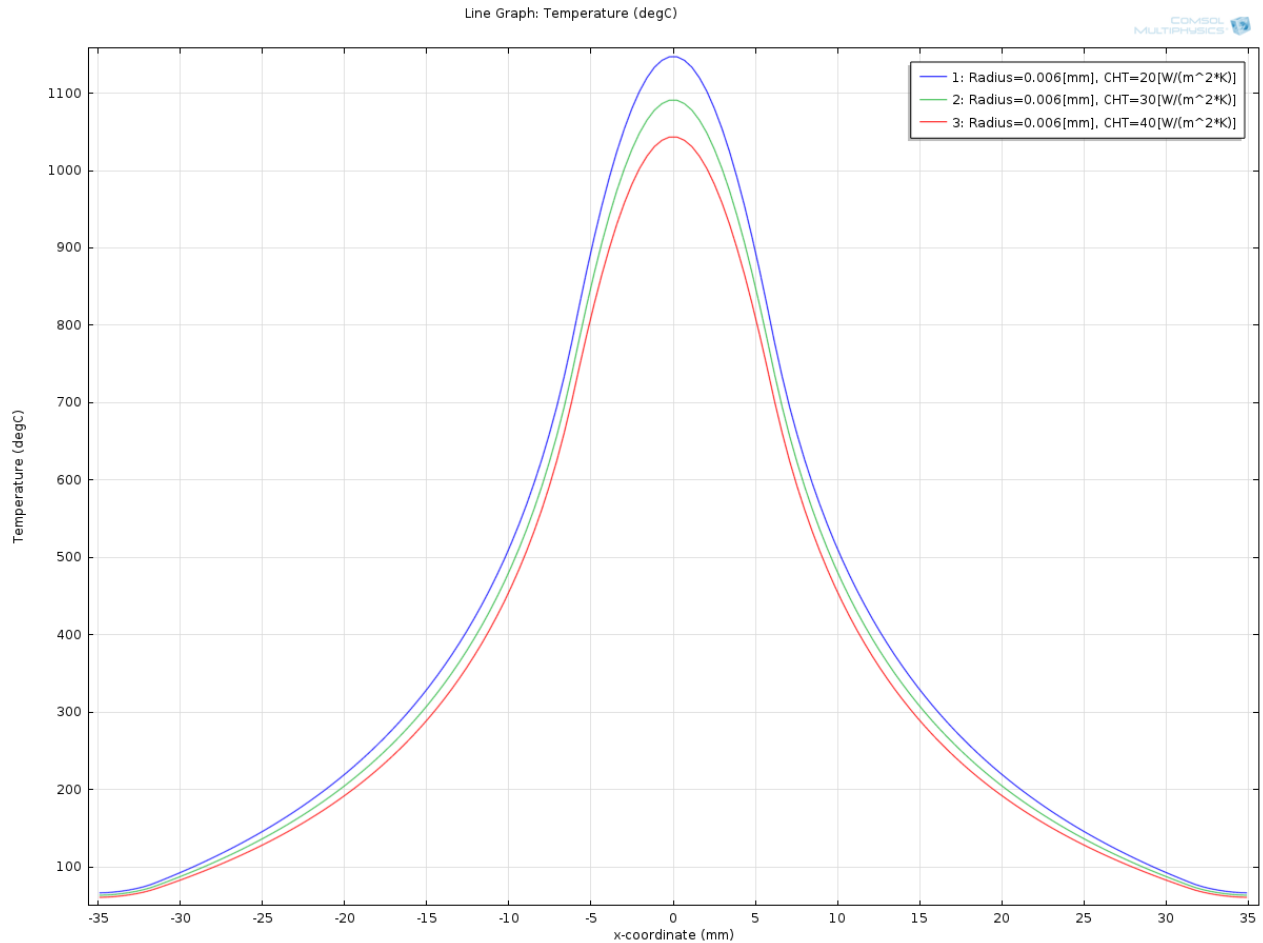
### Beam Exit Window

The electron beam exit window must be able to handle the current density of the beam without losing its thermal and structural integrity. The choice of material for the window is Beryllium (Be) due to its high melting point (1300 °C) and low density. The Be exit window (see below) will absorb nearly 600 W (at 5 mA) of beam power and should have sufficient heat handling capacity to maintain its integrity. However, we recognize that at higher energy, (for example, at 40 MeV), the window needs to handle only 1.25 mA.

We have previously modeled a Be window of 6.35 cm aperture and 380  $\mu\text{m}$  thickness and concluded that the window will withstand 1 mA of current and hold accelerator vacuum when the flange and the window are cooled and the electron beam diameter is at least 12 mm. Cooling of the flange can be accomplished by circulating water and cooling of the window can be accomplished by a modest flow of (1m/s) of nitrogen gas. Through beam optics set up, it is possible to create a 12 mm beam spot on the window (Figures 2 and 3). We will continue the modeling and simulations to arrive at a Be window thickness and cooling schemes to handle 1.25 mA and higher beam currents.



**Figure 2. Beryllium exit window – Uniform cylindrical heat load applied to the center of window. Outer Diameter constrained and temperature HELD AT 20° C. 14.7 PSI applied to the back of the window. Convective Heat Transfer coefficients in the range of 20-40 W/m²K applied to the back of the window.**



**Figure 3. Beryllium exit window temperature in the CHT range 20-40 W/m²K at a beam radius of 6 mm**

### Tungsten Radiator

For the tungsten radiator, the low energy ( $\leq 10$  MeV) beam at 50 kW has similar features as the beam exit window with beam power deposition of about 22 kW (5 mA and 2 mm radiator). As with the Be exit window, at 40 MeV and 1.25 mA, the power deposition is a bit over 5 kW, removing this much heat from the radiator is non-trivial. The optimization of the radiator for the highest achievable photon flux will be investigated as part of the global optimization of  $^{67}\text{Cu}$  yields. (One of Jefferson Lab's investigators (P.D.) holds a patent on a rotating radiator for heat load distribution). We will investigate methods to handle 1.25 mA and higher beam currents.

### Gallium Target

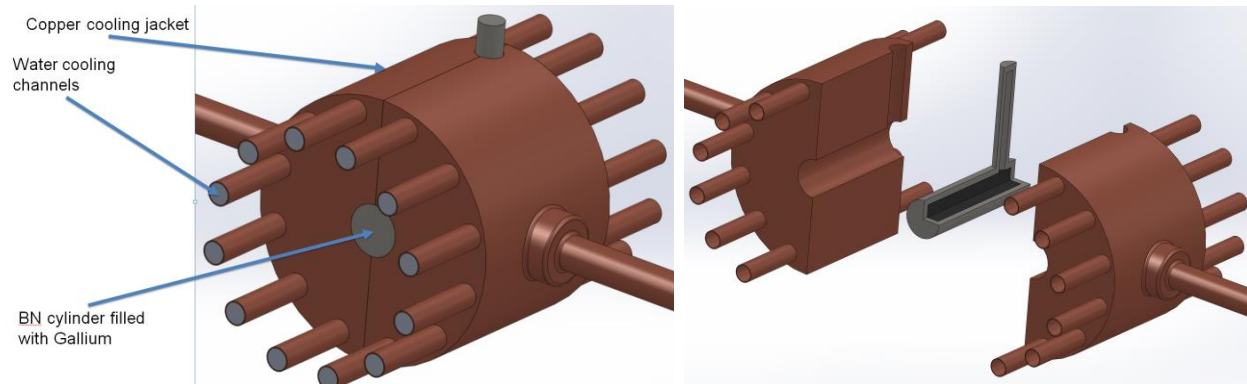
Gallium is a solid below 30 °C and a liquid above that temperature. Its high boiling point makes it an attractive target which can handle high beam power.

**Target – Material** - Gallium (99.9999% chemically pure)

**Target – Thermal** - Allowed Temperature rise: 2000<sup>0</sup> C, max. at 50kW of beam power

**Target Holder- Cooling** – Water cooled, cooling water temperature – 35<sup>0</sup> C (to ensure Ga stays as liquid)

**Target Holder- Chemical** – Lowest possible copper content to avoid contamination from other copper isotopes.

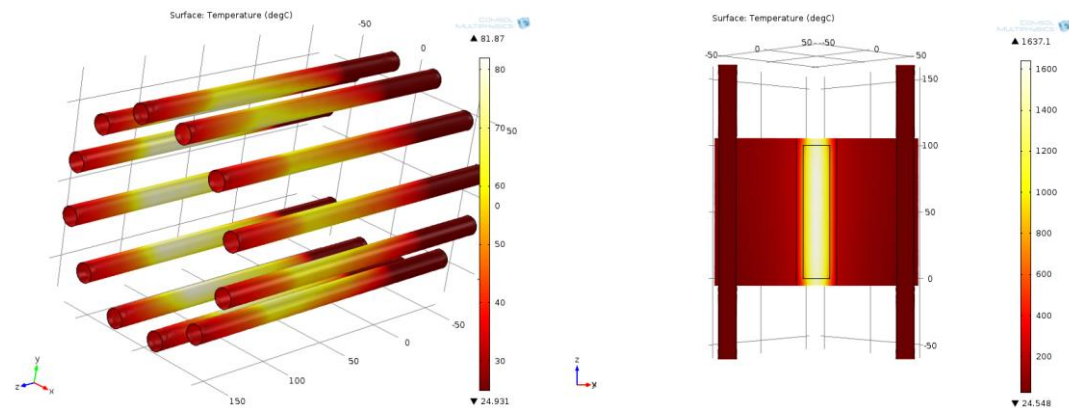


**Figure 4. Target System – Preliminary design**

Jefferson Lab has in-depth knowledge and experience in designing high power beam dumps (up to 1 MW). We bring this experience to the design of the target system. Figure 4 shows a preliminary design for the copper jacket that houses the gallium target holder. A boron nitride (BN) cylinder holds the gallium target avoiding contamination from copper. BN is chosen for its high melting point (3000 °C) and high thermal conductivity (BN's thermal conductivity can range from 3 to 600 W/(m K). We will use the hexagonal BN which has higher thermal conductivity.

In our simulations, we used BN at a modest 30 W/(m K). The gallium target is completely encased within the BN cylinder. The clam shell design of the copper jacket facilitates removal and installation of the cylinder. The challenge in this R&D is to maintain good thermal contact between the BN cylinder and the copper jacket.

The simulations shown in Figure 5 use a gallium cylinder with a radius of 10 mm and a length of 100 mm and a water flow rate of 5 GPM through each channel.



**Figure 5. Water wall temperature (left) and the temperature of the target (right)**

The simulations were under the following conditions:

- A water flow rate of 5 GPM through each channel
- The gallium cylinder has a radius of 10 mm and a length of 100 mm
- The boiling point of gallium is 2,205 °C
- The melting point of BN is 2,973 °C
- The melting point of Copper is 1,085 °C
- 50 kW total beam power
- 21.7 kW absorbed by Tungsten
- 735 W absorbed by BN (Front side)
- 27.3 kW absorbed by gallium
- 7 W absorbed by BN (Back side)
- Assume that the power distribution is a cylinder with a 6 mm radius
- BN thermal conductivity depends on material (a-BN, h-BN) and orientation ranging from 3 to 600 W/(m K) – used 30 W/(m K)

These preliminary studies indicate that neither the gallium target nor the cooling water will boil and neither the copper nor the BN will melt to nearly 30 kW. We will extend these simulations to 50kW. The advantage of using BN cylinder, apart from its lack of copper content, is that its cost is low and thus reduces the need to be reused. It also appears that gallium does not attach to its walls at normal temperatures, whether this holds true after irradiation is to be seen.

#### Bench Tests without beam

We will conduct beam tests for thermal and mechanical integrity only after doing bench tests. The most important test will be on the BN cylinder with gallium target. One of Jefferson Lab's investigators (KJ) is an expert in RF inductive heating and will guide the tests. Jefferson Lab has the power sources that can create power in excess of 50kW. Figure 6 shows a BN cylinder of planned dimensions inside a coil. The test setup will be immersed in a flowing low conductivity water bath. This experiment will give us data which will guide our target system design.



*Figure 6. BN Cylinder and Coil*

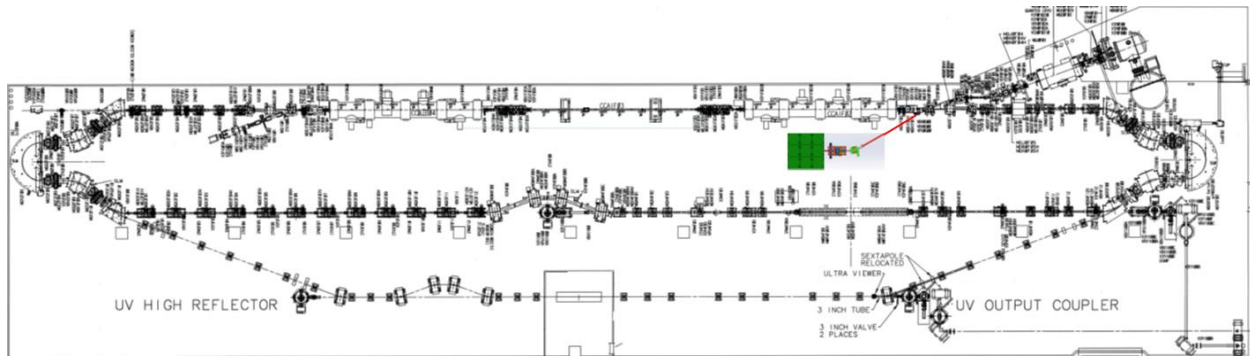
We plan a series of bench tests for understanding the thermal resistivity between the copper jacket and the BN cylinder. For these tests, we will heat both the BN and copper jacket and investigate methods for reducing thermal resistivity.

#### Setup for gallium irradiation at LERF

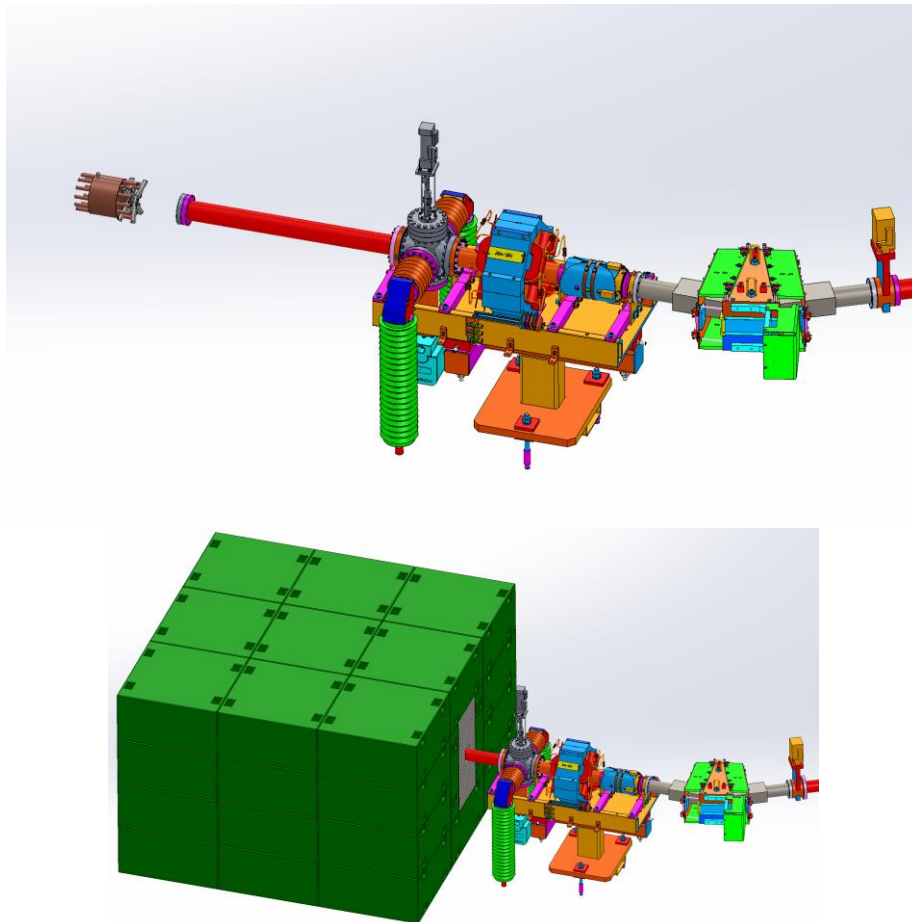
We will test the Be window and radiator at  $\geq 1.25$  mA at the injector of LERF (Figures 7a,7b) at lower than 10 MeV which is radiologically a simpler set up for shielding and low levels of activations. For the



target system tests, we have to use higher currents. We will accomplish this by removing the window and the radiator and directly exposing the target system in vacuum. This requires thermal isolation of the target system from the beam pipe flanges, which we think can be accomplished.



*Figure 7a. LERF's injector area for high power beam tests. Detailed view of the insert (green area) is shown in figure below.*



*Figure 7b. View of the beamline (above) with target system and with the target system enclosed in the shielding (below)*

#### Planned Beam Tests and validation of simulations

At  $\leq 10$  MeV,  $\geq 1.25$  mA (LERF injector)

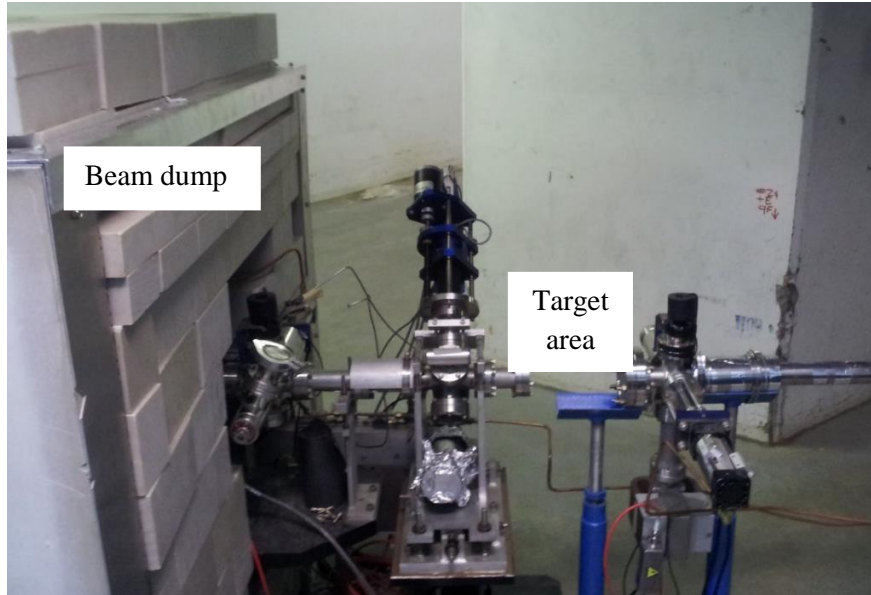
1. Tests of Beryllium window for thermal and structural integrity
2. Tests of radiator for thermal integrity (thickness guided by modeling and simulations)



At  $\leq 10$  MeV,  $\geq 5$  mA (LERF injector)

3. Tests of target system (gallium in BN cylinder with copper cooling jacket), no Be window and no radiator in the beam path. The target will be in vacuum.

