History of the Former Medical Department at Brookhaven National Laboratory

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General Audience Abstract

Brookhaven National Laboratory (BNL) has been a center for scientific breakthroughs since its inception in 1947. The opening of the Brookhaven Graphite Research Reactor (BGRR) – in 1950 and the construction of the Brookhaven Medical Research Reactor (BMRR) – the first reactor specifically made for medical research in the United States were the venues for inaugural medical research. This study of the historical prominence of BNL's former Medical Department is an investigation into the research and contributions for medical science conducted between 1950-2000. The goal of this research is to create a fully encompassing understanding of the research and accomplishments of radiotherapy development recorded at the former Medical Department at BNL. The research of the former Medical Department at Brookhaven National Laboratory, now the contemporary Environmental, Biology, Nuclear Non-proliferation (EBNN), building 490, was conducted through collection of both primary and secondary sources, relating them together to create a coherent informational research analysis of the history of scientific achievement and breakthrough conducted at the Brookhaven medical research building. Sources of scientific studies on the experimentation and advancement of groundbreaking radiotherapy techniques were collected in the form of published scientific studies, digitally archived newspapers, BNL memorial publishing's, biographical publications of BNL's history, and photographs. As a result of this study, I have gained an increased understanding of the contributions and accomplishments of the former Medical Department. This anatomizing of the history of the Medical Department provided firsthand experience to the process of quantifying historical documents and records understanding the full process of the cultural resource program at Brookhaven National Laboratory.

Introduction

The Medical Department at BNL was first established in 1948 as one of the 6 departments present in the early days of BNL. The construction of building 490 and the Brookhaven Medical Research Reactor was completed in December of 1958, and was ready for clinical trials in March of 1959. The Medical Department at BNL has a rich history of advanced research and innovation, being one of the most influential centers for medical development for the past sixty years. Groundbreaking research at BNL is felt all around the world, several breakthroughs in medicine, specifically nuclear medicine, were achieved at BNL. BNL's list of contributions to modern medicine include FDG-PET imaging, BNCT clinical trials, L-Dopa Parkinson's treatment, tritiated thymidine, first ever Human insulin synthetization, dopamine and addiction research, diagnostic medical isotopes including Technetium 99m, Thallium 201, Tin 117m DPTA, the link between hypertension and salt intake, and the creation of a protein data bank. However, with the time limitations set on this summer semester internship I focused my research on three breakthroughs: BNCT treatment, FDG-PET imaging, and medical isotope production.

Methods/Materials

For this study on radiotherapy breakthrough at BNL, sources were collected in the form of published scientific studies, digitally archived newspapers, BNL memorial publishing's, biographical publications of BNL's history, BNL scientific research library and online research archive and archived photographs from the period of clinical testing at the Medical Department. During this period of data collection, it was important to understand the history of the building from firsthand accounts. Mr. Robert 'Bob' Colichio is the current Research Operations Coordinator and EBNN directorate for building 490. Bob kindly gave me a tour of the remnants of the vacated Medical Department and the newly transformed parts of Bldg. 490 that were once part of the Medical Department. This extensive tour highlighted major parts of the Medical Department: two of the four intact nursing wings, the research lab portion of the building, outside shielding of the BMRR, the basement storage, and the history of the patient care and procedures that were ongoing. Bob lent a bin with vintage photos of the operations and practices of the Medical Department dating back to the 1950's. The utilization of these photographs, biographical findings of BNL, primary documents of specific research initiatives and more allowed for a comprehensive understanding of the rich past of innovation at BNL.

Constructed in 1947 opened in August 1950, the BGRR (Brookhaven Graphite Research Reactor) was the first reactor built after World War two in the United States. The BGRR was the first reactor built during peacetime and was specifically to be used for peaceful applications. The primary function of the BGRR was to create neutrons for interdisciplinary experiments relating to physics, biology, chemistry, and material science. The initial fuel source of the BGRR was natural uranium (NU). In 1958 the BGRR fuel source was changed to Highly enriched uranium (HEU), this HEU has a higher isotope composition of uranium-235 nearing 93%. The BGRR was put on standby in June 1968 after 18 years of operation, being declared 'obsolete'. In 2012 the BGRR was fully decommissioned. Throughout its lifetime nearly 25,000 experiments were conducted and its contributions to nuclear science and medicine are still felt today.

