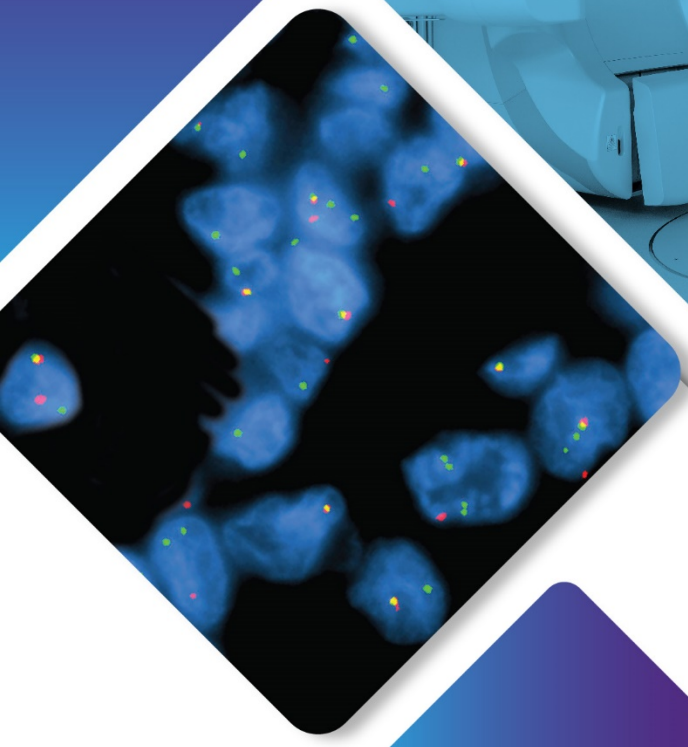
Contributions of the U.S. Department of Energy National Laboratories and Facilities to Advance Industry

Medical Imaging, Diagnostics, and Treatment



U.S. DEPARTMENT OF ENERGY | *Office of* TECHNOLOGY TRANSITIONS

Cover photos top to bottom: negatoscope images of a MRI scan, a medical linear accelerator used for proton therapy, analysis of the cell's chromosomes using Abbott's Vysis FISH Probe (Image provided by Abbott).

Contents


$x = \frac{\sum_{i,j} x_{i,j} I_{i,j}}{\sum_{i,j} I_{i,j}}$
$y = \frac{\sum_{i,j} x_{i,j} I_{i,j}}{\sum_{i,j} I_{i,j}}$
$\langle \epsilon^2_{phot} \rangle = \frac{4\pi^2}{n} \left(\frac{\beta d}{\lambda}\right)^2$
$= qvB \Rightarrow \omega = \frac{v}{r} = \frac{qB}{m}$
Space
Time
$\pm 0.5°$
120
130
GAT AAAT CT GG TCT T AT
$\hat{f}(\xi) = \int_{-\infty}^{\infty} f(x) e^{-2\pi i x \xi} dx$
$= \int_{-\infty}^{\infty} f(x(z), y(z))\, dz$
$= \int_{-\infty}^{\infty} f((z \sin\alpha + s\cos\alpha), (-z\cos\alpha + s\sin\alpha)) dz$
$\rho\left(\frac{\partial V}{\partial t} + V \cdot \nabla V\right) = \nabla P + \rho g + \mu \nabla^2 V$
OH
HO
HO
O
^{18}F

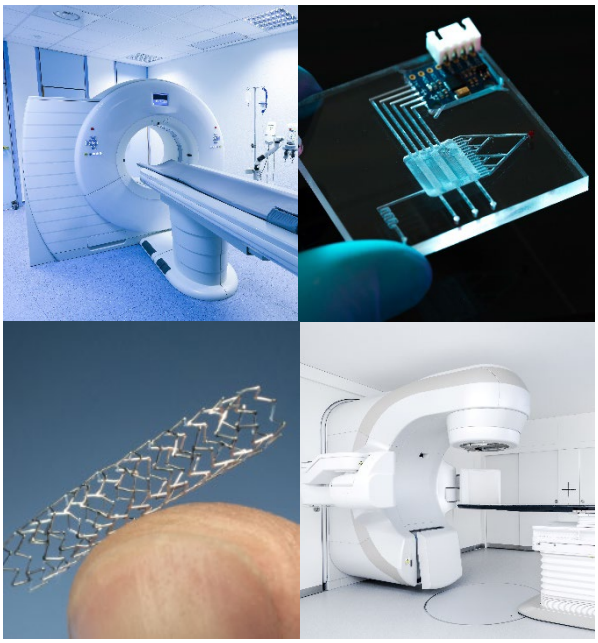
Contributions to Medical Technology

Exciting new medical tools and treatments offer great promise to millions of Americans who now face a variety of serious diseases or conditions. A surprising number of today's medical breakthroughs evolved from basic and applied research that was conducted at the U.S. Department of Energy (DOE) National Laboratories to advance national economic, energy, and security interests. Many products and therapies later became even more effective, affordable, and user-friendly through the efforts of academia and industry.

Roots in Basic and Applied Research

The DOE National Laboratory System pursues basic research to push the limits of science and help meet future challenges. Scientists engaged in basic research often cannot anticipate how their findings will be used. Medical isotopes were an unexpected benefit of early basic DOE research (see inset at right and page 2).

The National Laboratories also conduct applied research often with government, industry, and university partners tapping into their unique facilities and expertise to solve pressing national problems. As described on the following pages, many Lab-developed solutions have directly and indirectly improved medical technology in the following four areas:



Many life-saving diagnostic tools and treatments revolutionizing medicine today can trace their origins to basic or applied research at DOE Labs. Clockwise from top left: computed tomography scanner, a Lab-on-a-chip device, a medical linear accelerator used for proton therapy, and a platinum-chromium coronary stent from Boston Scientific Corporation Inc.

Isotopes or radioisotopes are essential to modern imaging technologies and treatments. The DOE National Laboratories played a key role in their discovery and continue to support their safe production, effectively helping shape the field of nuclear medicine as we know it today.

Diagnostics advances originating from the National Laboratories include such mainstays as positron emission tomography-computed tomography (PET-CT) and magnetic resonance imaging (MRI) as well as highly specialized instrumentation for identifying genetic conditions, health risks, and infectious diseases.

Treatment of disease has improved with the development of better drugs, therapies, and management techniques. The National Laboratories have worked with industrial partners to develop options for successfully treating such critical health risks as cancer and heart disease.

Precision medicine is based on recent advancements in the understanding of human DNA and proteins—enabling individualized patient treatment and management. This field was made possible by the completion of the Human Genome Project, which received significant support from our National Laboratories.

Outcomes

This document summarizes some key technology advancements achieved at the DOE National Laboratories that have contributed to modern medicine. These summaries draw upon available data to show how innovative ideas grew into valuable products and processes.

Specific ***health***, ***economic***, or ***knowledge transfer*** benefits or outcomes due to DOE Lab-developed commercialized technologies are shown through a few examples at the right. Knowledge transfer outcomes include a range of associated licenses, spin-off companies, and awards (e.g., the Nobel Prize; see inset below) that suggest the extent to which our medical and scientific communities value these contributions.

Examples of Outcomes by Type

Technology		Outcome
Proton Beams for Cancer Therapy *(Page 15)*	*Health*	17,500 cancer patients treated at Loma Linda University Medical Center
Radiopaque Stent Alloys *(Page 17)*	*Economic*	>$4 billion in cumulative sales
T7 Protein Expression System *(Page 22)*	*Knowledge Transfer*	~800 associated patent licensees

An Investment in America

The National Laboratories receive $10–$15 billion in funding annually to conduct basic and applied research on a broad portfolio of projects (DOE OTT, 2018). This research is essential to our nation's global leadership in science and technology development. Scientific advances achieved through this research continuously improve our quality of life, support critical national energy and security goals, and help U.S. manufacturers maintain a competitive edge in global markets.