The tests at LERF will be conducted with the beam line extending well into the shielding hut. We will have instrumentation in place to monitor the temperature of the components along with radiation monitors. Tests 1 and 2 may be completed at the same time.



*Figure 8. CEBAF Injector beam line*

At  $\geq 18.5$  MeV, low current ( $\sim 5 \mu\text{A}$ ), gallium and zinc targets (CEBAF injector)

The higher energy tests will be conducted at CEBAF's injector area Figure 8. We will conduct a series of short exposures of targets at 18.5, 40 and 100 MeV. These energies are selected for the following reasons: 18.5 MeV electron energy was selected to stay below the  $^{69}\text{Ga}(\gamma, 2n)^{67}\text{Ga}$  reaction threshold because both  $^{67}\text{Cu}$  and  $^{67}\text{Ga}$  emit gamma radiation at the same energy. Using energy below  $^{69}\text{Ga}(\gamma, 2n)^{67}\text{Ga}$  threshold, one can be assured that the 184.6 keV gamma is due to  $^{67}\text{Cu}$  decay; 40 MeV appears to produce the fewer contaminants at a reasonable  $^{67}\text{Cu}$  production and 100 MeV has a higher  $^{67}\text{Cu}$  yield albeit with higher degree of contamination (Table 2 below). These tests will allow us to understand, as a function of energy, the contaminants, our isotope separation techniques and yields and optimize beam parameters.

*Results from a parasitic test at CEBAF Injector*

Information regarding photo-production of  $^{67}\text{Cu}$  from Ga targets is sparse. About a year ago, a short parasitic test, (Investigators PD, GK), was done at CEBAF's injector area to investigate Ga's viability for  $^{67}\text{Cu}$  production. The available beam energy for the parasitic test was 10 MeV and the test showed no clear indication of  $^{67}\text{Cu}$ , which can be detected via its gamma emission. This is not a surprising result because while the beam energy is above the production threshold, the cross section for the alpha particle emission is suppressed by the nuclear Coulomb barrier (Figure 9).

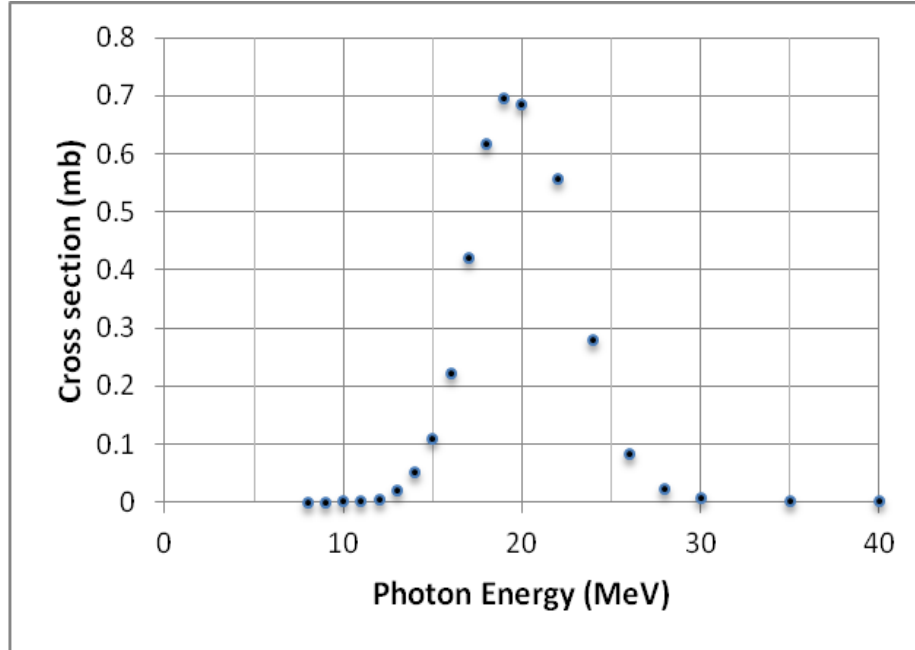


Figure 9. Cross section of  $^{71}\text{Ga}(\gamma, \alpha)^{67}\text{Cu}$  [17].

We used FLUKA [18] to calculate  $^{67}\text{Cu}$  yields in gallium. Results are generally in good agreement with TENDL-2014 data. However, there are discrepancies between both FLUKA and TENDL-2014 and the much lower cross sections reported by Antonov *et al.* [19] and Segebade *et al.*[13]. These discrepancies must be resolved experimentally.

		Natural Gallium Target			<sup>71</sup> Ga Target		
Energy of Electron Beam [MeV]		18.5	40	100	18.5	40	100
Nuclide & dominant production reaction	T <sub>1/2</sub>	Calculated Yield [ mCi / (50 kW · h) ]					
<sup>67</sup> Cu <sup>71</sup> Ga(γ,α) <sup>67</sup> Cu	61.8 h	1.4	13	18	3.5	32	44
<sup>64</sup> Cu <sup>69</sup> Ga(γ,αn) <sup>64</sup> Cu	12.7 h		298	521			72
<sup>71m</sup> Zn <sup>71</sup> Ga(n,p) <sup>71m</sup> Zn	4 h		0.1	0.8		0.2	1.1
<sup>69m</sup> Zn <sup>69</sup> Ga(γ,np) <sup>69m</sup> Zn <sup>71</sup> Ga(γ,np) <sup>69m</sup> Zn	13.8 h	0.1	17	45	0.1	40	109
<sup>69</sup> Zn <sup>69</sup> Ga(γ,np) <sup>69</sup> Zn <sup>71</sup> Ga(γ,np) <sup>69</sup> Zn	56 m	0.7	181	494	1	434	7
<sup>72</sup> Ga <sup>71</sup> Ga(n, γ) <sup>72</sup> Ga	14.1h		43	63	8.7	49	71
<sup>70</sup> Ga <sup>71</sup> Ga(γ,n) <sup>70</sup> Ga <sup>69</sup> Ga(n, γ) <sup>70</sup> Ga	21 m	8.5	1.7 x 10 <sup>5</sup>	2.1 x 10 <sup>5</sup>	1.1 x 10 <sup>5</sup>	4.1 x 10 <sup>5</sup>	5.2 x 10 <sup>5</sup>
<sup>68</sup> Ga <sup>69</sup> Ga(γ, n) <sup>68</sup> Ga	68 m	4.4 x 10 <sup>4</sup>	1.3 x 10 <sup>5</sup>	1.7 x 10 <sup>5</sup>		941	4770
<sup>67</sup> Ga <sup>69</sup> Ga(γ, 2n) <sup>67</sup> Ga	3.26 d	2.9 x 10 <sup>4</sup>	380	581		0.02	35
<sup>66</sup> Ga <sup>69</sup> Ga(γ, 3n) <sup>66</sup> Ga	9.5 h		6.2	121			29

Table 2. Yields of <sup>67</sup>Cu and other notable radionuclides at 50 kW beam power in full absorption natural gallium and <sup>71</sup>Ga targets calculated using FLUKA

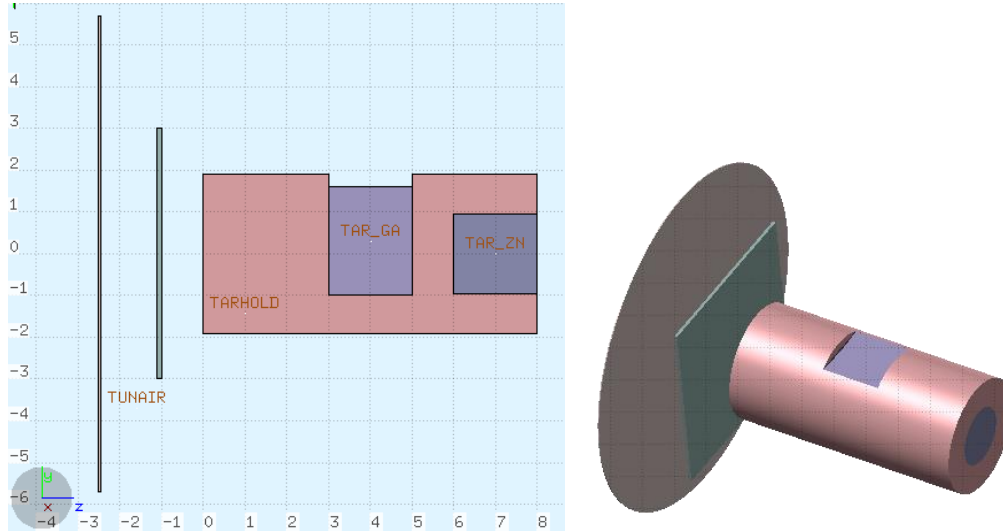
A few weeks ago, another beam time opportunity at CEBAF injector arose for a test. We requested and were given electron beam to irradiate both Ga and Zn samples. We selected 18.5 MeV electron energy for reasons stated above. Irradiation parameters are presented in Table 3.

Electron Beam Energy [MeV]	Average Beam Current [ $\mu$ A]	Duration of Irradiation [min]	Beam Power [W]
<b>18.5</b>	<b>2.4</b>	<b>60</b>	<b>4.4</b>

*Table 3. Irradiation parameters*

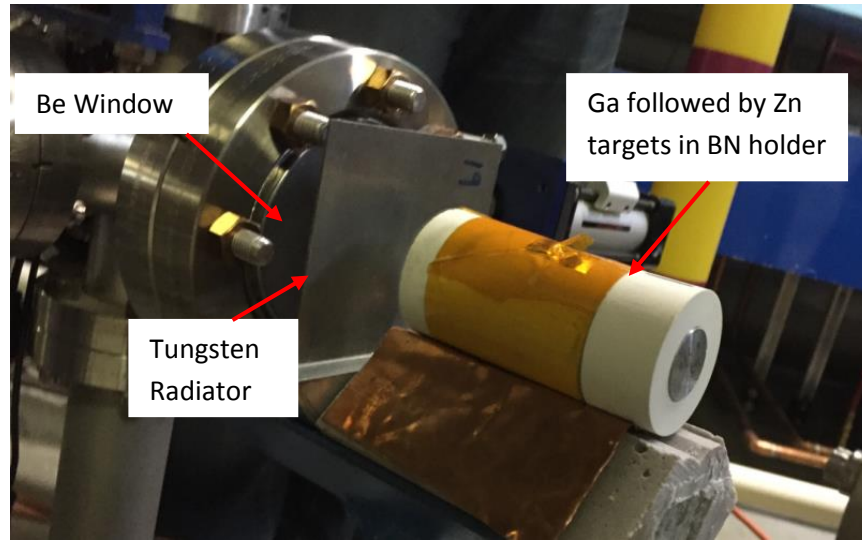
In order to save time both Ga and Zn targets were irradiated at the same time, with Zn target placed behind the Ga target of about 1 radiation length.

Irradiation setup consisted of 381  $\mu$ m thick Be window, 1 mm thick tungsten radiator, 3 cm thick hexagonal boron nitride (hBN) filter, 2 x 2.6 x 2 cm<sup>3</sup> gallium target inside and hBN sample holder. This was followed by a 2 cm diameter, 2 cm zinc target with another cm of BN between the targets (Figure 10). The test setup is shown in Figure 11.

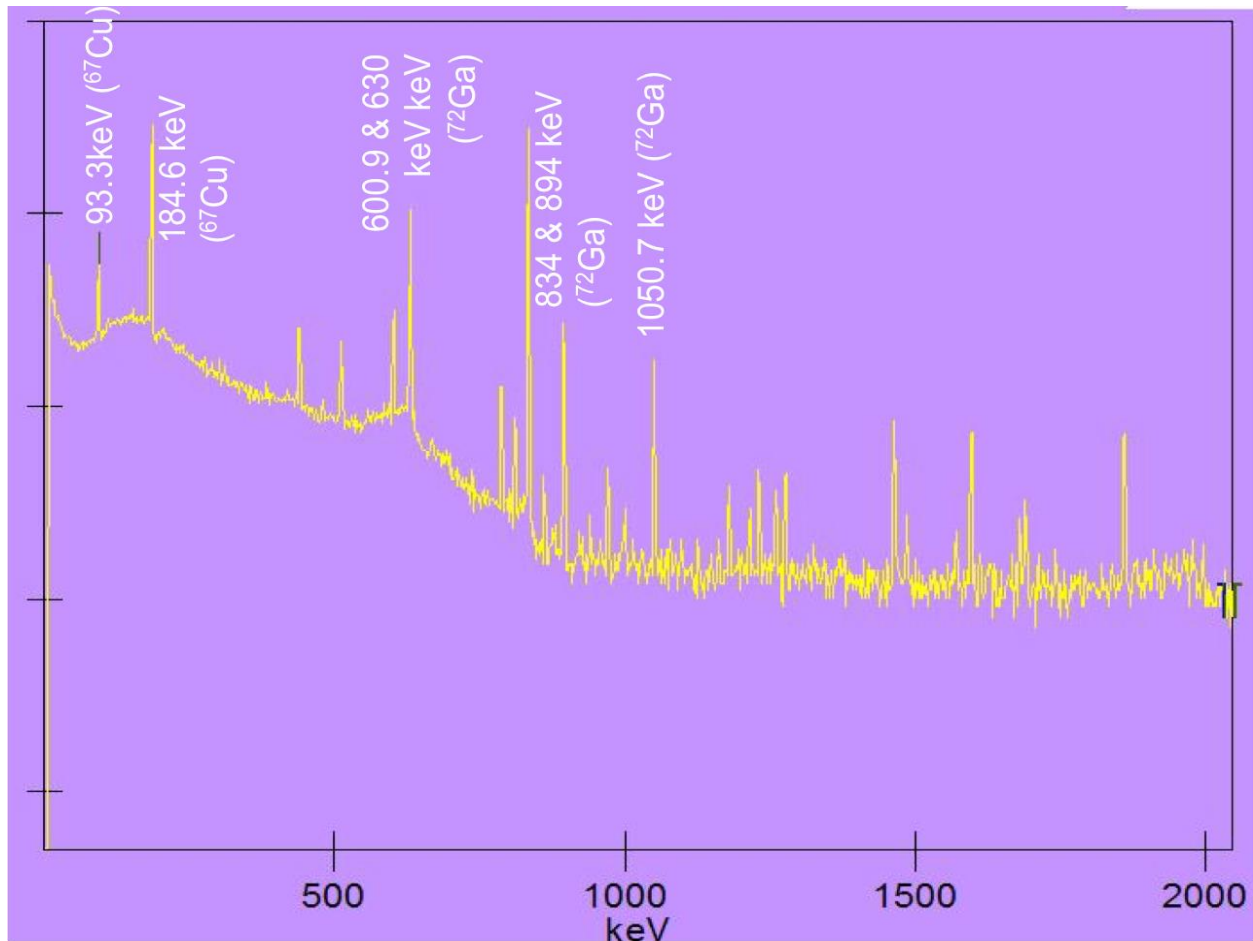


*Figure 10. 3 dimensional drawings used in FLUKA model*

The short-lived radioactivity induced in the irradiated setup was allowed to decay for approximately 18 hours. Gamma spectroscopy analysis of the gallium and zinc samples was performed using a high purity germanium detector, GENIE-2000 spectroscopy software and ISOCS/LabSOCS calibration software by Canberra. <sup>67</sup>Cu Gamma signal from irradiated gallium sample is shown in Figure 12.



*Figure 11. Test setup at CEBAF Injector*



*Figure 12. Measured decay photon spectrum of gallium target 25 hours after the irradiation.*

Detailed models of each irradiation were created in FLUKA. Results of activation measurements and FLUKA calculations are presented in Table 4. FLUKA overestimates  $^{67}\text{Cu}$  production in gallium at 18.5 MeV maximum bremsstrahlung energy by approximately a factor of 2 and underestimates  $^{67}\text{Cu}$  production in zinc by approximately a factor of 0.7. It should be noted that this was a demonstration experiment and

lacked the set up and controls needed for measurement precision. The experiments during this proposal period will be rigorously planned and executed. The error estimates in measured yield in the table are due to activity measurement errors, not experimental errors.

Target	Measured $^{67}\text{Cu}$ Yield (Bq/W·h)	FLUKA $^{67}\text{Cu}$ Yield (Bq/W·h)	Ratio FLUKA/measurement
<b>Ga</b>	$111 \pm 18$	$228 \pm 7$	$2.05 \pm 0.33$
<b>Zn</b>	$103 \pm 17$	$75.7 \pm 3.3$	$0.73 \pm 0.12$

*Table 4. Comparison of measured and calculated  $^{67}\text{Cu}$  yields in gallium and zinc.*

#### Material handling post irradiation

The limits for shipping will comply with the DOT shipping limits for the isotopes. For shipping purposes, the material will almost certainly be classified as a Type A shipment and will be factored into our irradiation times at CEBAF injector. This does require a certain specification packaging, and the packing and shipment of the material must be done by DOT-qualified HAZMAT shippers. Jefferson Lab keeps at least two people in RadCon current on DOT RAM shipping certifications. Shipping can be done through FedEx. VCU has processes in place to receive the irradiated material

#### Isotope Separation and Purification

Radiochemical separation of  $^{67}\text{Cu}$ , from Ga and Zn targets as well as from stable and radioactive impurities, will be performed using a combination of solvent extraction and ion-exchange chromatography. Following target irradiations at Jefferson Lab, radioactive targets will be delivered to the radiochemistry laboratory at VCU for processing. Target processing will be carried out inside a lead shielded hot cell fitted with remote manipulators. By remote manipulation, the irradiated target material will be removed from the target holder and will be measured in a dose calibrator inside the hot cell to determine the total radioactivity in the target. This total activity will contain not only the desired radioisotope, but also other co-produced radioisotopes. Next, the target material will be dissolved in the appropriate solvent and a small fraction ( $\mu\text{Ci}$ ) of the solution will be taken and processed for pre-separation initial Gamma spectroscopy analysis. This will determine the identity of the isotopes induced in the target solution. Following radiochemical separation, gamma spectroscopy analysis will be repeated on the purified radioisotope product as well as the other separated isotopes to determine the efficiency of the purification method and to quantify yield of all produced radioisotopes. Radiochemical separation will be performed on both the Ga and Zn targets.