The BMRR (Brookhaven Medical Research Reactor) was opened in late 1958, becoming operational just a few months later in March of 1959. The BMRR had a long lifespan at BNL as it went completely offline in December of 2000, today being partially decommissioned. The BMRR was a center for nuclear medical research at BNL. Over the course of its life the BMRR was integral in experimental research into the effects of ionizing radiation on both humans and seedlings, thermal neutron irradiation of bacteria, epithermal neutron irradiation studies on animals, and different applications of neutron radiography on biological material. As its first operative use was during clinical trials of BNCT treatment. During this period the patients would be irradiated in a 'coffin' within the shielding of the reactor and be rushed down to the nursing wing of building 490, where the patient would be housed and observed. The BMRR later turned into a source of medical isotope production before being overtaken by the BLIP (Brookhaven Linac Isotope Producer). The BMRR was used consistently for over 40 years in a variety of experiments ranging from BNCT to myocardial imaging.

BNCT

BNCT treatment was first brought to BNL by the Medical Department chairman Dr Lee E. Farr in 1950. Farr led the largest and boldest campaign for atomic energy use in radiotherapy treatment. BNCT follows a complex procedure where the BMRR creates epithermal neutrons, these neutrons penetrate bodily tissue, as they continue through the body the neutrons lose energy and thus the now low energy thermal neutrons are captured by B^{10} atoms, the following decay results in the production of high-energy alpha particles that kill the localized cancer cells that have taken up the B^{10}. The B^{10} reaction ($^{10}B + n_{th} \rightarrow [^{11}B]^* \rightarrow \alpha + {}^{7}Li + 2.31$ MeV) was discovered in 1934 by Maurice Goldhaber and James Chadwick, these two colleagues would joke in the lab that this reaction could cure cancer[3]. Several years later in 1940 the first in vivo trials of BNCT irradiation were conducted. The methodology looked favorable to Farr and was subsequently placed as priority for the medical department's research. BNCT treatment at BNL began in 1951 involving the use of the BGRR (Brookhaven Graphite Research Reactor). Initially patients administered ^{10}B enriched sodium tetraborate (Borax) intravenously as the patients would be placed on a stretcher as the BGRR would be started up and be lowered into the shielding of the BGRR to received irradiation[1][3]. Patients would receive irradiation for periods ranging from 17 minutes to 40 minutes in duration[4]. The first group of 10 patients beginning in 1951 prevailed unsuccessful results. Patient selection criteria were focused on treating patients afflicted with GBM – Glioblastoma Multiforme- a form of malignant brain tumor, which during the 1950's and 1960's was a terminal diagnosis. In 1959 new optimism prevailed with the updated protocol for the use of the new BMRR (Brookhaven Medical Research Reactor), a reactor commissioned specifically for medical research involving atomic energy. During this new period of testing using the BMRR seventeen new patients would receive experimental BNCT treatment for GBM from 1959 through 1961 when the BNCT program was terminated. Though the course of the BNCT treatment at BNL overall proved to be unsuccessful in the eradication of cancerous cells within patients. The average life expectancy after BNCT was about 3 months, however outliers existed on both sides of the spectrum. One patient lived 151 days after treatment and another lived nearly 5 years after treatment, conversely four of the seventeen patients seen in the BMRR trials lived for merely 2 weeks after irradiation. Autopsies of those patients revealed acute swelling of the brain which was most likely brought on or perpetuated by the large doses of radiation each patient received. Although BNCT clinical trials at BNL was largely unsuccessful, the resulting experimental knowledge recorded on the effects of radiation on organic tissue in the human body and the effects of radiation treatment of cancer on the human body were monumental to nuclear medicine and set the building blocks of nuclear medical research for decades to come at BNL.

FDG PET imaging

([^{18}F]Fluorodeoxyglucose-Positron Emission Tomography) scan is one of the most influential medical breakthroughs in the history of modern medicine. The original idea of a 2D glucose tagging molecule that could be used to image the brain was first created at the National Institute of Health (NIH) by scientist Louis Sokoloff and UPenn researcher Martin Reivich. The development of the FDG radiotracer happened at BNL where scientists Tatsuo Ido, Al Wolf, Joanna Fowler, Vito Casella, and Chung Nan Wan successfully synthesized the compound with a radioactive half-life of 110 minutes. In 1976 the first brain images showed the concentration of FDG in the brain as desired. The initial use of PET imaging was to study the function and mechanisms of the brain. Imaging of the brain would proceed after the patient is administered with a radioisotope intravenously. The compound would decay, and emission of gamma radiation would be tracked, and the path of the radiation took would be traced, with help from advanced in software and computing the resulting brain imaging were revolutionary. At BNL addiction and brain research from 1980s-2000s utilizing PET and MRI technology to study the effect of addictive drugs on the brain showed how the brain responds. The research was the first research that showed that additive drugs localize in the brains pleasure center and influences the levels of dopamine[1]. These studies went further to study the effects of environmental and genetic factors that play a role in addiction and potential treatments for addiction. Later research observed the neurological mechanisms of ADHD and neurodegenerative diseases like epilepsy. PET-CT imaging is most prominently used around the world today with FDG being the most widely used radiotracer with about 1.5 million FDG-PET scans being performed annually[2].