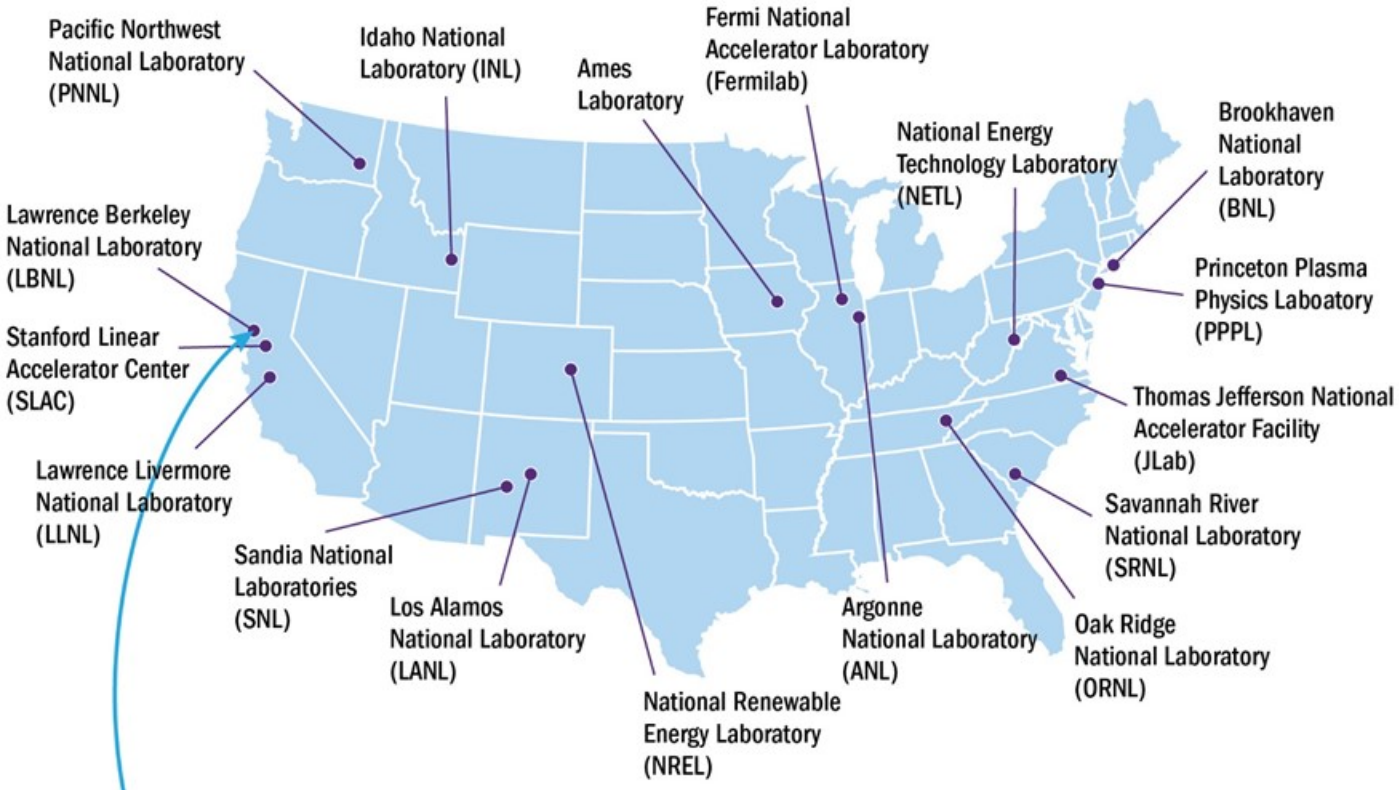
Credit: Argonne National Laboratory Flickr (CC BY-NC-SA 2.0)

The Advanced Photon Source (APS) provides high-energy x-ray beams that help map the structure of crystalline materials, including proteins. APS beamlines support advanced research in pharmaceuticals, biosciences, and other medical disciplines.

Since opening in 1996, the APS at Argonne National Laboratory (ANL) has characterized more proteins and supported more protein structure research than any other x-ray facility. Users have imaged proteins from anthrax, meningitis-causing bacteria, salmonella, and other pathogenic bacteria. In 2009, the three winners of the **Nobel Prize in Chemistry** studied the structure and function of ribosomes using data collected at the APS. (Koppes 2019)

DOE National Laboratories

The DOE National Laboratory System includes 17 National Laboratories (Labs) and numerous related facilities that provide our Nation with world-class scientific and technological capabilities. Individual Labs mentioned throughout the remainder of this document may use the acronyms or shortened names shown on the map below.



Ernest Lawrence (right) developed a unique circular particle accelerator known as the cyclotron. He quickly recognized the machine's medical applications—and brought in his brother, John Lawrence, M.D. Treatments for leukemia and polycythemia were first administered in 1936 using the 60-inch cyclotron. The 184-inch cyclotron (housed in the dome shown) continued the legacy of medical treatment at the Lawrence Berkeley National Laboratory, which was named in honor of Ernest Lawrence.

Helium atoms were used for targeted cancer therapy on 2,054 patients, and neon atoms were used to treat 433 patients. Today, particle accelerators dedicated to medical treatment and diagnostics have become the norm.

(Chu 2005)

Credit: Berkeley Lab Flickr (CC BY-NC-ND 2.0)

MEDICAL TECHNOLOGIES

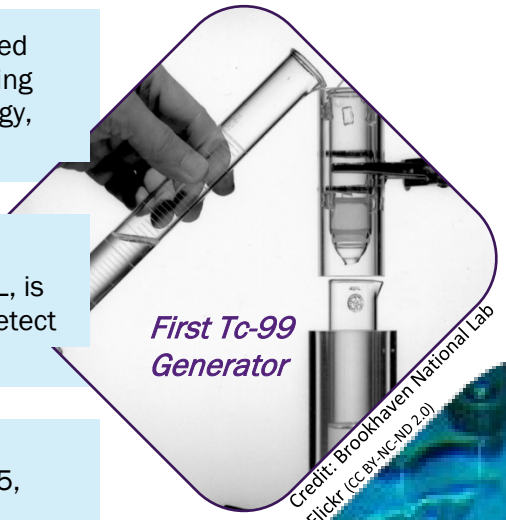
The DOE National Laboratories have long played a pivotal role in nuclear medicine—beginning with the production of radioactive isotopes (or radioisotopes). Radioactive isotopes make it possible for modern clinicians to image internal organs, diagnose injuries and disease, destroy tumors and cancers, and guide or evaluate treatment. Doctors select medical isotopes in concert with the appropriate treatment based on the location, size, and other aspects of the target tissue. The National Labs are closely linked to many isotopes, such as those listed below.

^{14}C Carbon-14

Early Radioactive Tracer: The cyclotron at LBNL produced some of the first medically useful radioisotopes, including C-14 (Kahn 1996), which helped revolutionize physiology, geology, biochemistry, biomedicine, and more.

^{18}F Fluorine-18

Metabolic and Cancer Scans: F-18 or FDG (for fluorodeoxyglucose), which was first synthesized at BNL, is used in PET imaging to assess metabolic activity and detect cancer (BNL 2012).



First Tc-99 Generator

Credit: Brookhaven National Lab Flickr (CC BY-NC-ND 2.0)

^{75}Se Selenium-75

Cancer Detection: ORNL's High Flux Isotope Reactor generates a variety of medical isotopes, including Se-75, which is used for gamma radiography, W-188/Re-188 (prostate cancer), and Cf-252 (cervical and ovarian cancers) (NIDC 2019).

^{99}Tc Technetium-99

Widest Use: Tc-99 is the most widely used radioisotope in medicine. It serves as a tracer element in about 40 million procedures each year and makes up 80% of nuclear diagnostic imaging globally (WNA 2019). BNL developed a Tc-99 generator that lets hospitals produce the isotope on their own premises.