#### **Radiochemical separation of $^{67}\text{Cu}$ from Ga**

Photon irradiation of natural gallium target (60%  $^{69}\text{Ga}$  / 40%  $^{71}\text{Ga}$ ) leads to the production of  $^{67}\text{Cu}$  mainly by the  $^{71}\text{Ga}(\gamma, \alpha)$  reaction and, depending on photon energy, there will also be a contribution from  $^{69}\text{Ga}(\gamma, 2p)$  reaction, albeit at a much lower level. Irradiation of natural Ga target will also lead to the production of Ga, Zn and Cu isotopes, including stable  $^{65}\text{Cu}$  by the  $^{69}\text{Ga}(\gamma, \alpha)$  reaction. Production of stable Cu will be greatly minimized when an enriched  $^{71}\text{Ga}$  target is used, leading to significant increase in the specific activity of produced  $^{67}\text{Cu}$ . Previous reports, on the production of  $^{67}\text{Cu}$  from Zn target, have indicated that reaction leading to the production of stable isotopes ( $^{63}\text{Cu}$ ,  $^{65}\text{Cu}$ ) is the major source of the reduction in specific activity [20]. The same group has reported a 5-fold increase in specific activity when an enriched  $^{68}\text{Zn}$  target was used [21].

The radionuclide separation approach planned is a modified version of previously published methods [22,23] used to separate  $^{64}\text{Cu}/^{67}\text{Cu}$  from radioactive waste generated during the proton-induced production of  $^{67}\text{Ga}$  from Zinc target. We will employ a combination of solvent extraction and ion exchange

chromatography to separate  $^{67}\text{Cu}$  from the liquid Ga target material and from other trace metals co-produced during the irradiation. The initial step will involve removal of the bulk Ga using isopropyl ether (IPE) solvent extraction in which Ga will be retained in the organic phase and  $^{67}\text{Cu}/\text{Cu}$  will remain in the aqueous phase. A second IPE extraction of the aqueous phase further removes residual Ga. The aqueous phase containing  $^{67}\text{Cu}/\text{Cu}$  will be evaporated to near dryness and re-dissolved in dilute HCl. The  $^{67}\text{Cu}/\text{Cu}$  activity will be extracted into dithizone phase; this organic agent has high selective affinity for Cu and not Ga, Fe or Zn. The  $^{67}\text{Cu}/\text{Cu}$  will be back extracted into an aqueous phase prior to ion exchange purification using CG-71 amberchrome column impregnated with dithizone. This chromatography step purifies the final product from traces of Ga, Zn and any other elemental impurities. The scheme of its workflow is outlined below in Figure 13.

### **Radiochemical Separation of $^{67}\text{Cu}$ from Zn**

Previously reported methods for the separation of  $^{67}\text{Cu}$  from Zn targets will be employed for the separation [23, 24]. Three ion-exchange matrices will be used for the separation of  $^{67}\text{Cu}$  from the Zn target. These are the cation-exchanger AG 50 W ( $\text{H}^+$ ); Chelex 100 ( $\text{H}^+$ ) and the anion-exchanger AG 1X8 ( $\text{Cl}^-$ ). Irradiated Zn target will be dissolved in 6M HCl. Following complete dissolution of Zn, the HCl solution will be loaded into the cation-exchanger which retains Ga radioactivity, but not that of  $^{67}\text{Cu}$  and Zn isotopes. The 6M HCl eluate will be neutralized to pH 3-4 by NaOH. This solution will then be loaded on the chelex 100 column which retains the  $^{67}\text{Cu}$  activity, while Zn and other metal impurities such as Ni OR Co, will be eluted. Further elution with 2M HCl elutes  $^{67}\text{Cu}$  with potential trace quantities of Zn (monitored by  $^{69\text{m}}\text{Zn}$ ). The 2M HCl eluate will be passed through the final anion-exchanger, which retains any traces of Zn, and elutes the final  $^{67}\text{Cu}$  activity.

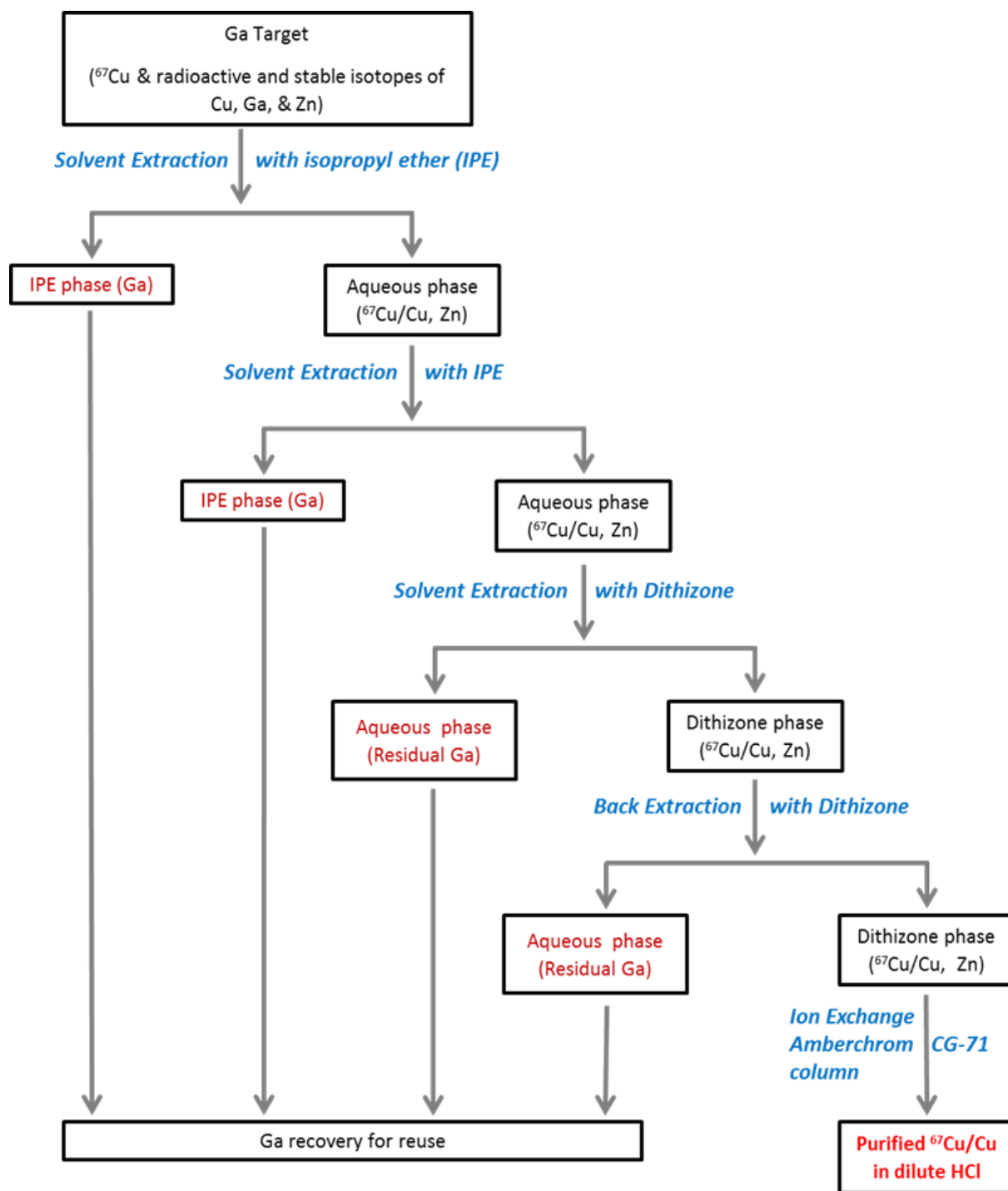


Figure 13. Schematic workflow showing the steps and processes involved in the separation of <sup>67</sup>Cu/Cu from irradiated gallium target



## Radiochemical Analysis

*Gamma-ray spectroscopy:* High purity Germanium based Gamma spectroscopy (Ortec, USA) will be used to analyze the samples for radionuclide purity and to accurately measure absolute yields. The detector is calibrated for both energy and efficiency using standard point sources ranging from 20 keV to 2 MeV. In addition to identifying the produced radionuclides by gamma-ray spectroscopy, half-life analysis will also confirm the identity of the detected gamma rays. The measured activity will be extrapolated to the total volume of the purified isotopes and verified by dose calibrator measurements at the mCi level. Since the gamma-ray emissions of  $^{67}\text{Cu}$  and  $^{67}\text{Ga}$  are similar, albeit with different intensities, identification of  $^{67}\text{Cu}$  gamma-ray peaks will be confirmed by relative intensity of the peaks as well as half-life analysis of repeatedly measured samples over a period of several half-lives.

*Inductively Coupled Plasma Mass Spectrometry (ICP-MS):* ICP-MS will be used to quantitatively measure stable isotopes of both the desired elemental isotope (Cu) as well as other stable isotopes. These measurements will yield data on the amount of the trace isotopes in the ppb sensitivity. Using standards of Cu, Zn, and other metals, absolute mass (ng –  $\mu\text{g}$  range) of each element will be determined from these measurements.

*Specific Activity measurements and determination:* From the gamma spectroscopy measurements and ICP-MS analysis, the specific activity of the purified  $^{67}\text{Cu}$  will be determined from these measurements. The experimentally determined value will be compared to theoretical calculation based on amount of radioactivity and number of atoms present in that radioactivity.

## Time Table of Activities

The timelines shown in Figure 12 represent the activities during that period and not the start and end dates. The exact dates for irradiations will depend on the schedule of the CEBAF accelerator. The present accelerator schedule shows irradiation opportunities during the 3<sup>rd</sup> quarter of 2017 and 2<sup>nd</sup> and 3<sup>rd</sup> quarters of 2018. The irradiations will not take place all at once, but at different times during the R&D period and the samples will be analyzed between beam runs.

### Year 1

We will use the first year to model and simulate isotope production as well as thermal and mechanical processes and begin the designs for the beam exit window, the radiator and the target system. During this year, we will prepare LERF's injector beam line. During the first two quarters, we will also develop separation techniques to carry out radionuclide measurements and radiochemical separation of irradiated targets in the 3<sup>rd</sup> quarter. At CEBAF injector, we will conduct the first set of irradiation experiments of both gallium and Zinc targets, at low power but high energy, to establish processing protocols for isotope separation and chemical and radiochemical purity. Designs of components during this year will lead to their fabrication spanning quarters 3 to 5. Prior to the first runs at we will prepare the injector beam lines for the tests, compile the experiment readiness documents and assure approvals from Accelerator Operations, JLab Management and from DOE representatives at JLab.

### Year 2

During quarters 4 to 5, the target system will be evaluated without beam, e.g., RF inductive heating test at 50kW, investigating thermal conductivity between the target capsule and the copper jacket. Any required modifications will be made. During quarters 6 and 7, low power isotope production at beam energies at one or more of energies 18,5, 40 or 100 MeV will be carried out at Jefferson Lab's CEBAF injector, followed by radiochemical separation. In quarters 6 and 7, high power beam test of target system will be done at Jefferson Lab's LERF. During this period, remaining low power high energy tests will be done at Jefferson Lab's CEBAF injector followed by radiochemical separation, radionuclide measurements and purity analysis, at VCU. The final report of findings will be completed by quarter 8.

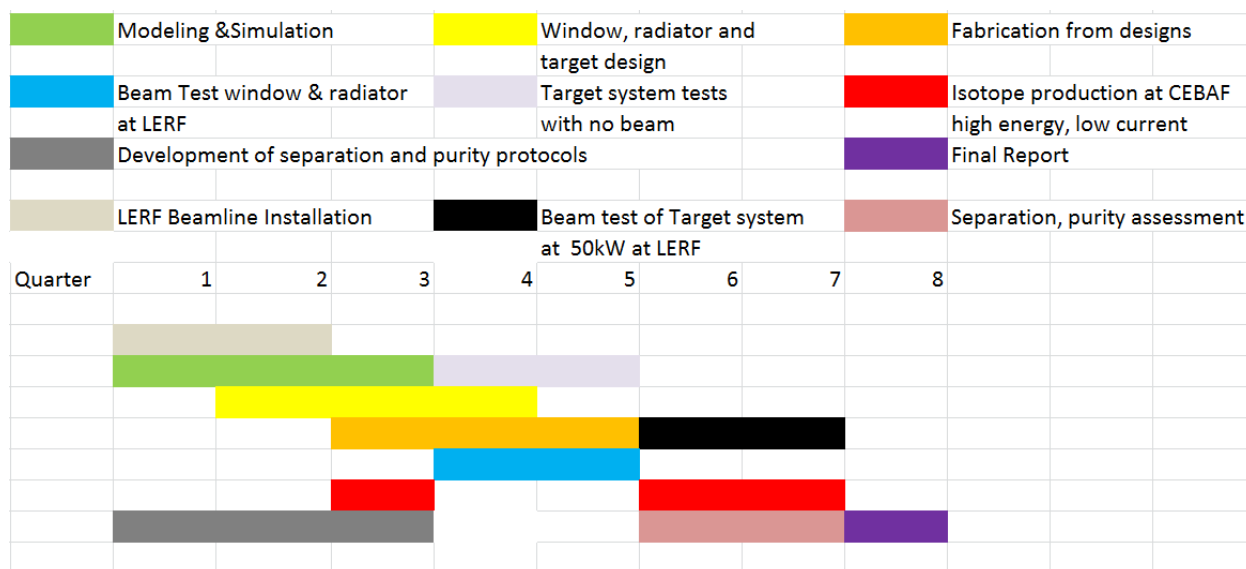


Figure 14. Timeline

#### Legend details

- Modeling and Simulation of photo-production process, thermal and mechanical stresses of the beam exit window, radiator and BN target system (BN and the copper jacket).
- Design of the Be window, radiator and target system
- Fabrication of the Be window, radiator and target system
- Beam tests of Be window and radiator at LERF
- Bench tests of target system (no beam)
- Low current Irradiations of Ga and Zn targets at CEBAF injector at 18.5, 40 and 100 MeV (not all at the same time), followed by radiochemical separation and radionuclide & chemical analysis
- Preparation of LERF Beamline for beam delivery and beam dump installation
- Beam test of target system at LERF
- Preparation for isotope separation, development of protocols
- Radiochemical separation, purity assessment and chemical analysis, using the protocols developed in year 1
- Preparation and submission of final report to DOE Office of Science

SDSMT will participate through the two years in modeling and simulations, irradiation tests and verifying the test results with model calculations. The work will be carried out by a graduate student under the guidance of all PIs. The student will also participate in the chemistry and radiochemistry aspects of the program under the guidance of VCU investigators.

#### Project Goals/Objectives

We propose a two-year project, by the end of which the following deliverables will be complete:

1. Prepare and configure LERF's injector beamline for low energy, high current electron beam delivery
2. Simulation (GEANT4, MCNP, FLUKA and ANSYS) studies of:
  - a. Beam exit window optimization for thermal distribution and power handling
  - b. Converter optimization (thickness, type, configuration) for thermal distribution and power handling
  - c. Target system to handle up to 50 kW of beam power
3. Experimental verification of the simulations of exit window and radiator capabilities at LERF injector

4. Experimental verification of the power handling capability of target system at LERF injector
5. Determination of currents for high energy runs for isotope production at CEBAF injector
6. Validation of the simulation code with experimental results by irradiation at CEBAF injector and measurement at VCU
7. Extraction and purification of  $^{67}\text{Cu}$  from both Ga and Zn targets after each irradiation
8. Measurement of yields, radiochemical and chemical purity after each irradiation
9. Training of a graduate student

### Project Management Plan

Dr. Andrew Hutton of Jefferson Lab will lead the project. The core competencies of the collaborating institutions are sufficiently distinct that project management does not need to be hierarchical.

At the beginning, the overall planning of each major aspect of this R&D, namely, the high power target system, irradiation of targets, measurement of yields at different energies, optimization of beam parameters, separation of the desired isotope, and delivery of the isotope to targeted area will be discussed and reviewed by all PIs and investigators. Once a month, the three PIs will meet over the phone to discuss the project progress and track the goals for the current quarter as shown in the timeline. Once the goals for the quarter are set, carrying out that activity and communicating the findings is the responsibility of the PI of the expert institution. Problems or conflicts will be discussed by all PIs and jointly resolved. Jefferson Lab and VCU, where the experimental activities take place, are geographically close to each other. This facilitates quarterly in-person meetings, alternating between Jefferson Lab and VCU with the PI from SDSMT joining over the phone. All PIs assume responsibility for training of students.

### Student Training

The work described in this proposal provides an excellent training ground for a graduate student (SDSMT has identified a suitable student). The student will receive a comprehensive, interdisciplinary and hands on training during this proposal period. The expertise developed will include modeling and simulations of thermal and mechanical aspects, photo-nuclear process simulations, executing bench tests and irradiation tests, learning chemical separation processes and analyzing the gathered data. Past the proposal's funding period, we will support the students with other funds. We also wish to expose summer undergraduates at the lab (SULI, Student Undergraduate Laboratory Internship program, funded by DOE and REU; Research Experience for Undergraduates, joint ODU/JLAB program funded by NSF) to this exciting field of which they may be quite unaware. We will design projects that can give a student a valuable experience during the 10 weeks the students spend at the lab. We have been running these programs in accelerator and nuclear physics for many years and have experience in developing short term projects with great impact on the student learning experience.