Medical isotopes

Medical isotope research has been a center of medical research at BNL since 1950. The production of medical isotopes from the BGRR and later the BLIP (Brookhaven Linac Isotope Producer). Isotope production is important as researchers can identify that medical isotopes can be used for a wide variety of medical applications. Before the production of isotopes researchers hypothesize that specific elements may have desirable diagnostic imaging capabilities. From this hypothecation of potentially valuable medical isotopes the ensuing research heavily involves the use of one of the several reactors at BNL that have contributed hundreds of isotopes for nuclear medical research. During the lifespan of the Medical Department the synthetization of groundbreaking isotopes allowed for great leaps in nuclear medicine and medical diagnostics. The production of three specific isotopes produced at BNL would significantly impact the field of nuclear medicine and be utilized by physicians across the globe. These three isotopes are Thallium-201, Technetium-99m, and Tin-11m DPTA

Thallium 201 was created at BNL by a team of researchers led by E. Lebowitz. Thallium-201 was deemed a potentially useful radioisotope for its application for various medical procedures including myocardial imaging, visualization, and assessment of physiology and damage, renal medullary imaging, and tumor detection. Thallium-201 was synthesized by the irradiation of regular Thallium using the 60inch Brookhaven cyclotron[6]. Later outshined by ^{99m}Tc, Thallium-201 was the main compound for nuclear cardiography and cardiac stress tests. Thallium-201 is still used today in stress test primarily in patients that are at risk for coronary artery disease (CAD)

Tc-99m Technetium red blood cell targeting kit: Technetium 99 was created at BNL by Isotope development program head Walter Tucker and Powell Richards. Tucker's group discovered ^{99m}Tc as a contaminant while trying to purify ^{132}I. ^{99m}Tc became the ideal radiotracer for diagnostic testing of heart disease and a wide range of internal organ imaging[4]. ^{99m}Tc was a huge breakthrough in nuclear medicine, being the most used medical radioisotope in the world today administered to millions of patients every year.

Sn-117m DTPA was developed at BNL by scientist Suresh Srivastava for treatment of the agonizing pain of advanced bone cancer patients. Developed in the 1990's, the idea of using tin-117m (an isotope of regular tin) attached to DPTA to allow for the compound to reach the bone without being sidetracked began clinical trials. Researchers found that the tin isotope (synthesized using the High Flux Beam Reactor at BNL) allowed for localized dose of electrons to the bone easing patient pain without affecting the surrounding tissue or the bone marrow. The results of clinical studies showed the promising data of Sn-117m DTPA as patient pain reduction with no resulting damage was recorded simultaneous with a weak gamma ray emission that allowed for imaging equipment to be used to map the region of the body it had traveled.

Conclusion

The Medical Department at BNL is responsible for numerous esteemed awards in medicine. Through interdisciplinary operations and experiments BNL has become cemented in history as a pioneer of nuclear medicine research. Although the BMRR was decommissioned in 2000, medical research continues in building 490 today. Contributions of the Medical Department after the permanent shut down of the BMRR include developments in microPET imaging and micro-MRI procedure allowing for non-invasive high resolution brain imaging research allowing researchers to uncover the neural mechanisms of neurological conditions like Alzheimer's Disease and Autism[7]. The impact of the Medical Department at BNL has been felt around the world by tens of thousands of people every day.

The importance of studying history is integral in understanding the world we live in today. Studying history allows us to contextualize the world we live in on a micro and macro scale. Understanding how a person, system, or society arrived at the point they are at is important in dictating how to progress into the future. The importance of history in the field of science is crucial to the understanding of science. Science is a discipline where change is a constant and a necessity for the advancement of the discipline itself. By being able to observe and study the changes that happen within science you are enabling yourself to see the full arc of transformation the discipline has experienced and use that knowledge to help progress science more effectively by avoiding the errors of our predecessors.

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