^{99}Mo Molybdenum-99

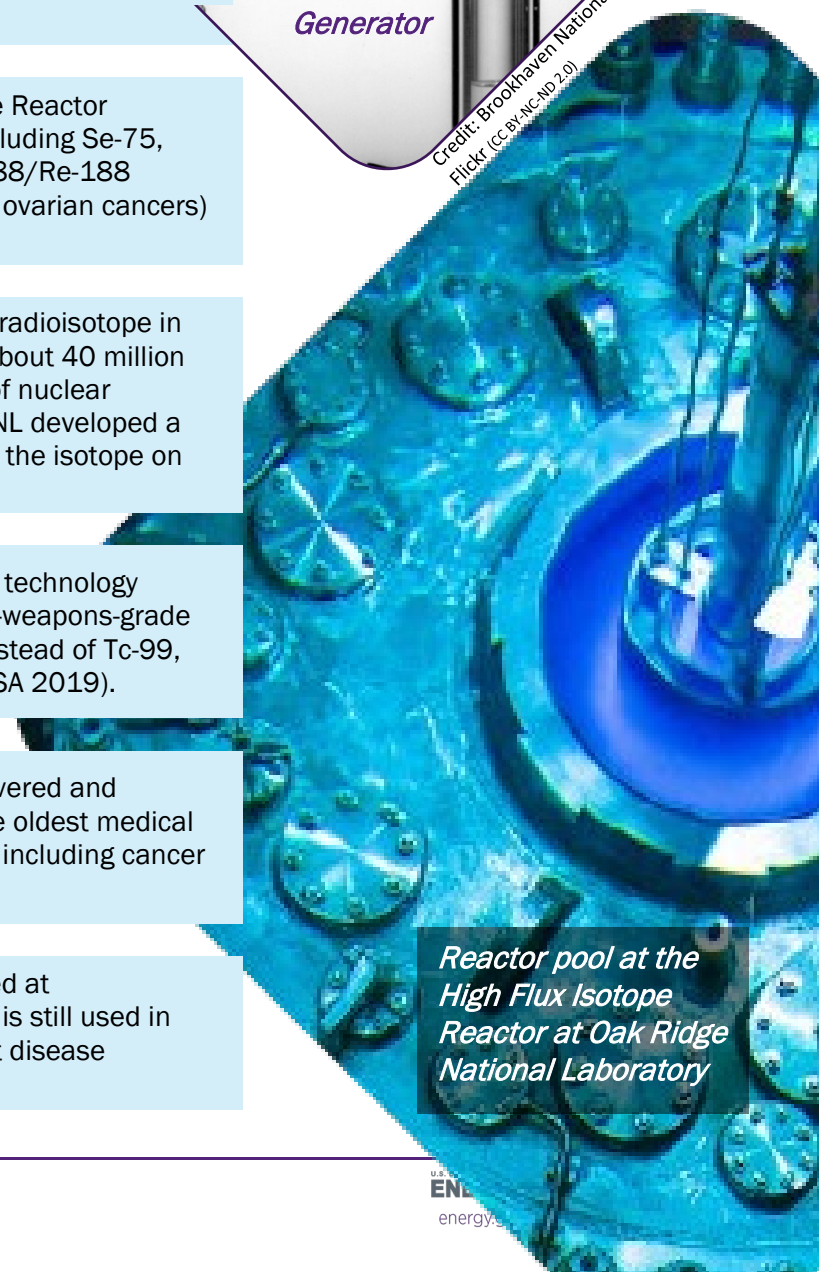
Safety: The National Labs have contributed technology knowledge to enable the production of non-weapons-grade Mo-99 (NASEM 2016). Mo-99 is stocked instead of Tc-99, owing to the latter's very short half-life (NNSA 2019).

^{131}I Iodine-131

Thyroid Treatment: I-131 was initially discovered and generated at LBNL (Kahn 1996). One of the oldest medical isotopes, it is used to treat thyroid disease, including cancer (WNA 2019).

^{201}Tl Thallium-201

Stress Tests: Tl-201 was originally generated at LBNL's cyclotron (Kahn 1996). The isotope is still used in stress tests for patients with coronary heart disease (WNA 2019).



Reactor pool at the High Flux Isotope Reactor at Oak Ridge National Laboratory

TIMELINE OF MEDICAL ISOTOPES AT THE NATIONAL LABORATORIES

1930

1929 – Ernest O. Lawrence invents the cyclotron, which produces the world's first useful medical radioisotopes.

1937 – Iodine-131 is created. With a half-life of only eight days, it was first used to treat hyperthyroidism in 1940.

1940

1938 – Tc-99m is discovered by Emilio Segre.
1939 – Ernest Lawrence is awarded the Nobel Prize.

1950

1952 – Scintillation camera (Anger Camera) is invented at LBNL. This device uses gamma rays to detect tumors.

1961 – James S. Robertson, a scientist at BNL, develops the precursor to PET scans.

1960

1965 – BNL scientists develop the Tc-99m generator.
1965 – High Flux Isotope Reactor at ORNL becomes operational, producing medical isotopes like Cf-252.

1970

1973 – Scientists at BNL develop a faster way to produce Tl-201 for use in diagnostic scanning and imaging.

1980

1976 – Colleagues at BNL synthesize FDG, which is used for PET imaging of glucose metabolism.

1990

1980s – LBNL scientists are first to develop heavy ion beams for clinical applications like cancer radiotherapy.

1990s – Tl-201 is used about one million times a year (in 13% of nuclear medicine scans).

2000

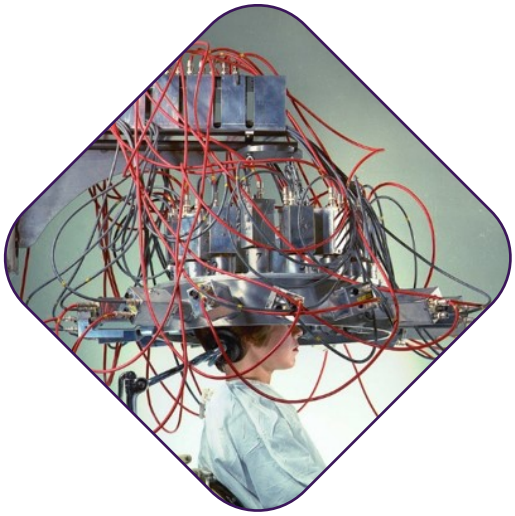
Late 1990s – The 3D PET camera is developed to image brain chemistry.

2010

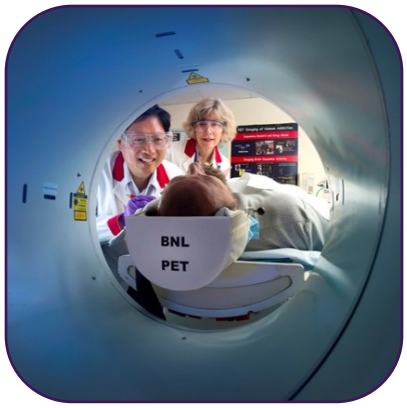
2018 – Mo-99 is cleared for U.S. production. Domestic production becomes a DOE Lab priority as supplies become limited. The Tc-99 isotope derived from Mo-99 is used in 40,000 scans in the United States each day.

2020

First working model of Ernest Lawrence's cyclotron
Credit: Berkeley Lab Flickr (CC BY-NC-ND 2.0)



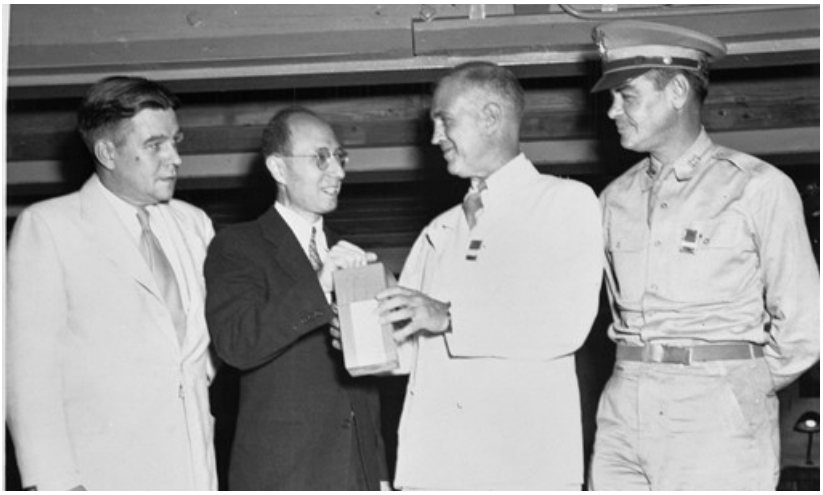
Pre-PET headgear at BNL
Credit: Brookhaven National Lab Flickr (CC BY-NC-ND 2.0)



PET facility at BNL
Credit: Brookhaven National Lab Flickr (CC BY-NC-ND 2.0)

Production and Distribution of Medical Radioisotopes

Radioisotopes are among the most important scientific byproducts of the Manhattan Project. Following World War II, ORNL began producing and distributing them for peacetime purposes.