### **Summary**

Gallium is an attractive target for its potential power handling capability. This target has not been used for photo-production of  $^{67}\text{Cu}$  and opens up a new opportunity for producing  $^{67}\text{Cu}$ , which has both diagnostic and therapeutic value and whose supply is unreliable.

This R&D describes a logical path to address the thermal and mechanical issues associated with high power operations through modeling and simulations, bench tests without beam and finally with beam. The strategy adopted limits the amount of beam time (beam time is expensive), and controls the local activity due to beam operations. By using a BN cylinder to hold the gallium, a major concern of copper contamination of the target gallium is alleviated. The data generated during this R&D will be made available to other researchers via standard communications such as presentations at conferences and publications. The high

power targetry techniques developed for this particular isotope may be adopted for other targets, accounting for the properties of the target materials.

While we have done a few preliminary analysis and tests, there are a number of issues that can only be resolved experimentally. High power radiation effects, e.g., on the thermal conductivity of hBN, need to be understood as is the thermal contact between the BN cylinder and the copper jacket for effective heat transfer. It was reported [25] that hBN irradiated by protons or neutrons could be weakened. The behavior of hBN under irradiation by electrons and photons will be investigated during this study. This R&D will add to the knowledge base regarding some radiation hardness aspects of this material. As alternatives to hBN, we will investigate other suitable materials such as Beryllia. Our low energy high power beam test of the target system, namely, the copper jacket housing the BN cylinder will be in vacuum with no windows. We need to ensure that the thermal gradient from the target system to the beamline could be managed.

With the different materials in the beam tests, namely, Be, W, BN and a small amount of gallium, we plan detailed simulations to determine the electron energy at LERF to keep the local activity to a minimum. Additionally, we will use the guidance of simulations to determine the best beam current at CEBAF injector at 18.5, 40 and 100 MeV that will produce  $^{67}\text{Cu}$  which could be separated and which will lead to measurable yields. Additionally, this will determine the shielding necessary at CEBAF injector. We will compare the separation and isolation processes for  $^{67}\text{Cu}$  from both Ga and Zn targets and measure the contaminants in each target at different energies, which has not been done before. The graduate student who participates in this R&D will receive interdisciplinary training in physics, engineering and radiochemistry; a training not usually available to most students. We also expect a few undergraduates will participate in this program during the two summers at Jefferson Lab.

The collaboration has the necessary expertise to design high power targets and has described the work done to date in this area. LERF is a very unique electron accelerator which not only can provide beam power in excess of 100 kW but within the power envelope is tunable of energy and current simultaneously. Due to the nature of experimental work done at Jefferson Lab, the lab is highly experienced in high power beam dumps and radiological calculations. The extensive expertise of the VCU group enables the separation, purity assessment and yields of the desired isotope after irradiations. The facilities at both Jefferson Lab and VCU along with the well-developed infrastructures make us well prepared to pursue the proposed work. This is evidenced by our ability to do preliminary simulations and parasitic beam tests in support of this proposal.

The final report to the DOE's Office of Science will include all the findings from this project.

As a result of this project, it is fully expected that LERF can become a reliable source of  $^{67}\text{Cu}$  and potentially for other photo-produced research isotopes that are not readily available.

#### *Path to a reliable supply of $^{67}\text{Cu}$ at Jefferson Lab's LERF*

Successful demonstration of the feasibility of  $^{67}\text{Cu}$  production will pave the way for developing a reliable supply of this isotope using the high power electron beam at LERF. The bulk of the capital cost of the LERF facility was provided from contracts with Office of Naval Research and grants from the Commonwealth of Virginia. The beam time at LERF is lightly subscribed compared to accelerators that are used primarily for physics or other research, where isotope production takes a lower priority. This makes the availability of dedicated beam time for isotope production much more certain.

For this proposal, our strategy is to use only low energy beam at LERF's injector in order to minimize local activity. For production of isotopes in reasonable quantities, i.e., higher energy ( $> 18.5$  MeV)  $\sim 50$  kW operation, a permanently shielded enclosure to house the radiator and target system at the high energy end of LERF would be necessary. Jefferson Lab has the needed expertise and facilities for this design and installation (Figure 15 shows the high energy section of LERF and the area for permanent shielded

enclosure for target irradiation). A robotic handler for installing and retrieving the target is an essential device which can be designed and may even be available for purchase. The third ingredient is isotopically enriched targets which are expensive, (50 gms of 99.8% gallium costs about \$150K), but the target material can be recovered and recycled for further use. Thus, the isotopically enriched target, shield enclosure and robotic manipulator for target handling are onetime costs. The recurring costs will be for the operation of LERF and separation and purification of  $^{67}\text{Cu}$ , with beam time being the most expensive.



*Figure 15. LERF Accelerating Section (left), Irradiation area for isotope production (right)  
(Beam Dump will be upgraded for full production)*

We note that the technology that will be developed during this research is transferable and can be adopted by industries that wish to produce reliable supply of interesting but not readily available isotopes.

## APPENDIX 1: Biographical Sketches

### Andrew Michael Hutton

Thomas Jefferson National Accelerator Facility  
12000 Jefferson Ave, Newport News, VA 23606

andrew@jlab.org  
phone: 757-269-7396

### Education and Training

London University	Physics	Ph.D.
Cambridge University	Natural Sciences	M.A. (Honours)
Cambridge University	Natural Sciences	B.A. (Honours)
Cambridge University		Entrance Scholarship

### Research and Professional Experience

2007-present	Associate Director Accelerator Division, Thomas Jefferson National Accelerator Facility
1995-2007	Director of Operations, Thomas Jefferson National Accelerator Facility
1992-1995	Deputy Accelerator Division Leader for Commissioning and Operations, Thomas Jefferson National Accelerator Facility
1989-1992	Head of B Factory Machine Design Group, SLAC, Stanford University
1986-1989	SLC Project, System Commissioner for the Arcs, then Head of Beam Delivery Section, SLAC, Stanford University
1975-1982	Physicist, Conseil Européen pour la Recherche Nucléaire
1970-1975	Physicist, Institute of Photochemistry and Radiation Chemistry

### Publications

#### RADIOACTIVITY INDUCED IN TISSUES BY 600 MEV PROTONS

M. Barbier, A. Hutton, A. Pasinetti  
CERN Publication 66-34, 1966

#### NEUTRON PRODUCTION IN THE LEP VERSION 8 VACUUM CHAMBER

A. Hutton  
Technical Note LEP-135, 1979

#### ACCELERATOR PROSPECTS FOR PHOTON PHYSICS

A. Hutton  
Paper presented at Photon 92, San Diego California Mar 23-26, 1992 and SLAC-PUB-5462, May 1992

#### COMMISSIONING OF CEBAF

A. Hutton  
Proc. Fourth European Particle Accelerator Conference June 27-July 1, 1994 and CEBAF-JC-94-007

#### A SYNCHRONIZED FEL-SYNCHROTRON RADIATION FACILITY AT JEFFERSON LAB

A. Hutton, R. May, H. Dylla, G.P. Wilson, G. Neil, O. Garza, R. Lauze, S. Prior, S. Benson  
Proceedings of PAC 2001, IEEE (2001), p2668

#### CEBAF ENERGY RECOVERY EXPERIMENT

A. Bogacz, K. Beard, J. Bengtsson, C. Butler, Y. Chao, S. Chattopadhyay, H. Dong, D. Douglas, A. Freyberger, A. Guerra, W. Hicks, A. Hofler, J. Hovater, A. Hutton, R. Lauze, N. Merminga, T. Plawski, Y. Roblin, M. Spata, C. Tennant, M. Tiefenback, A. Bernard, H. Toyokawa  
Proceedings of PAC 2003, IEEE (2003), p195

#### **WORLD-WIDE EXPERIENCE WITH SRF FACILITIES**

A. Hutton, A. Carpenter

Proceedings of PAC 2011, IEEE (2011), pg. 2575

#### **UPGRADING THE CEBAF INJECTOR WITH A NEW BOOSTER, HIGHER VOLTAGE GUN, AND HIGHER FINAL ENERGY**

R. Kazimi, A. Freyberger, A. Hofler, A. Hutton, F. Hannon

Proceedings of IPAC'12, IEEE (2012), pg. 1945

#### **FIELD EMISSION AND CONSEQUENCES AS OBSERVED AND SIMULATED FOR CEBAF UPGRADE CRYOMODULES**

F. Marhauser, R. Johnson, R. Rodriguez, P. Degtiarenko, A. Hutton, G. Kharashvili, C. Reece, R. Rimmer

Proceedings of SRF2013, JACoW (2013), pg. 694

#### **Synergistic Activities**

Executive Committee Member, Accelerator Application Division for American Nuclear Society

Chair of Organizing Committee of International Particle Accelerator Conference 2015

Member of Virginia Commonwealth University Mechanical Engineering Advisory Board

Jointly with ODU, established Center for Accelerator Science in ODU's Physics department for graduate education in Accelerator Sciences

Appointed Chairman of Board of Directors of the Virginia Quality Institute

#### **Collaborators and Co-editors**

Prof. Jamal Zweit, Director, Molecular Imaging Center

Prof. Douglas Wells, Dean of Graduate Education, South Dakota School of Mines and Technology

#### **Graduate and Postdoctoral Advisors and Advisees**

Ph. D. Adviser for a Columbia University graduate student

#### **Patents**

Compact push-pull free electron laser, US 74994476 B1

**Jamal Zweit, PhD, DSc**

Professor of Radiology, Radiation Oncology, Pathology, Biochemistry & Molecular Biology and Chemistry

Director, Center for Molecular Imaging

eRA COMMONS USER NAME (credential, e.g., agency login) jzweit

University of Kansas, Lawrence, KS	B.S.	1976-1980	Radiation Biophysics
JFK Medical Center/The City University, New York, NY	M.S. Diploma	1980-1981	Nuclear Medicine/ Oncology
Medical Center, The Brooklyn Hospital, New York, NY	Board Certification	1981	Nuclear Medicine
University of Manchester, Manchester UK	-Ph.D, Radiochemistry & Radiopharmacology	1989	PET Imaging
	-D.Sc., Molecular Imaging	2004	Cancer Biology & Therapeutics

**Positions and Employment**

2008-	Professor of Radiology, Director, Center for Molecular Imaging, VCU
2008-	Affiliate Faculty, Radiation Oncology, Pathology, Biochemistry & Molecular Biology and Chemistry, Virginia Commonwealth University
2002-2008	Reader in Biomolecular Imaging, University of Manchester
1999-2008	Joint Head, Manchester Positron Emission Tomography Centre (ManPET)
1999-2008	Group Head, CRCUK/UM Radiochemical Targeting and Imaging, Paterson Institute for Cancer Research and UM
1998-2002	CRUK/UM Senior Lecture in Biomolecular Imaging Science, University of Manchester Institute of Science and Technology
1994-1997	Appointed Lecturer, University of London/ Institute of Cancer Research
1994-1997	Senior Research Scientist, Institute of Cancer Research, UK
1993-1994	Honorary Clinical Fellow, Royal Marsden NHS Trust, UK
1991-1994	Clinical Scientist, Institute of Cancer Research, UK
1989-1994	Post-doctoral Research Fellow, University of Manchester
1981-1985	Medical and Health Physicist, Tripoli Central Hospital and University of Tripoli

**Synergistic Activities (Relevant Professional and Scholarly Activities)**

Member, Society of Nuclear Medicine and SNMMI Radiopharmaceutical Council

Grant Proposal Reviewer, various national/international funding organizations

Member, Society of Molecular Imaging

Member, American Association for Cancer Research

Member, Journal of Cancer Science & Research Editorial Board

**Relevant Publications (Selected from 110 peer reviewed publications)**

1. Sun M., Yang L., Jose P., Wang L., **Zweit J.** (2013). Functionalization of quantum dots with multidentate zwitterionic ligands: impact on cellular interactions and cytotoxicity. *J. Mater. Chem. B*, vol. 1, no. 44, pp. 6137–6146.
2. Yang L, Sundaresan G, Sun M, Jose P, Hoffman D, McDonagh PR, Lamichhane N, Cutler CS, Perez JM, **Zweit J.** (2013). Intrinsically radiolabeled multifunctional cerium oxide nanoparticles for



- in vivo studies. *J. Mater. Chem. B* 1, 1421–1431.
3. Sun M, Hoffman D, Sundaresan G, Yang L, Lamichhane N, **Zweit J** (2012). Synthesis and characterization of intrinsically radio-labeled quantum dots for bimodal detection. *American Journal of Nuclear Medicine and Molecular Imaging*, 2(2): 122-135.
  4. Keen, H.G., Dekker, B.A., Disley, L., Hastings, H., Lyons, S., Reader, A.J., Ottewell, P., Watson A., and **Zweit, J.**, (2005), Imaging apoptosis in vivo using <sup>124</sup>I-annexin V and PET. *Nucl. Med. Biol.*, 32, 395-402. PMID: 15878509
  5. **Zweit J**, Downey S, Sharma H. A method for the production of iron-52 with a very low iron-55 contamination. *Int J Rad Appl Instrum A*. 1988;39(12):1197-201. Review. PubMed PMID: 2851001.
  6. **Zweit J**, Goodall R, Cox M, Babich JW, Potter GA, Sharma HL, Ott RJ. Development of a high performance zinc-62/copper-62 radionuclide generator for positron emission tomography. *Eur J Nucl Med*. 1992;19(6):418-25. PubMed PMID: 1618233.
  7. **Zweit J**. Radionuclides and carrier molecules for therapy. *Phys Med Biol*. 1996 Oct;41(10):1905-14. Review. PubMed PMID: 8912370.
  8. Blower PJ, Lewis JS, **Zweit J**. Copper radionuclides and radiopharmaceuticals in nuclear medicine. *Nucl Med Biol*. 1996 Nov;23(8):957-80. Review. PubMed PMID: 9004284.
  9. Brooks RC, Carnochan P, Vollano JF, Powell NA, **Zweit J**, Sosabowski JK, Martellucci S, Darkes MC, Fricker SP, Murrer BA. Metal complexes of bleomycin: evaluation of [Rh-105]-bleomycin for use in targeted radiotherapy. *Nucl Med Biol*. 1999 May;26(4):421-30. PubMed PMID: 10382846.
  10. Jayson GC, **Zweit J**, Jackson A, Mulatero C, Julyan P, Ranson M, Broughton L, Wagstaff J, Hakansson L, Groenewegen G, Bailey J, Smith N, Hastings D, Lawrance J, Haroon H, Ward T, McGown AT, Tang T, Levitt D, Marreaud S, Lehmann F.F, Herold M, Zwierzina H. (2002). Molecular Imaging and Biological evaluation of HuMV833 anti-VEGF antibody: Implications for trial design of anti-angiogenic antibodies. *JNCI*, 94, 1484- 1493.

#### **Principal Graduate and Postdoctoral Advisors**

Prof. Harbans Sharma, PhD, DSc, University of Manchester  
 Prof. Robert Ott, PhD, DSc, University of London and Institute of Cancer Research  
 Prof. Nic. Jones, PhD, Director, CRUK Manchester Cancer Center and Paterson Institute for Cancer Research

#### **Graduate and postdoctoral Advisees (selected from 35 graduate and postdoctoral fellows)**

##### **Graduate students mentored:**

Jason Lewis, PhD, Memorial Sloan Kettering Cancer Center, NY. USA  
 Heather Keen, PhD, AstraZeneca Pharmaceuticals, UK  
 Dermot Burke, MD/PhD, University of Leeds Hospital, UK  
 David Hoffman, PhD, University of California, Davis, USA  
 Naru Lamichane, PhD, University of Miami  
 Fatma Youniss, PhD, University of Benghazi, Libya  
 Jane Sosabowski, PhD, Kings College, London, UK

##### **Postdoctoral Fellows mentored:**

Bronwen Dekker, PhD, Nature Protocols Journal, UK  
 Minghao Sun, PhD, Virginia Commonwealth University, USA  
 Gajanan Dewkar, PhD, Virginia Commonwealth University, USA  
 Likun Yang, Virginia Commonwealth University, USA  
 Purnima Jose, PhD, Virginia Commonwealth University, USA  
 Philip McDonagh, MD/PhD, Virginia Commonwealth University, USA

**Douglas P. Wells, Ph.D.**

South Dakota School of Mines and Technology  
501 E. Saint Joseph St., Rapid City, SD 57701

wells@physics.isu.edu  
phone: 605-394-1763

**Professional Preparation**

Rutgers University	Physics, Mathematics	B.S., 1982
University of Virginia	Mathematics,	M.S., 1984
University of Illinois	Physics,	M.S., 1985
University of Illinois	Physics,	Ph.D., 1990
University of Washington	Physics	Post Doc, 1990-1992

**Appointments**

2012-present	Dean of Graduate Education and Professor of Physics, SDSM&T
2011-2012	Chair and Professor of Physics, Idaho State University
2006-2012	Director and Professor of Physics, Idaho Accelerator Center at Idaho State University
2003-2006	Chair, Department of Physics at Idaho State University
2003-present	Associate Professor of Physics at Idaho State University
1997-2003	Assistant Professor of Physics at Idaho State University
1996-1997	Associate Professor of Health Physics at Idaho State University
1993-1996	Radiation Health Physicist for Washington State Department of Health

**Products: Selected Publications (over 100 peer-reviewed publications in all)**

D.P. Wells, Medical Isotope Production with Electron Linacs and Accelerator Driven Subcritical Systems (ADSS), Plenary Presentation, AccApp'15-12th International Topical Meeting on the Nuclear Applications of Accelerators, 10–13 November 2015, Washington, DC, USA

L. Jiwen, V.N. Starovoitova, D.P. Wells, *Long-term variations in the surface air <sup>7</sup>Be concentration and climatic changes*, Journal of Environmental Radioactivity, 116 (2013) 42-47.

V.N. Starovoitova, L. Tchelidze, D.P. Wells, *Production of medical radioisotopes with linear accelerators*, Accepted for publication in the Journal of Nuclear Medicine (2013).

Z.J. Sun, D.P. Wells, V.N. Starovoitova, and C.R. Segebade, *Testing the Quasi-absolute Method in Photon Activation Analysis*, 22nd International Conference on the Application of Accelerators in Research & Industry (CAARI 2012), accepted for publication, AIP press, (2013).

J.F. Harmon, D.P. Wells and A.W. Hunt, *Neutrons and Photons in Nondestructive Detection*, Reviews of Accelerator Science and Technology, Vol. 4 (2011) 83–101, World Scientific Publishing Company.

D.P. Wells and C.R. Segebade, *An Overview of Activation Analysis Techniques and Applications*, Proceedings of 21<sup>st</sup> International Conference on the Application of Accelerators in Research & Industry, AIP press, Vol. 1336, pg. 452, (2011).

V. Starovoitova, D. Foote, J. Harris, V. Makarashvili, C.R. Segebade, V. Sinha and D.P. Wells, *Cu-67 Photo-nuclear production*, Proceedings of 21<sup>st</sup> International Conference on the Application of Accelerators in Research & Industry, AIP press, Vol. 1336, pg. 502, (2011).

Mestari, M.A., D.P. Wells, L.C. DeVeaux, and S. F. Naeem, *Real-Time Dosimetry System for Radiobiology Experiments Using a 25 MeV LINAC*, Proceedings of 20<sup>th</sup> International Conference on the Application of Accelerators in Research & Industry, AIP press, Vol. 1099, pgs. 3-6, (2009).

G. Kharashvili, V. Makarashvili, M. Mitchell, W. Beezhold, R. Spaulding, D.P. Wells, T. F. Gesell, W. Wingert, *Development and Testing of Gallium Arsenide Photoconductive Detectors for Ultra Fast, High Dose Rate Pulsed Electron and Bremsstrahlung Radiation Measurements*, Proceedings of 20<sup>th</sup> International Conference on the Application of Accelerators in Research & Industry, AIP press, Vol. 1099, pgs. 55-58 (2009).

L. Tchelidze, D. P. Wells and S. A. Maloy, *Positron Annihilation Energy and Lifetime Spectroscopy Studies for Radiation Defects in Stainless Steel*, Proceedings of 20<sup>th</sup> International Conference on the Application of Accelerators in Research & Industry, AIP press, Vol. 1099, pgs. 985-988 (2009).

### **Synergistic Activities:**

My research and education activities include many collaborative projects with radio-biologists (extremophiles, bio-threat reduction), anthropologists (photon activation analysis and artifact attribution), chemists (radio-isotope production), engineers (nuclear fuels characterization, nuclear non-proliferation), and homeland security (nuclear detection technique development).

### **Collaborators and Other Affiliations**

B. Blackburn, Raytheon; S. DasSarma University of Maryland Baltimore; J. L. Jones, INL; S. Maloy, Los Alamos National Laboratory (LANL); T. Roney, INL; T. White, INL; M. Espy (LANL); F. Merrill (LANL); K. Pitts (PNNL).

### **Graduate and Postdoctoral Advisors**

Ph.D. Advisors: A. Nathan (retired), B. Eisentein, (retired) University of Illinois.  
Postdoctoral Advisor: K. Snover (retired), E. Adelberger, University of Washington.

### **Thesis Advisor and Postgraduate-Scholar Sponsor**

Greg Gibbons, Doug Walker, Liu Jiwen, Tobin Mott, John Kwofie, Dr. Wade Scates, Jason Williams, Yoshi Toyoda, Vakhtang Makarashvili, Lali Tchelidze, Scott Thompson, Syed Naeem, Nino Tchelidze, Dr. Cecilia Hoffman, Amine Mestari, John Ralph, Ee Lin Roethlisberg, Kristin Smith, Jonathon Case, Jonathon Walker, Jay Kumar, Kiran Billa, Dr. Farida Selim, Dr. Khalid Choffani, Dr. Marc Mitchell, Charles Taylor.

**Pavel Degtiarenko**

pavel@jlab.org  
phone: 757-269-6274

110 Sharps Lane, Williamsburg, VA 23185

## **Education and Training**

Institute of Theoretical and Experimental Physics/Moscow Institute for Physics and Technology,  
Experimental, Physics, Ph.D., 1987

Moscow Institute for Physics and Technology, Physics and Engineer, M.S., 1978

## **Research and Professional Experience**

1996- Present	Staff Scientist, Jefferson Lab
1996-1996	Post Doctoral Fellow, CTR Corporation
1992-1995	Visiting Research Assistant Professor, Medium Energy Nuclear Physics Group
1986-1992	Scientist & Senior Scientist, Laboratory for High Energy Nuclear Physics ITEP

## **Publications**

*"Activation by 2.25 and 3.36 GeV electrons: Comparison of measurements with FLUKA calculations"*  
by G. Kharashvili and P. Degtiarenko

Shielding Aspects of Accelerators, Targets and Irradiation Facilities – SATIF 12 Workshop,  
Batavia, Illinois, United States 28-30 April 2014

Proceedings published by OECD Nuclear Science, NEA/NSC/R(2015)3, p. 149, 2015

*"Radiation dose rates resulting from the Experimental Program at JLab", P. Degtiarenko*  
Internal semiannual or quarterly JLab reports (Radiation Control Department Notes), 1996-2012

*"New Techniques of Low Level Environmental Radiation Monitoring at JLab", P. Degtiarenko,*  
V. Popov

IEEE Transactions on Nuclear Science, Vol. **57**, No. 5, 2010, 2000

*"Recent Skyshine Calculations at Jefferson Lab", P. Degtyarenko*  
Proceedings of the Third Workshop on Simulating Accelerator Radiation Environment (SARE3), 7-9 May 1997, KEK, Tsukuba, Japan, p. 264-273, 1997

*"Initial Measurements of Site Boundary Neutron Dose and Comparison with Calculations",*  
P. Degtyarenko, D. Dotson, R. May, S. Schwahn, and G. Stapleton  
in: Proceedings of the Health Physics Society 30th Midyear Topical Meeting on Health Physics of  
Radiation-Generating Machines, 5-8 January 1997, San Jose, California, p. 205-212, 1997

*"Applications of the Photonuclear Fragmentation Model to Radiation Protection Problems",*  
P. Degtyarenko  
Proceedings of the Second Specialist's Meeting on Shielding Aspects of Accelerators, Targets and  
Irradiation Facilities (SATIF2), 12-13 October 1995, CERN, Geneva, Switzerland, p. 67-91, 1995

*"Multiple hadron production by 14.5 GeV electron and positron scattering from nuclear targets"*  
P. Degtyarenko et al. (12 co-authors)  
Phys. Rev. C, **50**, R541-R54, 1994

*"Monte Carlo program for nuclear fragmentation", P. Degtyarenko and M. Kossov*  
Preprint ITEP-11, 1-18 (1992)

*"Inelastic Electron-Nucleus Interactions at 5 GeV detected by ARGUS", P. Degtyarenko et al. (4 co-authors)*

Z.Phys.A, **335**, 231-238 , 1990

*"Correlations between neutrons with small relative momenta produced in (pPb) interactions at 7.5 GeV/c"*

*with Yu.D.Bayukov et al. (13 co-authors)*

Phys.Lett.B, **189**, 291-294, 1987

*"Correlations of identical  $\pi^+\pi^-$  mesons produced in pion-nucleus interactions at 3.7 GeV/c"*

*with Yu.D.Bayukov et al. (5 co-authors)*

Yad.Fiz., **33**, 727-732, 1981

### **Synergistic Activities:**

American Physical Society, Division of Nuclear Physics

American Nuclear Society

American Health Physics Society

### **Patents**

*"Moving Core Beam Energy Absorber and Converter", P. Degtiarenko*

United States Patent 8,334,523 B1, 2012

*"Method of Multi-Channel Data Readout and Acquisition", P. Degtiarenko and V. Popov*

United States Patent 7,737,874 B1, 2010

*"Method and Apparatus for Measuring properties of Particle Beams*

*Using Thermo-Resistive Material Properties", P. Degtiarenko and D. Dotson*

United States Patent 7,279,882 B1, 2007

*"Cooled Particle Accelerator Target" , P. Degtiarenko*

United States Patent 6,904,957 B1, 2005

*"Heat Exchange Apparatus" P. Degtiarenko*

United States Patent 6,604,575 B1

**Sundaresan Gobalakrishnan**  
ASSISTANT PROFESSOR

**Education and Training**

Bharathiar University, India.	B.Sc.	1982-1985	Zoology
Bharathiar University, India.	M.Sc.	1985-1987	Zoology
University of Madras, India.	M. Phil.	1987-1988	Physiology
AIIMS, New Delhi, India.	Ph.D.	1993-2000	Physiology
NII, New Delhi, India	Postdoctoral	2000	Virology
Univ. of California at Los Angeles, USA.	Postdoctoral	2000-2005	Molecular Imaging
Stanford University, Stanford, USA.	Postdoctoral	2005-2006	Molecular Imaging

**Research and Professional Experience**

- (1) **Assistant Professor** (Research), Head of Multi-modality Imaging Laboratory, Center for Molecular Imaging, Department of Radiology, Virginia Commonwealth University, Richmond, VA, USA; February, 2013 to till date.
- (2) **Scientist Manager**, Center for Molecular Imaging, Department of Radiology, Virginia Commonwealth University, Richmond, VA, USA; April 2009 to February, 2013.
- (3) **Principal Scientist** (Molecular Imaging Lead), Oncology CEDD (Biology), GlaxoSmithKline R&D, Collegeville, PA, USA; October 2006 to December 2008.
- (4) **Research Associate** (Molecular Imaging), Laboratory of Prof. Sanjiv S. Gambhir MD, PhD, Molecular Imaging Program at Stanford, Stanford University, Stanford, USA; November 2005 to September 2006.
- (5) **Postgraduate Researcher** (Molecular Imaging), Laboratory of Prof. Sanjiv S. Gambhir MD, PhD, Crump Institute for Molecular Imaging, Department of Molecular and Medical Pharmacology, UCLA School of Medicine, Los Angeles, USA; August 2000 to October 2005.
- (6) **Postdoctoral Fellow** (Virology), Laboratory of Dr. Akhil C. Banerjee, PhD, Virology Laboratory, National Institute of Immunology, New Delhi, India; Apr-Jul 2000
- (7) **Lecturer in Physiology**, SVM Dental College, Salem, Tamil Nadu, India; Feb-Sep 1989.

**Publications (Publishing as Gobalakrishnan Sundaresan or G Sundaresan)**

1. Hoffman D, Sun M, Yang L, McDonagh PR, Corwin F, **Sundaresan G**, Wang L, Vijayaragavan V, Thadigiri C, Lamichhane N, Zweit J. Intrinsically radiolabelled [(59)Fe]-SPIONs for dual MRI/radionuclide detection. *Am J Nucl Med Mol Imaging*. **4**(6):548-60, 2014.
2. Sun M, **Sundaresan G**, Jose P, Yang L, Hoffman D, Lamichhane N, Zweit J. Highly stable intrinsically radiolabeled indium-111 quantum dots with multidentate zwitterionic surface coating: dual modality tool for biological imaging. *J. Mater. Chem. B*. **2**:4456-4466, 2014.
3. Rex K, Lewis XZ, **Sundaresan G**, Glaus C, Silva MD, Radinsky R, Burgess TL, Gambhir SS, Coxon A. Evaluation of the antitumor effects of rilotumumab by PET imaging in a U-87 MG mouse xenograft model. *Nuclear Medicine and Biology*. **40**(4):458-63, 2013.
4. Yang L, **Sundaresan G**, Sun M, Jose P, Hoffman D, McDonagh PR, Lamichhane N, Cutler CS, Perez JM and Zweit J. Intrinsically Radiolabeled Multifunctional Cerium Oxide Nanoparticles for in vivo Studies. *Journal of Materials Chemistry B*, **1**:1421-1431, 2013.
5. Dewkar GK, **Sundaresan G**, Lamichhane N, Hirsch JI, Thadigiri C, Collier T, Hartman MCT, Vaidyanathan G, Zweit J. Microfluidic radiosynthesis and biodistribution of [18F] 2-(5-fluoro-pentyl)-2-methyl malonic acid. *Journal of Labelled Compounds and Radiopharmaceuticals*, **56**(5):289-94, 2013.

6. Sun M, Hoffman D, **Sundaresan G**, Yang L, Lamichhane N, Zweit J. Synthesis and characterization of intrinsically radio-labeled quantum dots for bimodal detection. *American Journal of Nuclear Medicine and Molecular Imaging*, **2**(2): 122-135, 2012.
7. Olafsen T, Kenanova V, **Sundaresan G**, Anderson A, Crow D, Li L, Press M, Gambhir SS, Williams LE, Wong JYC, Raubitschek AA, Shively JE and Wu AM. Optimizing radiolabeled engineered anti-p185HER2 antibody fragments for in vivo imaging. *Cancer Research*, **65**(13): 5907-16, 2005.
8. Kenanova V, Olafsen T, Crow D, **Sundaresan G**, Subbarayan M, Carter N, Ikle D, Yazaki P, Chatziioannou A, Gambhir SS, Williams LE, Shively JE, Colcher D, Raubitschek AA and Wu AM. Tailoring the Pharmacokinetics of Engineered Antibody Fragments. Biodistribution and Small Animal PET Imaging of anti-CEA scFv-Fc and Variants. *Cancer Research*, **65**(2): 622-31, 2005.
9. **Sundaresan G**, Yazaki PJ, Shively JE, Finn R, Larson SM, Raubitschek AA, Chatziioannou AF, Gambhir SS and Wu AM. Iodine-124 Labeled Engineered Anti-CEA Minibodies and Diabodies allow High-Contrast, Antigen-Specific MicroPET Imaging in Athymic Mice. *Journal of Nuclear Medicine*, **44**(12): 1962-9, 2003.

#### **Synergistic Activities**

- Member, World Molecular Imaging Society
- Guest Editor, International Journal of Molecular Sciences
- Editorial Board Member, Austin Journal of Nuclear Medicine and Radiotherapy
- Reviewer for various scientific journals
- Invited Participant of the 11th Annual National Academies Keck Futures Initiative (NAKFI) conference, 'The Future of Advanced Nuclear Technologies: Building a Healthier and Safer Planet', at the National Academy of Science, Irvine, California, Nov 2013.

**Identification of Potential Conflicts of Interest or Bias in Selection of Reviewers: NONE**

#### **Principal Graduate and Postdoctoral Advisors**

- Prof. Usha Sachdeva, All India Institute of Medical Sciences, New Delhi, India
- Prof. Dr. Akhil C. Banerjee, PhD, Virology Laboratory, National Institute of Immunology, New Delhi, India
- Prof. Sanjiv S. Gambhir MD, PhD, Molecular Imaging Program at Stanford, Stanford University, Stanford, USA

**Graduate and Postdoctoral Advisors and Advisees: NONE**

## Joseph Gubeli

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12000 Jefferson Ave, Newport News, VA 23606

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mobile: 757-344-4159

## Education and Training

Christopher Newport University	Applied Physics	M.S., 1998
Christopher Newport University	Applied Physics	B.S., 1996

## Research and Professional Experience

2015-Present	Diagnostics Engineer, CASA, Jefferson Lab
2014-2015	Staff Engineer, Mechanical Engineer, Jefferson Lab
2005-2014	Optics Group Leader, Free Electron Laser, Jefferson Lab
1996-2005	Staff Engineer, Free Electron Laser, Jefferson Lab

## Publications

1. Fernanda H. Sakamoto, Apostolos G. Doukas, William A. Farinelli, Zeina Tannous, Michelle Shinn, Steve Benson, Gwyn Williams, H. Frederick Dylla and R. Rox Anderson, "Selective Photothermolysis to target Sebaceous Glands: Theoretical Estimation of Parameters and Preliminary Results Using a Free Electron Laser", *Lasers in Surgery and Medicine* **44** 175 (2012).
2. R. Rox Anderson, William Farinelli, Hans Laubach, Dieter Manstein, Anna N. Yaroslavsky, Joseph Gubeli III, Kevin Jordan, George R. Neil, Michelle Shinn, Walter Chandler, Gwyn P. Williams, Steven V. Benson, David R. Douglas, H.F. Dylla, "Selective photothermolysis of lipid-rich tissues: A free electron laser study", *Lasers in Surgery and Medicine* **38** 913 (2006).
3. G.R. Neil, C. Behre, S.V. Benson, M. Bevins, G. Biallas, J. Boyce, J. Coleman, L.A. Dillon-Townes, D. Douglas, H. F. Dylla, R. Evans, A. Grippo, D. Gruber, J. Gubeli, D. Hardy, C. Hernandez-Garcia, K. Jordan, M.J. Kelley, L. Merminga, J. Mammoser, W. Moore, N. Nishimori, E. Pozdeyev, J. Preble, R. Rimmer, M. Shinn, T. Siggins, C. Tennant, R. Walker, G.P. Williams, S. Zhang, "The JLab High Power ERL Light Source", *Nucl. Instr. & Methods* **A557** 9 (2006).
4. George R. Neil, G. L. Carr, Joseph F. Gubeli III, K. Jordan, Michael C. Martin, Wayne R. McKinney, Michelle Shinn, Masahiko Tani, G. P. Williams and X.- C. Zhang, "Production of High Power Femtosecond Terahertz Radiation", *Nuclear Instruments and Methods* **A507** 537 (2003).
5. M. N. Petrovich, A. Favre, D. W. Hewak, H. N. Rutt, A. C. Grippo, J. F. Gubeli III, K. C. Jordan, G. R. Neil, M. D. Shinn, "Near-IR Absorption of Ga:La:S and Ga:La:S:O Glasses by FEL-based laser calorimetry. *Journal of Noncrystalline Solids*, **326-327** 93-97 (2003).
6. M. D. Shinn, G. R. Baker, C. P. Behre, S. V. Benson, M. E. Bevins L. A. Dillon-Townes, H. F. Dylla, E. J. Feldl, J. F. Gubeli, R. D. Lassiter, F. D. Martin, and G. R. Neil, "Design of the Jefferson Lab IR Upgrade FEL optical cavity", *Nuclear Instruments and Methods* **A507** 196 (2003).
7. A. Christodoulo, D. Lampiris, K. Polykandriotis, W.B. Colson, P.P. Crooker, S. Benson, J. Gubeli, and G.R. Neil "Free-electron-laser oscillator with a linear taper", *Phys. Rev.* **E66**, 56502 (2002).
8. G. R. Neil, S. V. Benson, G. Biallas, H. P. Freund, J. Gubeli, K. Jordan, S. Myers and M. D. Shinn, "Second Harmonic FEL Oscillation" *Nuclear Instruments and Methods in Physics Research* **A483**, 119 (2002).