Eugene Wigner, ORNL Research Director (second from left), hands the first shipment of a reactor-produced radioisotope to E.V. Cowdry, Research Director of the Barnard Free Skin and Cancer Hospital. Credit: Oak Ridge National Lab Flickr (CC BY 2.0)

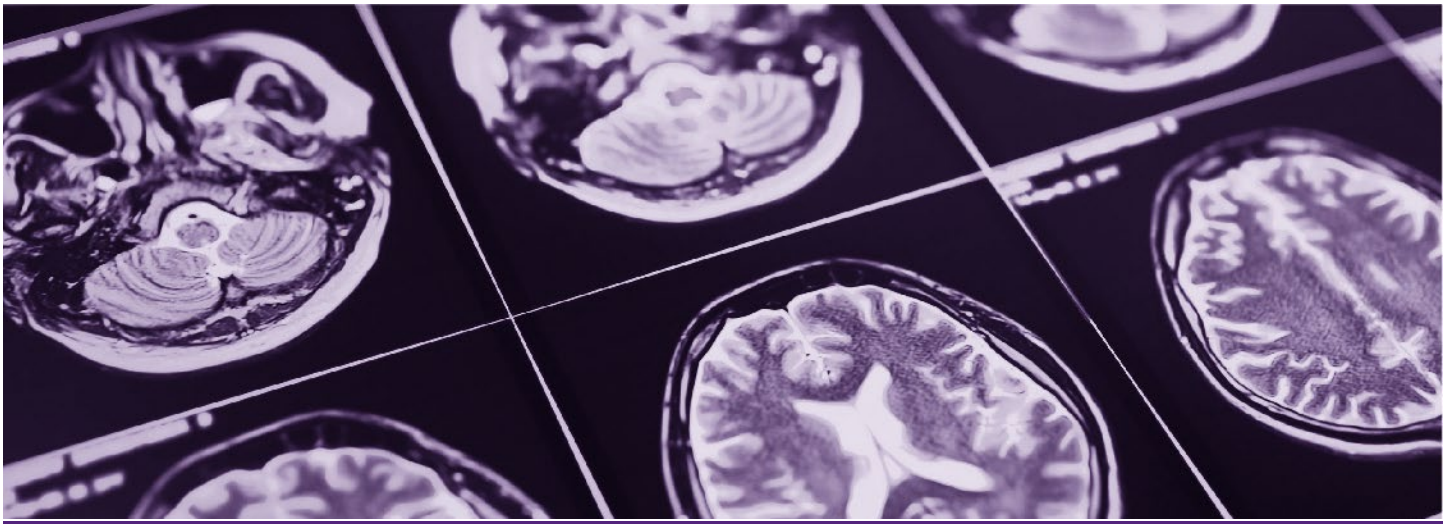
Today, the DOE Isotope Program continues to improve upon isotope production methods and produces radioactive and stable isotopes to bolster the supply for a wide range of domestic needs. These isotopes are essential to many research, medical, and industrial applications. The ***National Isotope Development Center (NIDC)*** at ORNL provides an interface with the broad user community and coordinates isotope production across the program facilities at Argonne, Brookhaven, Idaho, Los Alamos, Oak Ridge, Savannah River, and Pacific Northwest National Laboratories, Y-12 National Security Complex and the University of Missouri and University of Washington. These facilities use reactors, accelerators, and other methods to produce stable and radioactive isotopes, many of which are used for medical diagnostics and treatment. In 2019, the DOE Isotope Program provided 523 shipments of 23 different medical isotopes that are either rare or in short supply (provided by NIDC, March 30, 2020).

Medical isotopes available at NIDC*

Ac-225	*Ac-227*	*At-211*	*Bi-212*	*Bi-213*	*Co-60*
Cu-67	*Ge-68*	*He-3*	*Lu-117*	*Mo-100*	*Pb-212*
NIDC | NATIONAL ISOTOPE DEVELOPMENT CENTER MANAGED BY THE U.S. DEPARTMENT OF ENERGY ISOTOPE PROGRAM			*Ra-223*	*Se-72*	*Sr-82*
			Sr-90	*Th-227*	*W-188*
			Xe-129	*Yb176*	*Y-86*

*For a complete list visit the NIDC website

Customers interested in purchasing isotopes can use the NIDC website at www.isotopes.gov to request a quote.



Diagnostics

Through extensive work in nuclear medicine and experience with high-energy magnets, the DOE National Laboratories have advanced imaging technologies and other diagnostics tools that have drastically improved disease detection.

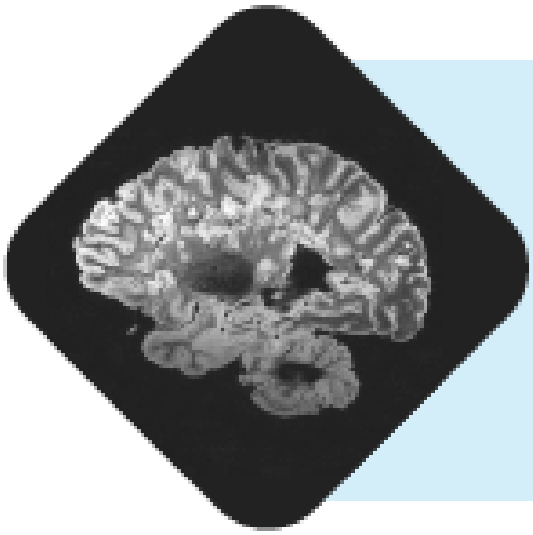
- **FDG, Radiopharmaceutical Tracer Used in PET Scans**
- **Breast-Specific Gamma Imaging (BSGI)**
- **Wavefront® Sensing and Binary Optics Technology**
- **Droplet Digital PCR Provides Unprecedented Accuracy**

Better Tools for Diagnosis

The rise of medical imaging technology in the early 20th century allowed doctors to move past their reliance on stethoscopes and microscopes—letting them see inside the living human body. Technologies that employ ultrasound, magnetic resonance imaging (MRI), computed tomography (CT), and positron emission tomography (PET) revolutionized the field of medical diagnostics.

Widely Used Diagnostic Imaging Technologies

The capabilities and expertise of the DOE National Laboratories were instrumental in developing a variety of advanced tools that allow doctors to look inside our bodies to make more accurate diagnoses. MRIs and PET-CTs are two of the most popular types of scans that trace their origins to the National Laboratories.



119 MRIs for every 1,000 people in the United States, 2018
(OECD Health Statistics: Health care utilization)

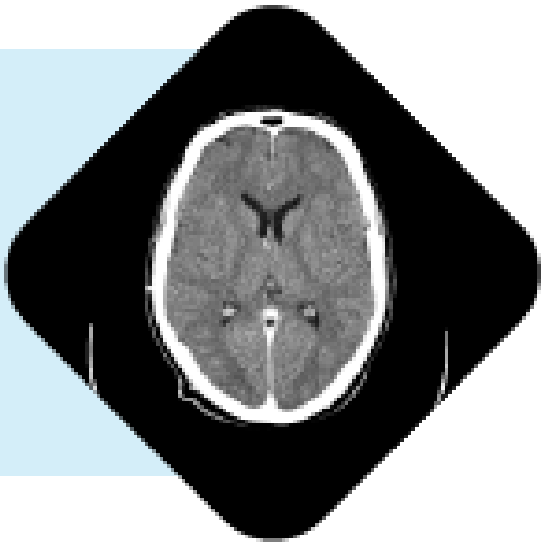
MRIs use a strong magnetic field to produce detailed internal images of the human body. Scans can image organs such as the liver, kidneys, and heart—as well as the head—to diagnose a wide array of ailments.

The magnets in these devices were originally a tool for physicists to accelerate protons. Made of superconducting wire, these magnets were used to build Fermilab's Tevatron, the world's first superconducting synchrotron.

271 CTs for every 1,000 people in the United States, 2018
(OECD Health Statistics: Health care utilization)

CT scans combine a series of x-ray images taken from different angles around the body. A computer then pieces these images together to create cross-sectional images of bones, blood vessels, and soft tissues.

CT and PET scans can be combined for a PET-CT. Nearly 90% of CT scanners are PET-CT scanners (Aranibar 2011). The PET was developed through extensive work at the DOE National Laboratories, including ORNL, BNL, and others (Jones 2017).



FDG, Radiopharmaceutical Tracer Used in Positron Emission Tomography (PET) Scans

Brookhaven National Laboratory (BNL) developed ^{18}F-fluoro-deoxyglucose (^{18}F-FDG) in late 1976. This radioactive drug is used as a tracer in PET imaging to differentiate between healthy tissue and diseased tissue. Before each PET scan, a small amount of ^{18}F-FDG is injected into the patient. Because cancer grows at a faster rate than healthy tissue, cancer cells absorb more of the tracer. The PET scanner detects the radiation given off by the ^{18}F radioisotope's decay and produces images of the body that show both normal and cancerous tissue. ^{18}F-FDG is now the standard radiotracer used for PET neuroimaging, with more than 1.5 million such scans performed annually. Hospitals and research centers around the world use ^{18}F-FDG PET scans to diagnose and monitor the progression of cancer and other neurological and psychiatric diseases.