9. Stephen V. Benson, Joe Gubeli, and Michelle Shinn, “Mode Distortion Measurements on the Jefferson Lab IR FEL” Nuclear Instruments and Methods in Physics Research **A483**, 434 (2002).

### **Synergistic Activities**

Co-winner R&D100 Award for Free Electron Laser

### **Patents**

Method for separating FEL output beams from long wavelength radiation, US 9,325,145

**Kevin Jordan**

Jefferson Lab

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Newport News, VA 23606

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email: [jordan@jlab.org](mailto:jordan@jlab.org)**Position Title:** Diagnostics Group Leader, CASA**A. Professional Preparation**

PE	Registered Professional Engineer	1995
BSEE	Old Dominion University	1991
AAET	Madison Area Technical College	1977

**B. Appointments**

2015-present:	Diagnostics Group Leader, CASA, Jefferson Lab
2013-2015:	CASA, Jefferson Lab
1996-2013:	Chief Engineer Free Electron Laser, Jefferson Lab
1987-1996:	Staff Engineer, SRF Division, Jefferson Lab
1985-1987:	Technischer Angestellter, Deutsches Elektronen-Synchrotron (DESY)
1978-1985:	Electronic Technician, Fermi National Accelerator Lab

**C. Recent Publications**

10. G. Ciovati, Steven M. Anlage, C. Baldwin, G. Cheng, R. Flood, K. Jordan, P. Kneisel, M. Morrone, G. Nemes, L. Turlington, H. Wang, K. Wilson, and S. Zhang “Low temperature laser scanning microscopy of a superconducting radio-frequency cavity” Review of Scientific Instruments **83**, 034704 (2012)
11. V. Raffa, C. Riggio, M. W. Smith, K. C. Jordan, W. Cao, A. Cuschieri “BNNT-Mediated Irreversible Electroporation: Its Potential on Cancer Cells” Technology in Cancer Research and Treatment ISSN 1533-0346, 2012 March 28
12. M.W. Smith, K.C. Jordan, C. Park, J.-W. Kim, P.T. Lillehei, R. Crooks and J.S. Harrison “Very long single- and few-walled boron nitride nanotubes via the pressurized vapor/condenser method” Nanotechnology **20** (2009) 505604 (6pp)
13. M.A. Holloway, R.B. Fiorito, A.G. Shkvarunets, P.G. O’Shea, S.V. Benson, D. Douglas, P. Evtushenko, K. Jordan, “Multicomponent measurements of the Jefferson Lab energy recovery linac electron beam using optical transition and diffraction radiation”, Phys. Rev. ST Accel. Beams **11** 082801 (2008).
14. C. Park, K. E. Wise, J. H. Kang, J.-W. Kim, G. Sauti, S. E. Lowther, P. T. Lillehei, M. W. Smith, E. J. Siochi, and J. S. Harrison, and K. Jordan, “Multifunctional nanotube polymer nanocomposites for aerospace applications: adhesion between SWCNT and polymer matrix”, Adhesion Society Meeting, Austin TX, Feb (2008)
15. P. C. Eklund, B. K. Pradhan, U. J. Kim, and Q. Xiong, J. E. Fischer, A. D. Friedman and B. C. Holloway, K. Jordan, M.W. Smith, “Large-Scale Production of Single-Walled Carbon Nanotubes Using Ultrafast Pulses from a Free Electron Laser,” Nano Letters, American Chemical Society, Volume 2, Issue 6 (June 12, 2002).
16. C.D. Tennant, K.B. Beard, D.R. Douglas, K.C. Jordan, L. Merminga and E.G. Pozdeyev, “First observations and suppression of multipass, multibunch beam breakup in the Jefferson Laboratory free electron laser upgrade”, Phys. Rev. Special Topics – Accelerators and Beams **8** 074403 (2005).

#### **D. Synergistic Activities**

Scientific program committee member International Beam Instrumentation Conference  
Winner R&D100 Award for Free Electron Laser

#### **E. Patents:**

1. High kinetic energy penetrator shielding and high wear resistance materials fabricated with boron nitride nanotubes (BNNTS) and BNNT polymer composites, US 9,067,385
2. Magnesium doping of boron nitride nanotubes, US 9,059,361
3. Efficient boron-carbon-nitrogen nanotube formation via combined laser-gas flow levitation, US 8,986,513
4. Apparatus for the production of boron nitride nanotubes, US 8,753,578
5. Integrated Rig for the Production of Boron Nitride Nanotubes via the Pressurized Vapor-Condenser Method, US 8,679,300
6. Efficient boron nitride nanotube formation via combined laser-gas flow levitation, US 8,673,120
7. Articulating feedstock delivery device, US 8,573,446
8. Apparatus and method for fast recovery and charge of insulation gas, US 8,522,817
9. Protective laser beam viewing device, US 8,334,899
10. Laser Ablative Synthesis of Carbon Nanotubes, US 8,317,983
11. Boron Nitride Nanotubes, US 8,206,674
12. Magnetic Chicane for Terahertz Management, US 7,859,199
13. Apparatus for Free Electron Laser Ablative Synthesis of Carbon Nanotubes, US 7,663,077
14. Laser Ablative Synthesis of Carbon Nanotubes, US 7,671,306
15. Laser Ablation for the Synthesis of Carbon Nanotubes, US 7,692,116

## **George Kharashvili**

*Jefferson Lab  
12050 Jefferson Avenue, Suite 602  
Newport News, VA 23606, USA*

*Phone: +1 (757) 269-6435  
e-mail: georgek@jlab.org*

### **Education**

- Postdoctoral Fellow in Health Physics, Jefferson Lab, 2009-2012
- Ph.D. in Applied Physics, Idaho State University, 2009
- M.S. in Physics, Idaho State University, 2004
- B.S. in Physics, Tbilisi State University, Georgia, 2001

### **Research and Professional Experience**

- Radiation Physicist, Jefferson Lab, Radiation Control Department, 2012 - present
  - Radiation transport calculations
  - Development and testing radiation transport models
  - Photon and electron activation analysis
  - Radiation metrology
  - FLUKA collaboration
- Postdoctoral Fellow, Jefferson Lab, Radiation Control Department, 2009 - 2012
  - Radiation physics
  - Radiation detection instrumentation
- Research Assistant, Idaho Accelerator Center, Idaho State University, 2004 – 2009
  - Electron and bremsstrahlung beam characterization studies
  - Radiation dosimetry
  - Machine protection
  - Experiment setup for radiation biology research
  - Modeling and characterization of photoneutron sources
- Research Assistant, Environmental Monitoring Laboratory, Idaho State University, 2002 – 2004
  - Radiation metrology

### **Professional Affiliations and Services**

- Member of the Health Physics Society since 2002
  - Board of Directors of the Accelerator Section, 2011 – 2014
- Member of the Virginia Chapter of the Health Physics Society since 2010
  - Secretary since 2014
- Member of the Student Branch of the Eastern Idaho Chapter of the Health Physics Society, 2001 – 2009
  - President, 2007 – 2008
- Founding member of the Georgian Health Physics Association, member since 2007

### **Presentations/Publications:**

- G. Kharashvili, P. Degtiarenko, “Activation by 2.25 and 3.36 GeV electrons: Comparison of measurements with FLUKA calculations”, SATIF-12 proceedings, 149-155, 2014.
- P. Degtiarenko, G. Kharashvili, “Contribution of the direct electronuclear processes to thin target activation”, SATIF-12 proceedings, 284-290, 2014.
- P. Degtiarenko, G. Kharashvili, “Comparison of Thin Foil Activation Measurements to FLUKA Predictions”, Health Physics Society 58<sup>th</sup> Annual Meeting, Madison, Wisconsin July 2013.

- P. Degtiarenko, M. Keller, G. Kharashvili, V. Vylet, K. Welch, “Radiation Safety Considerations of the New High Gradient Cryomodule Operation at Jefferson Lab”, Health Physics Society 58<sup>th</sup> Annual Meeting, Madison, Wisconsin July 2013
- P. Degtiarenko, G. Kharashvili, V. Vylet, “Comparison of Direct Electron and Photon Activation Measurements with FLUKA Predictions – Preliminary Results”, 2<sup>nd</sup> FLUKA Advanced Course and Workshop, Vancouver, 2012
- G. Kharashvili, P. Degtiarenko, A. Fassò, V. Vylet, K. Welch, “Shielding of RF Penetrations at Jefferson Lab”. 56<sup>th</sup> Annual Meeting of the Health Physics Society, West Palm Beach, Florida, June 2011
- G. Kharashvili, M. D. Mitchell, W. Beezhold, T. F. Gesell, “Development and Testing of Gallium Arsenide Photoconductive Detectors for Ultra Fast, High Dose Rate Pulsed Electron and Bremsstrahlung Radiation Measurements”. 54<sup>th</sup> Annual Meeting of the Health Physics Society, Minneapolis, July 2009
- G. Kharashvili, V. Makarashvili, M. D. Mitchell, W. Beezhold, R. Spaulding, D. P. Wells, T. F. Gesell, W. Wingert, “Development and Testing of Gallium Arsenide Photoconductive Detectors for Ultra Fast, High Dose Rate Pulsed Electron and Bremsstrahlung Radiation Measurements”. AIP Conference Proceedings Volume 1099, Application of Accelerators in Research and Industry: Twentieth International Conference, pp. 55-58, 2008.
- G. Kharashvili, W. Beezhold, R. R. Brey, T. F. Gesell, A. Hunt. “Study of GaAs Photo Conductive Detectors (PCDs)”. American Conference of Radiation Safety, HPS’s 51<sup>st</sup> Annual Meeting, 2006
- G. Kharashvili, R. R. Brey, D. P. Wells, J. F. Harmon, T. F. Gesell; “Determination of the Photonuclear Cross-Section of  $^{129}\text{I}(\gamma, n)^{128}\text{I}$ ”. American Conference of Radiation Safety, 48<sup>th</sup> Annual Meeting of the Health Physics Society, 2003

## Frank Strieder

South Dakota School of Mines and Technology  
501 E. Saint Joseph St., Rapid City, SD 57701

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Phone: 605-394-1227

### (a) Professional Preparation:

Ruhr-Universität Bochum, Germany, M.S. Physics (summa cum laude), 1996  
Ruhr-Universität Bochum, Germany, Ph.D. Physics (summa cum laude), 2000  
Ruhr-Universität Bochum, Germany, Venia Legendi (Habilitation, Permission to lecture), 2009

### (b) Appointments:

Associate Professor of Physics, South Dakota School of Mines and Technology, Rapid City,  
2015 – present  
Lecturer (Privatdozent), Ruhr-Universität Bochum, Germany, 2009 – 2014  
Visiting Assistant Professor, Seconda Università di Napoli, Caserta, Italy, 2013  
Research Associate, Ruhr-Universität Bochum, Germany, 2000 – 2009  
Pre-doctoral Associate, Ruhr-Universität Bochum, Germany, 1996 – 2000

### (c) Related Products and Other Significant Products (out of more than 100 peer-reviewed publications):

- R. J. deBoer, J. Görres, K. Smith, E. Uberseder, M. Wiescher, A. Kontos, G. Imbriani, A. Di Leva, **F. Strieder**, "Monte Carlo Uncertainty of the  $^3\text{He}(\alpha, \gamma)^7\text{Be}$  reaction rate", Phys. Rev. C 90 (2014) 035804  
<http://dx.doi.org/10.1103/PhysRevC.90.035804>
- A. Di Leva, D.A. Scott, A. Caciolli, A. Formicola, **F. Strieder**, M. Aliotta, M. Anders, D. Bemmerer, C. Broggini, P. Corvisiero, Z. Elekes, Zs. Fülöp, G. Gervino, A. Guglielmetti, C. Gustavino, Gy. Gyürky, G. Imbriani, J. Jose, M. Junker, M. Laubenstein, R. Menegazzo, E. Napolitani, P. Prati, V. Rigato, V. Roca, E. Somorjai, C. Salvo, O. Straniero, T. Szücs, F. Terrasi, D. Trezzi, "Underground study of the  $^{17}\text{O}(p, \gamma)^{18}\text{F}$  reaction for explosive hydrogen burning", Phys. Rev. C 89 (2014) 015803  
<http://dx.doi.org/10.1103/PhysRevC.89.015803>
- O. Straniero, G. Imbriani, **F. Strieder**, M. Junker, D. Bemmerer, C. Broggini, A. Caciolli, P. Corvisiero, H. Costantini, S. Cristallo, A. DiLeva, Z. Elekes, A. Formicola, Zs. Fülöp, G. Gervino, A. Guglielmetti, C. Gustavino, Gy. Gyürky, A. Lemut, B. Limata, M. Marta, C. Mazzocchi, R. Menegazzo, I. Piersanti, P. Prati, V. Roca, C. Rolfs, C. Rossi Alvarez, E. Somorjai, F. Terrasi, H.-P. Trautvetter, "Impact of a revised  $^{25}\text{Mg}(p, \gamma)^{26}\text{Al}$  reaction rate on the operation of the Mg-Al cycle", Astrophys. J. 763 (2013) 100  
<http://dx.doi.org/10.1088/0004-637X/763/2/100>
- D. Schürmann, L. Gialanella, R. Kunz, **F. Strieder**, "The astrophysical S factor of  $^{12}\text{C}(\alpha, \gamma)^{16}\text{O}$  at stellar energy", Phys. Lett. B 711 (2012) 35  
<http://dx.doi.org/10.1016/j.physletb.2012.03.064>
- **F. Strieder**, B. Limata, A. Formicola, G. Imbriani, M. Junker, H.W. Becker, D. Bemmerer, A. Best, R. Bonetti, C. Broggini, A. Caciolli, P. Corvisiero, H. Costantini, A. DiLeva, Z. Elekes, Zs. Fülöp, G. Gervino, A. Guglielmetti, C. Gustavino, Gy. Gyürky, A. Lemut, M. Marta, C. Mazzocchi, R. Menegazzo, P. Prati, V. Roca, C. Rolfs, C. Rossi Alvarez, C. Salvo, E. Somorjai, O. Straniero, F. Terrasi, H.-P. Trautvetter, "The  $^{25}\text{Mg}(p, \gamma)^{26}\text{Al}$  Reaction at Astrophysical Energies", Phys. Lett. B 707 (2012) 60  
<http://dx.doi.org/10.1016/j.physletb.2011.12.029>
- E.G. Adelberger, A.B. Balantekin, D. Bemmerer, C.A. Bertulani, J.-W. Chen, H. Costantini, M. Couder, M. Wiescher, R. Cyburt, B. Davids, S.J. Freedman, M. Gai, A. Garcia, D. Gazit, L. Gialanella, U. Greife, M. Hass, W.C. Haxton, K. Heeger, G. Imbriani, T. Itahashi, A. Junghans, K. Kubodera, K. Langanke, D. Leitner, M. Leitner, L.E. Marcucci, T. Motobayashi, A. Mukhamedzhanov, K.M. Nollett, F.M. Nunes, T.-S. Park, P.D. Parker, P. Prati, M. J. Ramsey-Musolf, R.G.H. Robertson, R. Schiavilla,

- E. Simpson, K. A. Snover, C. Spitaleri, **F. Strieder**, K. Sümmerer, H.-P. Trautvetter, R.E. Tribble, S. Typel, E. Uberseder, P. Vettel, L. Winslow, **Review article**: “*Solar fusion cross sections II: the pp chain and CNO bi-cycleI*”, Rev. Mod. Phys. 83 (2011) 195  
<http://dx.doi.org/10.1103/RevModPhys.83.195>
- H. Costantini, A. Formicola, G. Imbriani, M. Junker, C. Rolfs, **F. Strieder**, **Review article**: “*LUNA: a Laboratory Underground for Nuclear Astrophysics*”, Rep. Prog. Phys. 72 (2009) 086301  
<http://dx.doi.org/10.1088/0034-4885/72/8/086301>
  - **F. Strieder**, “*Reaction Data in Helium and Carbon Burning*”, Journal of Physics G 35 (2008) 014009  
<http://dx.doi.org/10.1088/0954-3899/35/1/014009>
  - **F. Strieder** and C. Rolfs, **Review article**: “*Reaction data for light element nucleosynthesis*”, Prog. Part. Nuc. Phys. 59 (2007) 562  
<http://dx.doi.org/10.1016/j.pnpnp.2007.02.001>

#### (d) Synergetic Activities

- Member of the International Advisory Committee (IAC) for the Jinping Underground Laboratory for Nuclear Astrophysics (JUNA), 2015 - present
- Member of the Collaboration Council for the SECAR experiment at the Facility for Rare Isotope Beams (FRIB) at Michigan State University, 2015 - present
- Member of the Review Panel of the European Science Foundation (ESF) EuroCores Programme EuroGENESIS, 2009 - 2014
- Co-Organizer of the “Solar Fusion II” Workshop in Seattle, USA, January 2009
- Referee for Physical Review Letters, Physics Letters B, Physical Review C, J. of Physics G, Nuclear Instruments and Methods A, Eur. Phys. J. A

#### (e) Awards

Recognition as an Outstanding Referee by Nuclear Instruments and Methods A, 2012

#### (f) Collaborators

Collaborators: Michael Wiescher, Dan Robertson, Manoel Couder, Richard DeBoer, University of Notre Dame; Uwe Greife, Colorado School of Mines; Jeff Schweitzer, University of Connecticut; Gianluca Imbriani, Università di Napoli (Italy); Lucio Gialanella, Seconda Università di Napoli (Italy); Alba Formicola, Matthias Junker, Laboratori Nazionali del Gran Sasso (Italy); Marialuisa Aliotta, Tom Davinson, University of Edinburgh (UK); Alessandra Guglielmetti, Davide Trezzi, Università di Milano (Italy); Piero Corvisiero, Paolo Prati, Università di Genova (Italy); Carlo Brogini, Roberto Menegazzo, Università di Padova (Italy); Daniel Bemmerer, HFZ Dresden (Germany); Oscar Straniero, Osservatori di Teramo (Italy), Zsolt Fülöp, György Gyürky, Atomki Debrecen (Hungary); Michael Smith, ORNL.

Ph.D. Thesis Advisor: Claus Rolfs (Ruhr-Universität Bochum, Germany)

Graduate Advisor: Hanns-Peter Trautvetter (Ruhr-Universität Bochum, Germany)

Former Ph.D. Students: Daniel Schürmann (INFN Napoli), Antonino Di Leva (Università di Napoli)

## STANLEY M. HOWARD

501 E St. Joseph Street

Dept of Materials and Metallurgical Eng SD School of Mines & Technology Rapid City, SD 57701  
(605) 394-1282; Fax: (605) 394-3369 stanley.howard@sdsmt.edu

### (a) Professional Preparation

- BS. Metallurgical Engineering, Colorado School of Mines, Golden, CO (1967)
- Ph.D. Metallurgical Engineering (Minor - Chemical Petroleum Refining Engineering), Colorado School of Mines, Golden, CO (1971)
- PE Registered Professional Engineer (SD #2219)

### (b) Appointments

- 1971 – present, Department of Materials and Metallurgical Engineering, Assistant Professor (1971 - 75), Associate Professor (1975 - 81) Professor (1981-present), Chair (1994-2000) South Dakota School of Mines & Technology; Rapid City, SD
- 2004 – 2007, Yucca Mountain Project, Consultant/Auditor, DOE Contractor, BSE, Summerlin, NV
- 2003 – 2004, Division of Metals and Ceramics, Consultant, Oak Ridge Nat'l Lab, Oak Ridge, TN
- 1992 – 2001, Caterpillar Corporation – Consultant, Technical Center, Peoria, IL
- 1988 – 1991, Electronic Manuf. & Prod. Facility, Consultant, U. S. Dep't of the Navy, Ridgecrest, CA
- 1986 – 1987, Kerr-McGee Corporation, Consultant, Oklahoma City, OK
- 1981 – 1988, Group V Metals, Inc. - President (81 - 84), Vice President (84 - 88), Rapid City, SD
- 1977 – 1982, Mintech, Inc. - President (77 - 82), Rapid City, SD
- 1976 – 1977, Stanford Research Center, NSF Visiting Scientist, Menlo Park, CA
- 1967 – 1971, Dept of Metallurgical Eng, Research Fellow, Colorado School of Mines, Golden, CO
- 1967 sum., Atomic Weapons Division – Engineer, Dow Chemical Company, Golden, CO

### (c) Selected Publications

- 1) S.M. Howard: *Direct Activity Measurements in the Liquid Ag-Cu System Using a Valved Knudsen Cell- Mass Spectrometer System*, Metall. Trans. B, 1989, vol. 20B, pp. 845-52
- 2) J. Lui, S.M. Howard, and K. H. Han: *Adsorption Behavior of Cadmium and Zinc Ions on Oxide/Water Interfaces*, Langmuir, 1993, vol. 9, No. 12, pp. 3635-9
- 3) S. M. Howard and Stone, G: "High Strength and High Electrical Conductivity Copper Alloys." US Patent #6231700. May 15, 2001
- 4) J. I. Lee, S.M. Howard, J. J. Kellar, W. Cross, and K. H. Han: *Electrochemical Interactions between Silver and Sulfur in Sodium Solutions*, Metall. Trans. B, 2001, vol. 32B, pp. 895-901
- 5) Bharat Jasthi, William Arbogast, Stanley M. Howard: *Thermal Expansion Coefficient and Mechanical Properties of Friction Stir Welded Invar (Fe-36%Ni)*, Journal of Materials Engineering and Performance, 2009, vol. 18(7), pp. 925-34
- 6) B.K. Jasthi, W. J. Arbogast, and S. M. Howard: *Effect of Thermal Aging on the Corrosion and Microstructure of Friction Stir Welded Alloy 22*, Metall. Trans. A, 2012, vol. 43A, pp. 3192-201
- 7) S. M. Howard and J. P. Hager: *Thermodynamic Properties of the Liquid Sn-Ge and Sn-Au System by Mass Spectrometry*, Metall. Trans. Vol. 9B, 1978, pp. 51-59
- 8) S. M. Howard and J. P. Hager, and J. H. Jones: *Thermodynamic Properties of the Ge-Cu and Ge-Au Systems by Mass Spectrometry*, Metall. Trans., 1973, vol. 4, pp. 2383-88
- 9) Daniel Cubicciotti, Robin L. Jones, S. M. Howard, et al.: *The Formation of Iodine Induced Stress Corrosion Cracks in Zircalloys*, Journal of Nuclear Metals, 1978, vol. 78, pp. 2-16
- 10) S. M. Howard: *Extractive Metallurgy of Uranium and Plutonium*, Encyclopedia of Materials, Science and Technology, 2<sup>nd</sup> ed., Elsevier Science, Oxford, England, ISBN: 0-08-0431526, pp. 9458-9, 2002



**(d) Synergistic Activities:**

Short Course Presenter:

- *Corrosion Control and Prevention*, South Dakota School of Mines & Technology, Rapid City (1976)
- *Recovery and Sampling of Secondary Precious Metals*, U. S. Department of Defense Sponsored, South Dakota School of Mines and Technology, Rapid City (1987)
- *Recovery and Sampling of Secondary Precious Metals*, U. S. Department of Defense Sponsored, South Dakota School of Mines and Technology, Rapid City (1988)
- *Personal Computer Applications in Materials and Metallurgical Engineering*, The Minerals, Metals, and Materials Society Annual Meeting, Anaheim (1990)
- *Personal Computer Applications for Metals and Materials Engineering*, The Minerals, Metals, and Materials Society Annual Meeting, New Orleans (1991)
- *Computer Software and Methods in Metallurgical and Materials Engineering*, The Minerals, Metals, and Materials Society Annual Meeting, San Francisco (1994)

Textbook Author:

- Applied Numerical Methods, 2008,  
[http://stanleyhoward.sdsmt.edu/Math373/\\_AppliedNumMethodsText\\_SMH/TextDirectory.htm](http://stanleyhoward.sdsmt.edu/Math373/_AppliedNumMethodsText_SMH/TextDirectory.htm)
- Thermodynamics and Thermochemistry for Metallurgical Engineers,  
2010 <http://showard.sdsmt.edu/MET320/Handouts/Text/Chapter 0-7c-2012.pdf>

## **APPENDIX 2: Current and Pending Support**

### **Andrew Hutton, Jefferson Lab**

#### **Pending**

Sponsor: U. S. Department of Energy, Office of Science, Office of Nuclear Physics

The award or other identifying number: This proposal; DE-FOA-0001588

Title: Isotope Production R&D at High Power Electron Accelerators

Total value of the project: \$799,110

Person weeks/year: 1

Funding Period: 2 years starting in 2017

Description:

Roles: Andrew Hutton (PI/PD), Jamal Zweit (Co-PI), Doug Wells (Co-PI), Sundaresan Gobalakrishnan (Co-I), Pavel Degtiarenko (Co-I), Kevin Jordan (Co-I), George Kharashvili (Co-I), Joseph Gubeli (Co-I).

### **Jamal Zweit, VCU**

#### **Current**

Sponsor: Cancer Research Institute (Zweit)

The award or other identifying number: Not available

Title: Immunotherapeutic targeting cell surface neoantigen

Total Value of the Award: \$80,761

Person Months/year: 0.6 cal mos

Funding Period: 08/01/2015 – 7/31/2016

Description: The overall goal of the proposed research aims to exploit the tumor selective properties of SAS1B to develop and evaluate immunotherapeutics targeting cell surface SAS1B using passive and active immunization strategies including antibody-drug conjugates, antibody-nuclide conjugates, chimeric antigen receptors, and a SAS1B targeted peptide vaccine.

Roles: John C Herr (PI); Jamal Zweit (Co-PI); Sundaresan Gobalakrishnan (Co-I).

Sponsor: National institute of neurological disorders and stroke

The award or other identifying number: 1R01NS093985

Title: Combination of HIPSCS and bioengineering to repair injured pediatric brain

Total Value of the Award: \$1,907,080.00

Person Months/year: 1.2 cal mos

Funding Period: 06/01/2016 – 05/31/2021

Description: Promote integration of iPSCs in the injured pediatric brain. Using bioengineering approach to enhance the survival and functional integration of transplanted iPS cells in the immature rat brain following traumatic injury

Roles: Dong Sun (PI); Xuejun Wen (Co-PI), Ning Zhang (Co-PI), Jamal Zweit (Co-PI)

#### **Pending**

Sponsor: NIH

The award or other identifying number: R01 (Investigator initiated)

Title: Aerosol Delivery Efficiency in Human Subjects During High Flow Nasal Cannula (HNFC) Therapy

Total Value of the Award: \$2,449,455.00

Person Months/year: 1.2 cal mos

Funding Period: 12/1/2016 – 11/30/2020

Description: Development and validation of human HFNC exposure system suitable for clinical use

Roles: Philip W Longest (PI); Michael Hindle (Co-PI); Jamal Zweit (Co-I); Sundaresan Gobalakrishnan

(Co-I).

Sponsor: NCI

The award or other identifying number: R01 (Investigator initiated)

Title: Recoupling Nitric Oxide Synthase to chemo and radiosensitize breast cancer

Total Value of the project: \$1,370,500.00

Person Months/year: 1.2 cal mos

Funding period: 07/01/2015 – 06/30/2017

Description: This proposal tests the hypothesis that recoupling nitric oxide synthase (NOS) activity with a tetrahydrobiopterin precursor enhances chemosensitivity in spontaneous mouse mammary carcinoma and colorectal tumor models by increasing tumor oxygenation via vascular normalization.

Roles: Ross Mikkelsen (PI), Jamal Zweit (Co-I), Sundaresan Gobalakrishnan (Co-I), Eleonora Mezzaroma (Co-I), Vasily Yakovlev (Co-I).

Sponsor: U. S. Department of Energy, Office of Science, Office of Nuclear Physics

The award or other identifying number: This proposal; DE-FOA-0001588

Title: Isotope Production R&D at High Power Electron Accelerators

Total value of the project: \$799,110

Person Months/year: 1.44 cal mos.

Funding Period: 2 years starting in 2017

Description:

Roles: Andrew Hutton (PI/PD), Jamal Zweit (Co-PI), Doug Wells (Co-PI), Sundaresan Gobalakrishnan (Co-I), Pavel Degtiarenko (Co-I), Kevin Jordan (Co-I), George Kharashvili (Co-I), Joseph Gubeli (Co-I).

### **Douglas Wells, SDSM&T**

#### **Current**

Sponsor: SD Science and Technology Board

Title: “*Demonstrator Project for Nuclear Astrophysics at the South Dakota Underground Facility (SURF)*”

Total Value of Project: \$1,00,000

Period of Performance: 2013 – 2016

Role: co-PI, partners include U. Notre Dame, Colorado School of Mines and SURF

#### **Pending**

Sponsor: U.S. Department of Justice

RFP ID: CFDA No. 16.560

Title: “*Photon Activation Analysis: a non-destructive, simultaneous multi-element forensic analysis tool for high-value samples*”

Total Value of Project: \$550K

Submission date: February 1, 2016

Funding Period: 2 years, starting 1 Oct 2016

Role: co-PI, partner is Idaho State University

Sponsor: U.S. Department of Energy

Phase 1 SBIR

Title: “*Isotope Production for Fracing Applications*”

Total Value of Project: \$150K

Funding Period: 1 year, beginning 1 Oct 2016

Role: co-PI, Niowave Inc. is the lead institution), Idaho State University is the other partner

Sponsor: U. S. Department of Energy, Office of Science, Office of Nuclear Physics  
The award or other identifying number: This proposal; DE-FOA-0001588  
Title: Isotope Production R&D at High Power Electron Accelerators  
Total value of the project: \$799,110  
Funding Period: 2 years starting in 2017  
Role: Co-PI

**Sundaresan Gobalakrishnan, VCU**

**Current**

Sponsor: Cancer Research Institute  
The award or other identifying number: Not Available  
Title: Immunotherapeutic targeting cell surface neoantigen  
Total Value of the Award: \$80,761.00  
Person Months/year: 0.6 cal mos  
Funding period: 08/01/2015 – 7/31/2016  
Description: The overall goal of the proposed research aims to exploit the tumor selective properties of SAS1B to develop and evaluate immunotherapeutics targeting cell surface SAS1B using passive and active immunization strategies including antibody-drug conjugates, antibody-nuclide conjugates, chimeric antigen receptors, and a SAS1B targeted peptide vaccine.  
Roles: John Herr (PI); Jamal Zweit (Co-PI); Sundaresan Gobalakrishnan (Co-I).

**Pending**

Sponsor: NIH  
The award or other identifying number: R01 (Investigator initiated)  
Title: Aerosol Delivery Efficiency in Human Subjects During High Flow Nasal Cannula (HNFC) Therapy  
Total Value of the Award: \$2,449,455.00  
Person Months/year: 1.2 cal mos  
Funding Period: 12/1/2016 – 11/30/2020  
Description: Development and validation of human HFNC exposure system suitable for clinical use  
Roles: Philip W Longest (PI); Michael Hindle (Co-PI); Jamal Zweit (Co-I); Sundaresan Gobalakrishnan (Co-I).

Sponsor: NCI  
The award or other identifying number: R01 (Investigator initiated)  
Title: Recoupling Nitric Oxide Synthase to chemo and radiosensitize breast cancer  
Total Value of the project: \$1,370,500.00  
Person Months/year: 1.2 cal mos  
Funding period: 07/01/2015 – 06/30/2017  
Description: This proposal tests the hypothesis that recoupling nitric oxide synthase (NOS) activity with a tetrahydrobiopterin precursor enhances chemosensitivity in spontaneous mouse mammary carcinoma and colorectal tumor models by increasing tumor oxygenation via vascular normalization.  
Roles: Ross Mikkelsen (PI), Sundaresan Gobalakrishnan (Co-I), Eleonora Mezzaroma (Co-I), Vasily Yakovlev (Co-I).

Sponsor: U. S. Department of Energy, Office of Science, Office of Nuclear Physics  
The award or other identifying number: This proposal - DE-FOA-0001588  
Title: Isotope Production R&D at High Power Electron Accelerators  
Total value of the project: \$799,110  
Person Months/year: 0.96 cal mos.  
Funding Period: 2 years starting in 2017

Description:

Roles: Andrew Hutton (PI/PD), Jamal Zweit (Co-PI), Doug Wells (Co-PI), Sundaresan Gobalakrishnan (Co-I), Pavel Degtiarenko (Co-I), Kevin Jordan (Co-I), George Kharashvili (Co-I), Joseph Gubeli (Co-I).

**Pavel Degtiarenko, Jefferson Lab**

**Pending**

Sponsor: U. S. Department of Energy, Office of Science, Office of Nuclear Physics

The award or other identifying number: This proposal; DE-FOA-0001588

Title: Isotope Production R&D at High Power Electron Accelerators

Total value of the project: \$799,110

Person Months/year: 1

Funding Period: 2 years starting in 2017

Description:

Roles: Andrew Hutton (PI/PD), Jamal Zweit (Co-PI), Doug Wells (Co-PI), Sundaresan Gobalakrishnan (Co-I), Pavel Degtiarenko (Co-I), Kevin Jordan (Co-I), George Kharashvili (Co-I), Joseph Gubeli (Co-I).

**Kevin Jordan, Jefferson Lab**

**Pending**

Sponsor: U. S. Department of Energy, Office of Science, Office of Nuclear Physics

The award or other identifying number: This proposal; DE-FOA-0001588

Title: Isotope Production R&D at High Power Electron Accelerators

Total value of the project: \$799,110

Person Weeks/year: 1 week

Funding Period: 2 years starting in 2017

Description:

Roles: Andrew Hutton (PI/PD), Jamal Zweit (Co-PI), Doug Wells (Co-PI), Sundaresan Gobalakrishnan (Co-I), Pavel Degtiarenko (Co-I), Kevin Jordan (Co-I), George Kharashvili (Co-I), Joseph Gubeli (Co-I).

**George Kharashvili, Jefferson Lab**

**Pending**

Sponsor: U. S. Department of Energy, Office of Science, Office of Nuclear Physics

The award or other identifying number: This proposal; DE-FOA-0001588

Title: Isotope Production R&D at High Power Electron Accelerators

Total value of the project: \$799,110

Person Months/year: 2.75

Funding Period: 2 years starting in 2017

Description:

Roles: Andrew Hutton (PI/PD), Jamal Zweit (Co-PI), Doug Wells (Co-PI), Sundaresan Gobalakrishnan (Co-I), Pavel Degtiarenko (Co-I), Kevin Jordan (Co-I), George Kharashvili (Co-I), Joseph Gubeli (Co-I).

**Joseph Gubeli, Jefferson Lab**

**Pending**

Sponsor: U. S. Department of Energy, Office of Science, Office of Nuclear Physics

The award or other identifying number: This proposal; DE-FOA-0001588

Title: Isotope Production R&D at High Power Electron Accelerators

Total value of the project: \$799,110

Person Months/year: 1.5.

Funding Period: 2 years starting in 2017

Description:

Roles: Andrew Hutton (PI/PD), Jamal Zweit (Co-PI), Doug Wells (Co-PI), Sundaresan Gobalakrishnan (Co-I), Pavel Degtiarenko (Co-I), Kevin Jordan (Co-I), George Kharashvili (Co-I), Joseph Gubeli (Co-I).

**Frank Strieder, SDSM&T**

***Current:***

Project Title: Compact Accelerator System for Performing Astrophysical Research (CASPAR); a DIANA Demonstrator Project  
Support: Current  
Source of Support: South Dakota Science and Technology Authority  
Total Award Amount: \$ 1,000,000  
Total Award Period: 2013 to March  
Location of Project: South Dakota School of Mines and Technology  
Month/Year Committed: 2 mo/yr (academic)

***Pending:***

Sponsor: U. S. Department of Energy, Office of Science, Office of Nuclear Physics

The award or other identifying number: This proposal; DE-FOA-0001588

Title: Isotope Production R&D at High Power Electron Accelerators

Total value of the project: \$799,110

Person Months/year: 1.44 cal mos.

Funding Period: 2 years starting in 2017

Description:

Roles: Andrew Hutton (PI/PD), Jamal Zweit (Co-PI), Doug Wells (Co-PI), Sundaresan Gobalakrishnan (Co-I), Pavel Degtiarenko (Co-I), Kevin Jordan (Co-I), George Kharashvili (Co-I), Joseph Gubeli (Co-I).