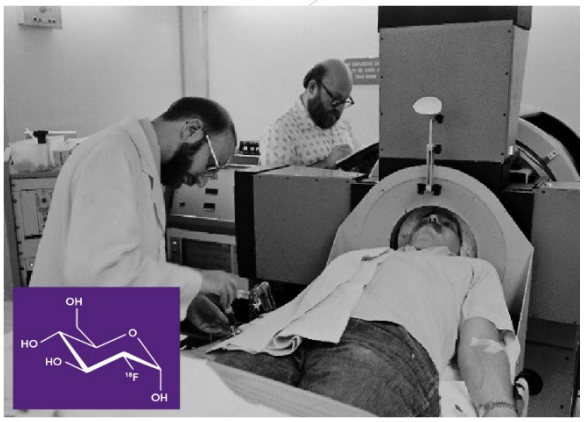
In 2009, BNL chemist Joanna Fowler received the National Medal of Science for her work in the development of ^{18}F-FDG.

Advantages

- Tissue uptake of ^{18}F-FDG closely correlates with certain types of tissue metabolism, enabling PET imaging to provide unique metabolic information.
- In contrast to conventional imaging, ^{18}F-FDG PET imaging can be used to screen the entire patient for local recurrence, lymph node metastases, and distant metastases during a single, whole-body exam requiring a single injection.
- The relatively long half-life of ^{18}F (110 minutes) eliminates the need for a cyclotron at PET facilities and allows for the commercial distribution of ^{18}F-labeled radiopharmaceuticals.

Sources: Gambhir et al. 2001; Burns 2010; BNL 2012; Kelloff et al. 2005

BROOKHAVEN NATIONAL LABORATORY



^{18}F-FDG is now the most frequently used radiotracer for the diagnosis of cancer and the evaluation of cancer therapy.

Facts and Figures

^{18}F-FDG-based PET imaging is 87%–90% accurate in diagnosing cancer, depending on the tumor location.

In 2011, approximately 1.8 million ^{18}F-FDG PET scans were conducted in the United States (94% were used to detect cancer).

In 2010, annual U.S. sales of ^{18}F-FDG reached $299 million.

"Development of ^{18}FDG is a testament to one of the key strengths of the National Laboratories, which bring together scientists from a range of disciplines in an environment that fosters collaborative approaches to address some of our nation's toughest challenges."

– Samuel Aronson, Brookhaven Laboratory Director

1968: ^{18}F-FDG first described in Czechoslovakia

1976: ^{18}F-FDG discovered at BNL

1976: ^{18}F-FDG first administered to a human patient

1990-98: Approximately 150 articles published involving clinical trials of ^{18}F-FDG in oncology

Today: ^{18}F-FDG is the primary tracer used in all PET imaging

Breast-Specific Gamma Imaging (BSGI)

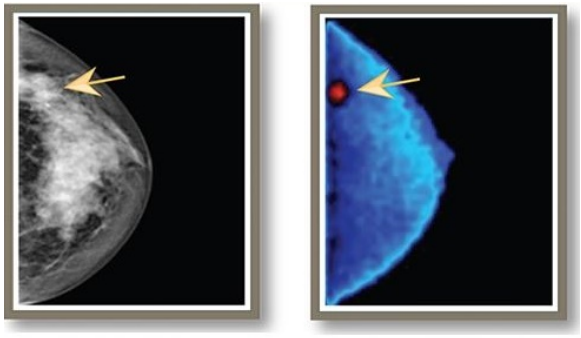
Jefferson Lab
Thomas Jefferson National Accelerator Facility

Early detection of breast cancer frequently leads to better outcomes. Basic research into nuclear physics led researchers at the Thomas Jefferson National Accelerator Facility (NAF) to develop a breast-specific gamma imaging (BSGI) technique, also known as molecular breast imaging (MBI), that improves the detection of early-stage breast cancers. The compact detector developed at JLab's NAF identifies cancerous lesions in the breasts via their uptake of gamma ray-emitting radio-pharmaceuticals.

In 1997, JLab licensed several patents relevant to BSGI/MBI to Dilon Technologies, Inc., a small high-tech company. JLab and the company worked together to develop the compact, user-friendly Dilon camera, which employs BSGI/MBI as an effective tool to distinguish benign tumors from malignant ones.

Advantages

- BSGI is effective at distinguishing between benign and malignant tumors at an early stage.
- It captures tumor information based on metabolism.
- BSGI complements inconclusive mammograms.
- It helps doctors more accurately diagnose breast cancer.
- BSGI overcomes image interpretation challenges in the presence of dense breast tissue due to age, scarring, or genetics.



Dense Breast Mammogram | Dense Breast MBI

MBI provides a valuable tool in breast cancer detection, particularly in dense tissue.

Facts and Figures

More than **200** cameras sold worldwide

More than **250,000** patients screened with BSGI/MBI worldwide

Proven to reduce benign biopsies by 50%

Nearly a four-fold increase in the non-invasive detection of cancer in women with dense breast tissue

"[BSGI/MBI] has a 98% predictive value. It changes treatment. It gives peace of mind."

– Robert Moussa, President of Dilon Technologies

Sources: Salasky 2011; Weisenberger et al. 2018; Dilon Diagnostics 2011; Dilon Technologies 2019; Choi et al. 2018; Huppe, Mehta, and Brem 2017; Holbrook and Newel 2015; Chufo 2009; Welch 2018

1997: JLab/NAF develops and licenses the BSGI technology to Dilon Technologies, Inc.

2004: Dilon Technologies releases the first commercially available camera using BSGI/MBI

2009: Receives Excellence in Technology Transfer Award from Federal Laboratory Consortium for Technology Transfer

Today: BSGI is used worldwide for early breast cancer detection

Wavefront® Sensing and Binary Optics Technology

Sandia National Laboratories

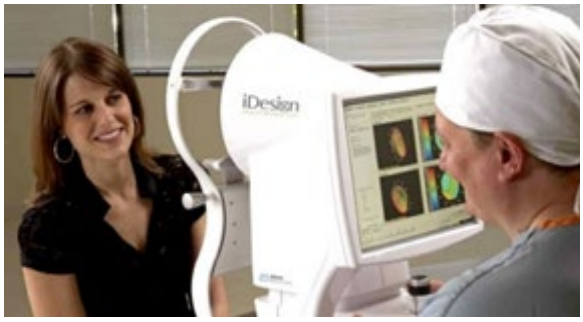
Research on lasers for defense applications led to an optical measuring system that now improves outcomes for patients undergoing Lasik surgery. The technology reduces the errors in measurements that can occur due to slight abnormalities across an optical lens. In the 1990s, scientists involved in research at Sandia National Laboratories saw the technology's market potential when integrated with developments in binary optics, expanded computer memory, digital camera arrays, and simplified electronics interfaces.

With three SNL licenses, spinoff company WaveFront Sciences (Albuquerque) designed the industry's highest-resolution Shack-Hartmann-based aberrometer, which can replace five conventional ophthalmological instruments in doctors' offices. The company's iDesign Advanced WaveScan System measures the detailed structure of the eye, from the shape of the cornea to the retina, for use in planning laser refractive surgery. The technology received U.S. Food and Drug Administration (FDA) approval for Lasik procedures in the United States and has also been approved for Lasik surgeries in Europe and Japan. A diagnostic version, the iDesign DX, has been sold in the United States since 2013. WaveFront Sciences was sold to Abbott Medical Optics, which was recently acquired by Johnson & Johnson Vision, where Wavefront sensing metrology continues to generate new products.

Advantages

- Wavefront metrology improves Lasik surgery results.
- The iDesign System generates a scan of the eye 25 times more precise than traditional methods.
- The system provides high-resolution measurements of the eye's interior and exterior and replaces five instruments.
- The FDA (U.S.) and CE (Europe) have both approved the system.

Sources: Zhang et al. 2013; Neal 2004; FDA 2003; Moussa et al. 2016



iDesign has been in U.S. markets since 2013.

Facts and Figures

Over 15 million Lasik procedures have been guided by the WaveScan WaveFront® System (2015).

94% of Wavefront-guided LASIK patients attained 20/20 vision, compared to 88% of conventional LASIK patients (2013).

This sensor technology is being used in NASA's James Webb Space Telescope.

"The technology developed at Sandia, commercialized by WaveFront Sciences, Abbott, and Johnson & Johnson Vision, has helped to improve the vision of many, many people."