**Stanley Howard, SDSM&T**

***Current:***

None.

***Pending:***

Sponsor: U. S. Department of Energy, Office of Science, Office of Nuclear Physics

The award or other identifying number: This proposal; DE-FOA-0001588

Title: Isotope Production R&D at High Power Electron Accelerators

Total value of the project: \$799,110

Person Months/year: 1.44 cal mos.

Funding Period: 2 years starting in 2017

Description:

Roles: Andrew Hutton (PI/PD), Jamal Zweit (Co-PI), Doug Wells (Co-PI), Sundaresan Gobalakrishnan (Co-I), Pavel Degtiarenko (Co-I), Kevin Jordan (Co-I), George Kharashvili (Co-I), Joseph Gubeli (Co-I).

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## APPENDIX 4: Facilities and Other Resources

### Thomas Jefferson National Accelerator Facility

The Thomas Jefferson National Accelerator Facility (Jefferson Lab, or JLab) occupies a 169-acre site in Newport News, Virginia. The primary mission of the laboratory is to utilize its unique Continuous Electron Beam Accelerator Facility (CEBAF) to explore the fundamental nature of confined states of quarks and gluons, including the nucleons that comprise the mass of the visible universe. Jefferson Lab is also a world leader in the development of superconducting radio-frequency technology utilized in CEBAF. This technology is the basis for an increasing array of applications at JLab and other DOE Laboratories, and in the international scientific community. JLab's core capabilities are experimental, theoretical and computational Nuclear Physics, Accelerator Science, Applied Nuclear Science and Technology and large scale user facilities/advanced instrumentation. Science conducted at JLab and CEBAF contributes to thesis research material for about one-third of all U.S. Ph.D.'s awarded annually in Nuclear Physics. The Free Electron Laser Facility is now renamed Low-energy Electron Recirculator Facility (LERF).

LERF offers advantages for production of isotopes. As an electron linac, it is a reasonably simple device to operate and maintain and can be run by a small group of trained technicians. Beam energy and current are 'tunable' allowing optimization of beam parameters for specific isotopes. For this proposal, we will limit our beam energy and current at the LERF injector to  $\leq 10$  MeV and  $\geq 5$  mA respectively in order to do high power tests under neutron production thresholds. For production of  $^{67}\text{Cu}$  isotopes, LERF can be operated at higher energies, up to 100 MeV.

Figure 1 shows the LERF building, which houses the accelerator and user labs. LERF begins with an injector, which provides the electron beam bunches, typically from a laser-driven photocathode. This beam is then accelerated by one or more SRF cavities. Typical accelerating gradients are 10–15 MV/m. The cavities are submerged in a helium bath within a cryomodule. The beam is steered and focused with magnets and beamline components until it is delivered to the target apparatus. Figure 2 shows the 100 kW beam dump in LERF.



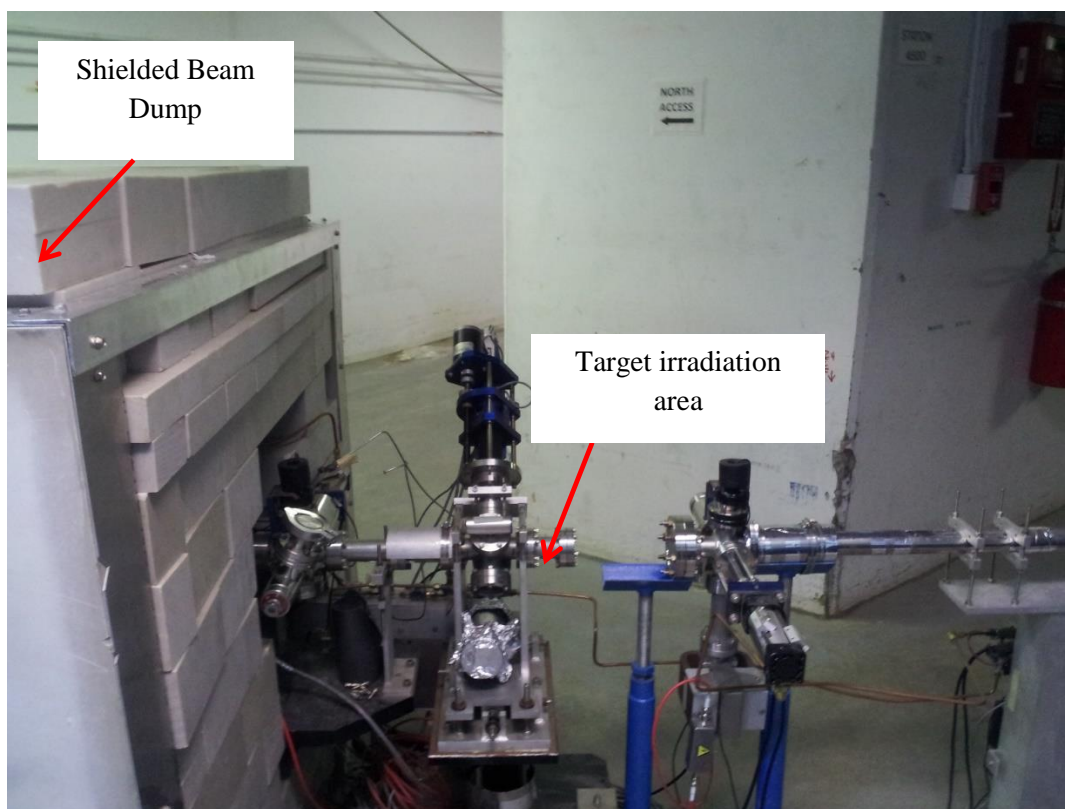
*Figure 1. LERF Building*



**Figure 2. LERF's 100 kW Beam Dump**

Handling of the radioactive materials will be managed by the Jefferson Lab Radiation Control Group. They will also bear responsibility for packaging and shipping of the target material to VCU for chemical separation.

CEBAF accelerator is a 12 GeV electron accelerator. CEBAF's injector beamline is capable of beam energies up to 120 MeV. Figure 3 shows the area where the irradiation experiments will take place.



**Figure 3. CEBAF Injector beamline showing the target irradiation area (left) and the beam dump (right)**

Other facilities at Jefferson Lab include LCW supply, beam dumps and many types of shielding material. As a premiere national lab, Jefferson Lab's has the infrastructure and the facilities needed for this research.

### **Virginia Commonwealth University**

Virginia Commonwealth University (VCU), located in downtown Richmond, Virginia has an excellent intellectual environment that is ideally suitable for this proposal. It is a major, urban public research university with national and international rankings in sponsored research. The Virginia Commonwealth University Medical Center campus occupies approximately six square blocks in downtown Richmond, Virginia. VCU is a state-supported, Carnegie Extensive research institution and, as such, has a number of resources and research-based centers to support research endeavors. Building on a heritage of established strengths in clinical and translational research, VCU has established the Center for Clinical and Translational Research (CCTR) to enhance research infrastructure and promote collaboration. Within the university, the CCTR provides the necessary longitudinal and cross-disciplinary networking, culture, and infrastructure for identifying promising discoveries made in the laboratory, testing them in animals and developing trials and studies for humans. VCU has subscriptions to numerous journals in electronic and hard copy versions and also has a very good collection of books in its libraries.

#### *Hospital, Clinical Teaching and Research*

The Medical College of Virginia Hospital of the VCU Health System, the Fairfax Inova Hospital, and the McGuire Veterans Administration Hospital together with their associated outpatient clinics provide the clinical teaching sites for medical students and, together with the General Clinical Research Center and the Massey Cancer Center, the sites for clinical research studies.

#### *Center for Molecular Imaging*

The Center for Molecular Imaging (CMI) is one of the VCU School of Medicine's Research Centers. CMI was established in 2008 to foster and facilitate multidisciplinary molecular imaging and nanotechnology research using advanced non-invasive imaging technologies. The emphasis is on multi-modality imaging approaches to study biology, biochemistry and pharmacology *in vivo*. Through these efforts, CMI provides a hub for translational research with basic and clinical scientists at VCU and beyond. The VCU Massey Cancer Center (MCC) is one of the centers that have imaging support provided by the CMI. VCU Massey Cancer Center is undergoing a major expansion of its cancer clinical research program. Through a focus on investigator-initiated therapeutic trials and the development of a clinical research affiliations network, the Center is extending its clinical trial offerings to patients across Virginia, helping to bring new drug discoveries to the state's residents. The CMI has Radio-Chemistry, Nano Chemistry, Cell Culture and Molecular Biology Laboratories, along with a dedicated wet laboratory and chemistry space. Additionally, the CMI investigators have direct access, from within its radiochemistry laboratory, to a 16 MeV Proton GE PETtrace self-shielded Cyclotron (GE Healthcare) operated through partnership with IBA Molecular Inc, USA. In addition, investigators have access to the other shared resources and facilities maintained and professionally staffed by VCU.

#### *VCU Chemistry Research Instrumentation Facility*

The VCU Chemistry departmental instrumentation facility houses several modern instruments for use by upper-level undergraduates, graduate students and other investigators. Instruments in the facility include liquid chromatography, gas chromatography-mass spectrometry, ion chromatography, inductively coupled plasma spectrometry, and infrared, Raman and fluorescence spectroscopy.



***Figure 4: The research hot-cell and few adjoining synthesis hot-cells (far right) at VCU are shown***

## **APPENDIX 5: Equipment (Relevant to the proposed research)**

### **Jefferson Lab**

Equipment relevant to this proposal includes inductive high power RF heaters for bench testing the target insert to assess the thermal stresses, vacuum equipment, instrumentation for radiation monitoring, thermal monitoring and pressure testing.

The laboratory has an electron beam welder if welding dissimilar metals in vacuum is required. In addition, there are sophisticated beam line diagnostic devices for beam position and beam profile measurements. Safety system equipment is standard in the accelerator enclosures.

### **Virginia Commonwealth University: Major Equipment**

#### **Center for Molecular Imaging:**

*Radiochemistry Laboratory (Gateway basement):* Our radiochemistry laboratory (480 SqFt) is fully equipped with one research hot-cell and six synthesis hot-cells. Three automated synthesizers that include two GE tracer labs (GE Tracer FFX-N) and one AllInOne™ Synthesizer from Trasis Inc. (Belgium). The AllInOne™ synthesizer is a flexible synthesis platform specially designed for the automated synthesis of short-lived labeled radiopharmaceuticals, with integrated HPLC capabilities. The laboratory is also equipped with radio HPLC systems (Waters, USA), a radio TLC scanner (AR2000, Bioscan) and Gas Chromatography (SRI Instruments Inc., USA). Gamma Spectroscopy facility within CMI supports radionuclide production development.

The Gateway basement houses the state-of-the-art Inveon PET/SPECT/CT multimodal imaging system (SIEMENS Preclinical Solutions, USA). The imaging facility in Gateway basement also houses fluorescent imaging modalities each with unique capabilities. The Inveon PET/SPECT/CT system is a state-of-the-art preclinical imaging platform, providing integrated small animal PET, SPECT and CT imaging with excellent sensitivity and resolution. Its innovative acquisition architecture unifies data collection from multiple modalities (PET, CT, and SPECT) integrated for fast, quantitative analysis.

*Gamma Spectroscopy facility:* The CMI's radiochemistry lab has a Gamma spectrometer (ORTEC) with the high purity germanium (HPGe) based detectors (FX-Series PROFILE GEM) that employ a proprietary thin entrance window in order to improve low energy efficiency and can detect signals from ~10 to 1500 keV. The FX-series can extend the useful energy range down to 10 keV and below, while maintaining the excellent peak shape and resolution characteristics. FX-Series PROFILE GEM detectors employ a proprietary thin entrance window in order to improve low energy efficiency.

*Cyclotron Facility (Gateway basement):* CMI has access to a 16 MeV Proton GE PETtrace self-shielded Cyclotron (GE Healthcare) operated through partnership with IBA Molecular Inc, USA. Targetry for the production of N-13, F-18 as well as solid targets for the production of I-124 and other inorganic PET radionuclides such as Zr-89, Mn-52 is available on this machine.

#### **VCU Chemistry Research Instrumentation Facility:**

The VCU Chemistry Department's instrumentation facility houses several modern instruments. Instruments in the facility include liquid chromatography, gas chromatography-mass spectrometry, ion chromatography, inductively coupled plasma spectrometry, and infrared, Raman and fluorescence spectroscopy.

The Varian (Agilent) ICP-OES: Inductively coupled plasma-optical emission spectroscopy (ICP-OES) is a very high temperature (7000-8000K) excitation source that efficiently desolvates, vaporizes, excites and

ionizes atoms. Molecular interferences are greatly reduced with this excitation source but are not eliminated completely. ICP sources are used to excite atoms for optical emission spectroscopy.

Varian – Vista MPX, CCD Simultaneous ICP-OES: This instrument offers simultaneous measurement of approximately 75 elements from parts-per-billion to percent levels. Samples either can be introduced for analysis individually or by the use of an autosampler.

Varian (Bruker) ICP-820MS: For metals analysis, with isotopic abundance data output. Has the option for metals speciation analysis, in where the oxidation state of the metals in the sample is able to be determined by utilizing an ion exchange column before the sample enters the ICP.

## **APPENDIX 6: Data Management Plan**

### **Sources of Data:**

1. Simulations of photo-production at different beam parameters (energy, current and power density)
2. Models and simulations, mechanical and thermal, of beam exit window, radiator and target assembly
3. Design of bench (no beam tests) of target assembly
4. Results of the bench tests
5. Drawings of the LERF injector beam line
6. Designs and procedures to be used of the irradiation experiments on the isotope targets
7. Logging of the shipping information
8. Data from in-beam tests of the Be window and the radiator
9. Data from in-beam tests of the target assembly
10. Data generated during spectral analysis of the composition of the target after irradiation
11. Generation of isotope separation protocols
12. Generation of purification protocols
13. Data from radio-chemical analysis
14. Data regarding the suitable purity of the isotope for clinical use.
15. Images and digital photographs of test and measurement setups
16. Videos of critical processes
17. Publications, talks and documents (e.g., papers in refereed journals, conferences and workshops, internal technical notes)

### **Content and Format:**

As much as possible, the data will be stored in standard formats. For example, photos and videos will be stored in jpeg and MP4 formats. Modeling and simulations are done using industry standard or public domain software (e.g. ANSYS, FLUKA). With the tools at our disposal, it is unlikely that any data we generate will be in a non-standard format.

### **Sharing and Preservation:**

Collaborators will have Memoranda of Understanding (MOU) with Jefferson Lab, enabling them to have user accounts on the Pansophy system. We will use Jefferson Lab's infrastructure to archive data.

Inventions and techniques developed during this program will be the property of the originating institution. Jointly developed inventions will be shared by the institutions through MOUs as needed. Once intellectual property rights and copyrights are in place, the data will be shared with other researchers.

Generated data may be transferred to industry following the standard practices of the collaborating institutions.

### **Data Management System:**

Our requirements for a Data Management System include:

- User-friendly graphical access to all collaborators
- Backup and archiving of data
- Compatibility with multiple formats (e.g., documents, spreadsheets, graphics, presentations)
- Access controls

We plan to use the Pansophy system developed at Jefferson Lab [1,2]. Pansophy has been used during the design, development, and fabrication of the cavities and cryomodules for the Spallation Neutron Source (SNS), and for the Jefferson Lab 12 GeV upgrade. Pansophy has also been adopted by Michigan State

University for the Facility for Rare Isotope Beams (FRIB), and is under consideration by Fermilab for PIP-II. Though Pansophy was developed specifically for accelerator systems, it meets all the above requirements. While Figure 1 illustrates the system with reference to a particular task, the system can be used for all our research and development tasks.

Pansophy integrates DocuShare, ColdFusion, Adobe Flex, MATLAB, Oracle, and Microsoft Office Suite, which are all commercial packages. In addition, it implements quality assurance elements of procedural control, automated data accumulation into a secured central database, prompt and reliable data query and retrieval, and online analysis tools, all accessed by users via their platform-independent web browsers. The graphical user interface enables navigation to either higher-level summaries or drill-down to the original source data. When data is generated locally at an institution, the data will be transferred to Pansophy.

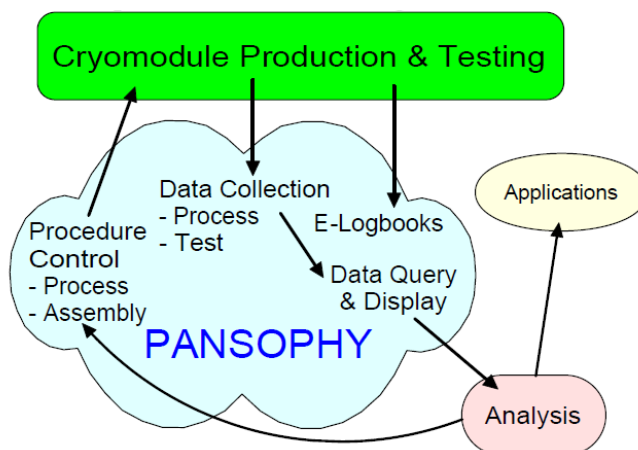


Figure 1: Pansophy System [1]

**Access Controls:** During data entry phase, an input module called a traveler is open to all users who have an account and is remotely accessible. The system logs the users who make access to the traveler. Once the module is closed, the data is accessible only to the system managers. This preserves the integrity of the raw data. The system implements multi-level privileged accesses to ensure integrity.

**Backup, Security and Archiving:** Pansophy is integrated into Jefferson Lab's Central Computing Facilities. Thus, all the information in the Pansophy system is regularly backed up. Jefferson Lab has robust cyber security processes and policies in place which will ensure data integrity and prevent unauthorized access.

## References:

1. C. Reece, V. Bookwalter, and B. Madre, "A System for Managing Critical Knowledge for Accelerator Systems: *PANSOPHY*",  
<http://accelconf.web.cern.ch/AccelConf/p01/PAPERS/MPPH304.PDF>
2. V. Bookwalter, B. Madre, C. Reece, "Flexible Application of the JLab *PANSOPHY* Information System for Project Reports, Process Monitoring, and R&D Sample Tracking",  
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