– Dan Neal, Research Fellow
Johnson & Johnson Surgical Vision, Inc.

1996: WaveFront Sciences spins off from SNL with three licenses

2013: Diagnostic version enters the commercial market

2015: FDA grants approval for use in Lasik surgery

Today: The system is utilized in Johnson & Johnson Vision products to diagnose, plan, and guide Lasik surgeries

Droplet Digital PCR Provides Unprecedented Accuracy

Lawrence Livermore National Laboratory

Polymerase chain reaction (PCR), a fast and affordable technique used in molecular biology, amplifies small strands of nucleic acids (DNA or RNA) by several orders of magnitude to produce millions of copies of a DNA sequence. PCR has become an indispensable tool in the diagnosis and monitoring of genetic and infectious diseases, forensic-based criminal identification, DNA paternity testing, and DNA/gene cloning for basic research.

In 2008, a team at Lawrence Livermore National Laboratory (LLNL) patented a fundamentally distinct digital PCR technique, regarded as the most accurate genetic analysis method available. LLNL co-exclusively licensed the method to RainDance Technologies and the startup QuantaLife. QuantaLife commercialized the technique, creating the Droplet Digital PCR™ (ddPCR™) System before being acquired by Bio-Rad Technologies.

The ddPCR system performs target molecule quantification, identifying diseases with unprecedented accuracy by detecting the DNA/RNA of infectious agents. This accuracy is based on the system's novel droplet partitioning method (which can partition a DNA sample into 20,000 individual nanoliter droplets) and its digital quantification of the resulting nucleic acid targets.

Advantages

- Unlike other PCR technologies, ddPCR provides absolute quantification of target DNA copies per input sample without the need to run standard curves.
- This cost-effective, high-resolution system can validate cutting-edge sequencing discoveries.
- The method is easy to use and can be simply integrated into clinical research and life science workflows.

Bio-Rad technologies QX200™ Droplet Digital™ PCR (ddPCR™) System

Facts and Figures

While still considered an emergent technology, ddPCR accounts for about 16% of the PCR market (2018).

Bio-Rad reported $643 million in revenue (2018).

The licensing agreement provides a significant source of revenue to LLNL that is being shared with inventors and funding research activities, per statutory provisions and DOE guidelines.

"This elegant solution expands the current state-of-the-art methods of quantitative PCR."

– Norman Schwartz, President and CEO of Bio-Rad

Sources: Paladin Capital Group 2011; Bio-Rad 2019; Frost and Sullivan 2019; Perkel 2014

1983: PCR first developed

2008: LLNL patents ddPCR and co-licenses the technology to RainDance and QuantaLife

2012: R&D 100 Award

2017: Bio-Rad acquires both licensees, consolidating the technology

Today: The licensing agreement continues to generate revenue for LLNL research

Treatment

The research at DOE National Laboratories has led to an array of new treatments for high-risk diseases, such as heart disease, in addition to conditions and diseases that receive less attention. Some discoveries have the potential to change the way that drugs are delivered to the body.

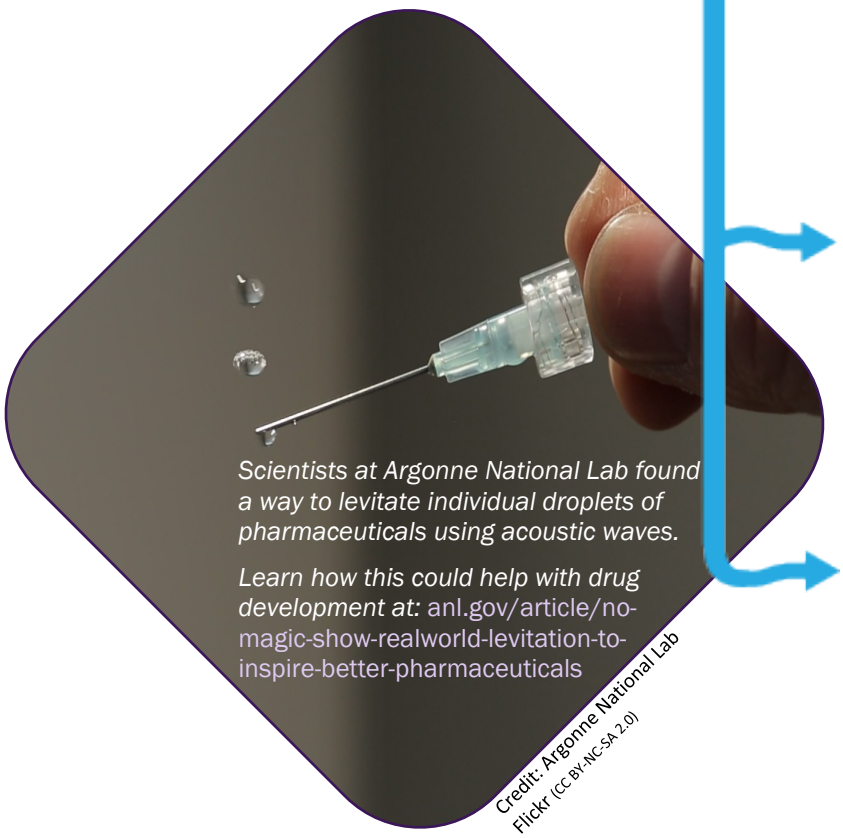
- Proton Beams for Cancer Therapy (Fermilab)
- Medication to Fight Skin Cancer (Zelboraf®) (ANL, LBNL, and SLAC)
- Radiopaque Stent Alloy (NETL)

The Department of Energy (DOE) recognizes that it can maximize its medical impact by preventing deaths from the most common causes. DOE advancements have addressed numerous causes—including many types of cancer.

Leading causes of death

(2017 in the United States) (CDC 2017)

- Heart disease: 647,457
- **Cancer: 599,108**
- Accidents (unintentional injuries): 169,936
- Chronic lower respiratory diseases: 160,201
- Stroke (cerebrovascular diseases): 146,383
- Alzheimer's disease: 121,404
- Diabetes: 83,564
- Influenza and pneumonia: 55,672
- Nephritis, nephrotic syndrome, and nephrosis: 50,633
- Intentional self-harm (suicide): 47,173



Scientists at Argonne National Lab found a way to levitate individual droplets of pharmaceuticals using acoustic waves.

Learn how this could help with drug development at: anl.gov/article/no-magic-show-realworld-levitation-to-inspire-better-pharmaceuticals

Credit: Argonne National Lab Flickr (CC BY-NC-SA 2.0)

Advances in Cancer Treatment at DOE National Laboratories

Skin Cancer

Zelboraf®, a drug developed largely due to discoveries at the Advanced Photon Source at ANL, has improved the outcomes for skin cancer patients (page 16).

Thyroid Cancer

Iodine-131, first produced at LBNL's cyclotron, remains a common treatment for thyroid cancer.

Lung Cancer

Proton beams at Loma Linda Medical Center treat a variety of cancers that affect the lungs, pancreas, and spine (page 15).

Myeloid Leukemia

DOE National Labs identified Actinium-225 as a potential cure for Myeloid Leukemia and other cancers (Eure 2012, Crocker 2018).

Prostate Cancer

ORNL produces actinium-227, the source for Bayer's FDA-approved treatment for metastasized prostate cancer, Xofigo®. ORNL is the only near-term production site for actinium-227 (ORNL 2018).

Proton Beams for Cancer Therapy

Fermilab

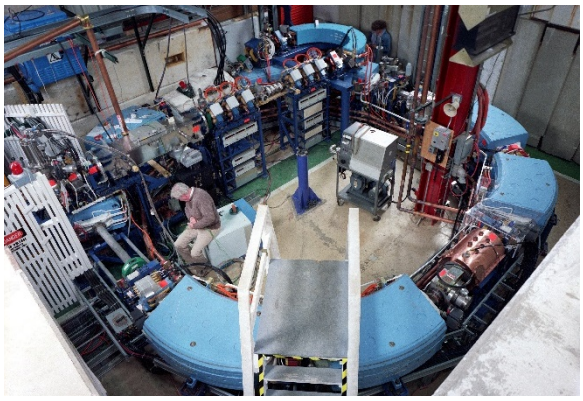
For radiation therapy, heavy particles like protons offer an advantage over X-rays or electrons in that the radiation dose can be better localized at the tumor site to avoid damaging healthy tissue. Fermilab's founding director Robert Wilson proposed the use of proton beams to treat tumors in 1946.

By varying the initial energy of a proton beam, radiation oncologists can control how deeply the beam penetrates a patient's body before it deposits most of its energy. Using computer simulations, clinicians can adjust the maximum reach of the protons to within a millimeter, sparing all tissue beyond the tumor. This unique capability makes proton beams an excellent choice for treating tumors located near sensitive organs, brain stems, spinal columns, or optic nerves.

In the late 1980s, Fermilab partnered with Science Applications International Corporation (later spun into the company Leidos) to build an accelerator and beam delivery system for treating cancerous tissue. In 1990, the nation's first hospital-based proton therapy accelerator was installed at Loma Linda University Medical Center (LLUMC) in Loma Linda, California, where it has continued to provide proton therapy for patients.

Advantages

- Charged-particle beams reduce radiation to surrounding healthy tissue (unlike X-rays).
- The therapy is appropriate for use on children, who have more time to develop secondary cancers.
- Northwestern Medicine research found that children who receive proton therapy for brain tumors show higher IQ, processing speed, and function (versus x-ray radiation).
- The therapy offers lower toxicities and positive survival outcomes for lung, pancreatic, and spinal cancers



Scientist working on the equipment that powers the Loma Linda particle therapy center [Photo: Fermilab]

Facts and Figures

Loma Linda has treated over **21,100** people, including **13,600** prostate patients.

600,000 successful proton treatments delivered.

240 different tumor sites treated at Loma Linda.

"Fermilab has led the way in particle therapy in many ways, designing and building America's first hospital-based proton therapy synchrotron, which is now housed at Loma Linda and has pioneered the clinical field of particle therapy."

– James Welsh, Chief of Radiation Oncology
Hines VA Medical Center

Sources: Wilson 1946, Cole et al. 1989, Loma Linda 2019, Gross et al. 2018

1946: Fermilab founding director Robert Wilson proposes use of proton beams to treat tumors

1980s: Fermilab partnership builds an accelerator and beam delivery system

1990: Loma Linda University Medical Center Proton Center opens

2005: LLUMC Proton Center treats its 10,000th patient

Today: There are 29 proton therapy centers across the United States

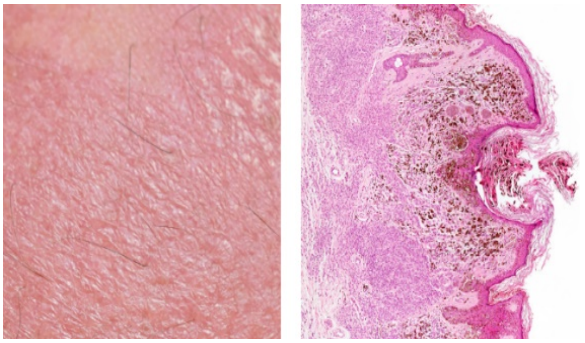
Medication to Fight Skin Cancer (Zelboraf®)

Melanoma is the leading cause of death from skin disease. Steadily rising melanoma rates in the United States and around the globe are attributed to ultraviolet rays from the sun, tanning beds, and sun lamps. Researchers at Plexxikon Inc., worked with drug producer Genentech to develop the melanoma-fighting drug Zelboraf® (vemurafenib), using specialized resources at the DOE National Laboratories: the Advanced Photon Source (APS) at ANL, the SLAC National Accelerator Laboratory, and research on the 3D structure of cancer-causing proteins at LBNL.

The research utilized the APS X-ray beams and an experimental technique called "macromolecular crystallography" to determine the structure of a specific cancer-causing mutated protein. This technique helped researchers examine hundreds of molecules to identify one that could hinder the cancer's spread. This discovery enabled the researchers to develop a drug that binds tightly to the mutated protein and blocks the signals that instruct cancer cells to multiply. Research at the APS was carried out on the Argonne Structural Biology Center X-ray beamlines. Zelboraf® was the first approved product in its class and pioneered a route for additional drug discovery.

Advantages

- Zelboraf® treats advanced melanoma by targeting a specific gene mutation.
- The drug slows the progression of late-stage and inoperable skin cancer (in patients whose cancer has a certain genetic mutation).



Frequently or severely sunburned skin (left) can cause skin cancer, as seen in the microscopic image (right). Zelboraf® can limit cancer's growth.

Facts and Figures

Approved for use in **90+** countries (2015).

Used to disrupt melanoma in **20K+** patients worldwide (2015).

First FDA-approved drug to treat a rare, previously untreatable blood cancer (Erdheim-Chester disease) with a 50% effectivity rate.

"The x-ray becomes a very useful technology because the (cancer) protein is so small you can't detect it with the eye or even with the most powerful microscope."

– Chao Zhang, Structural Biologist, Plexxikon Inc.

Sources: ANL 2016, Kenrick 2011, Genentech 2015, FDA 2017

2006: Clinical trials of Zelboraf® started

2011: FDA granted expedited approval of Zelboraf®

2012: Awarded Scrip Award for Best New Drug

Today: Zelboraf® is used to treat melanoma and a rare blood cancer (ECD)

Radiopaque Stent Alloy

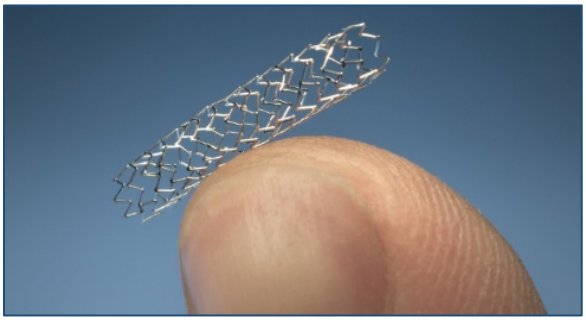
Stents are tiny, self-expanding, metal mesh tubes that hold an artery open to keep the blood flowing following balloon angioplasty. NETL developed a platinum-chromium alloy that shows up clearly on X-rays—making it easier for a doctor to both implant a stent made from this alloy and confirm its location. The high-yield strength of the new alloy enables thinner, more flexible stents that can be easily guided along narrow arteries without damaging small vessels in or near the heart.

Recognizing the need for better stent materials, Boston Scientific Corporation Inc. (BSCI) worked with NETL's Process Development Division in Albany, Oregon, to develop the new alloy and adapt the production technology for industrial-scale manufacturing. Boston Scientific acquired the technology and used the alloy's superior properties to develop new coronary stent products. The alloy became the foundation for the world's leading stent platform.

Advantages

Radiopaque stents enable the following:

- Enhanced patient safety
- Visibility on x-ray cameras
- Thinner profile and more flexibility to reach smaller arteries
- Less recoil
- Easier placement by doctors.



The platinum-chromium coronary stent avoids surgeries on small coronary arteries and reduces limb amputations.

Facts and Figures

BSCI's first stent product family was used in **8 million** stent implants worldwide.

BSCI stents captured **45%** of U.S. market and **33%** of global market (2012).

Stent series achieves **>$4 billion** in global sales between 2010—2012.

"The real tangible benefit is what [the new alloy] has done for physicians, their patients, and their outcomes."

– Jon Stinson, Principal R&D Engineer, Boston Scientific Corporation, Inc.

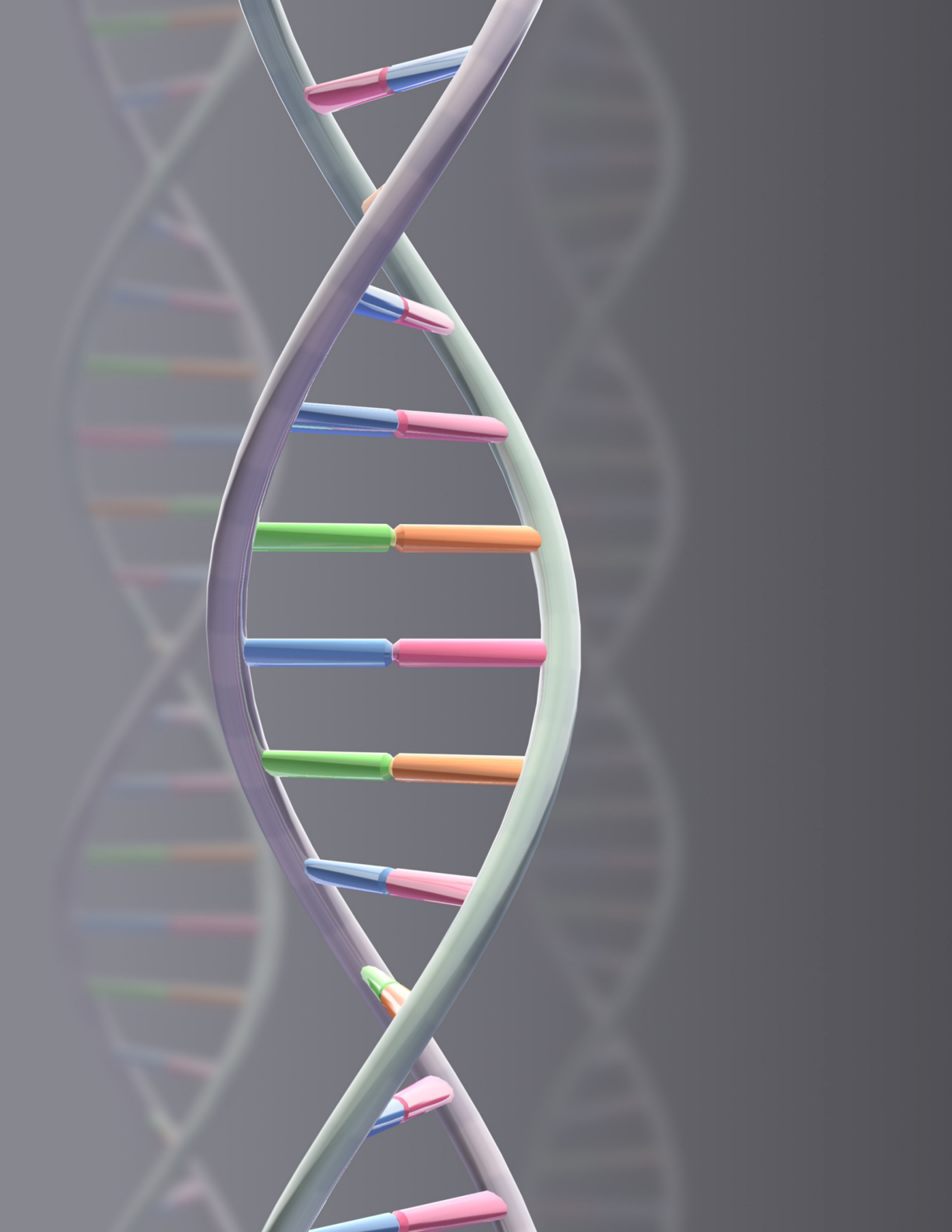
Sources: The Partnership for Public Service 2013, NETL 2012

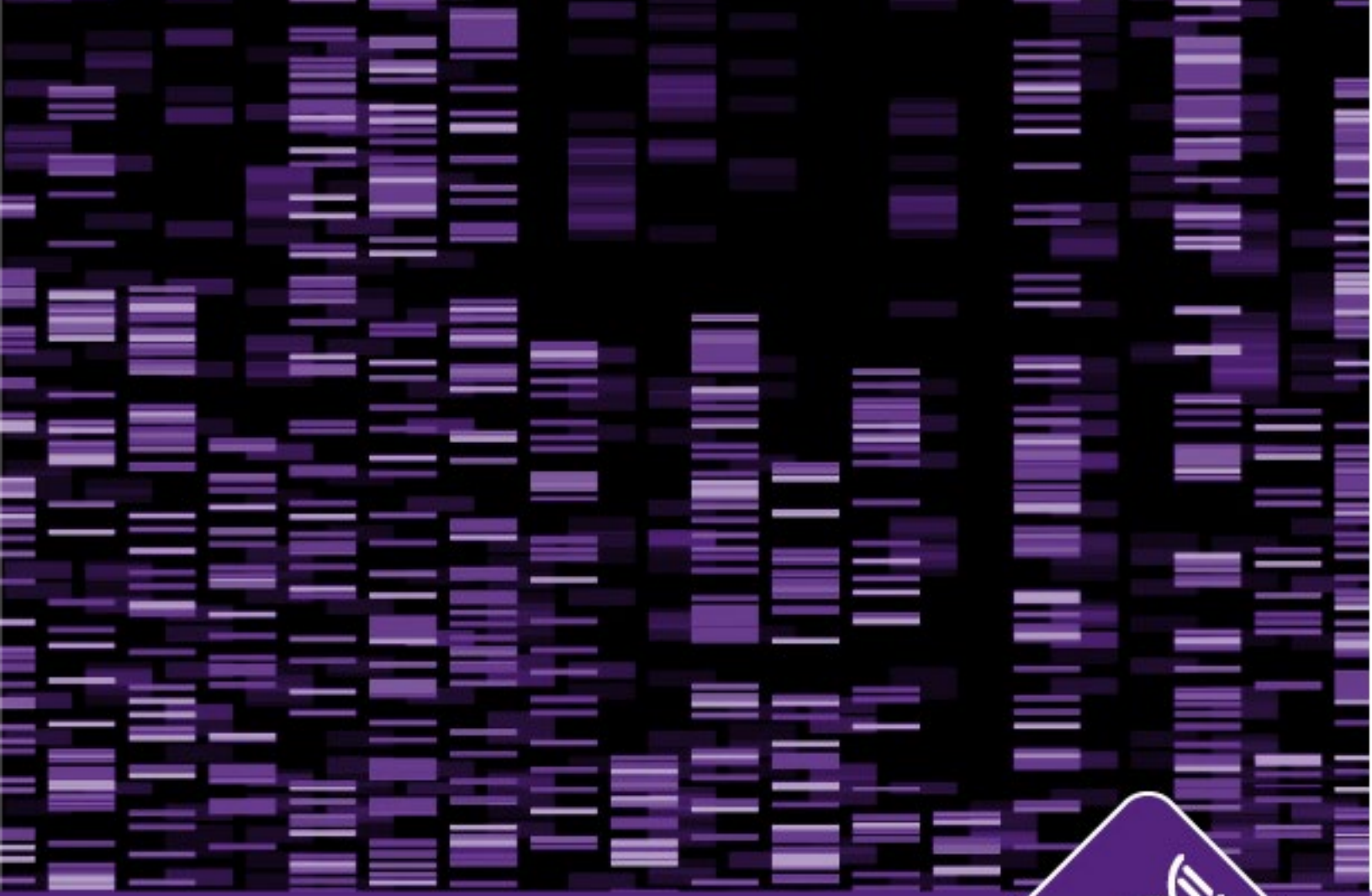
2009: Stent is first approved for sale in November of this year

2011: R&D 100 Award and Outstanding Commercialization Award from the Federal Laboratory Consortium for Technology Transfer

2012: U.S. Secretary of Energy's Achievement Award

2015: Alloy receives ASM Engineering Materials Achievement Award





Precision Medicine

Advances in precision medicine profoundly improve medical diagnoses and treatments. These technologies take advantage of an increased understanding of the human genome and protein production pathways.

- Chromosome Painting Improves Molecular Diagnostics (LLNL)
- Multiplexed Capillary Electrophoresis (Ames)
- T7 protein expression system (BNL)
- M3 Emitters (LBNL)
- Lab on a Chip: Microfluidic Technology Speeds DNA Analysis (ORNL)

Precision medicine is "an emerging approach for disease treatment and prevention that takes into account individual variability in genes, environment, and lifestyle for each person" (Garrido 2017). Designing specific treatments for individuals requires a greater understanding of both genetic make-up and unique body.

Human Genome Project

The Human Genome Project was a 13-year project coordinated by DOE and the National Institute of Health (NIH) to sequence the 3 billion base pairs in human DNA. This undertaking began in 1990 and was completed on April 14, 2003.

Key findings from this project include that human beings have approximately 22,300 protein coding genes and our genome contains many more segmental duplications, or identical gene sequences, than originally thought.

Multiple National Labs supported the Human Genome Project, including LBNL, LLNL, and ORNL. This project provided the foundation for much of personalized medicine and has led to the discovery of numerous protein pathways and genetic disorders.

The outcomes of this project are immense. The human genome project resulted in the following (Regier et al. 2017):

- Discovery of more than 1,800 disease genes
- 2,000 genetic tests for human conditions
- 350 biotechnology-based products in trials
- A drastic decline in the cost of genome sequencing
  - Enabling investigation of the underlying causes of rare genetic diseases
- Development of the field of pharmacogenomics to explore how genetic variations affect treatment.

The project cost about $2.7 billion, which is less than the $3 billion estimated and has made both anticipated and unexpected impacts on medicine (Gyles 2008, NHGRI 2019).

In 2007, James Watson's DNA was sequenced at a cost of $2 million (Gyles 2008). Today, the same DNA sequencing may cost only $700 (Dante, 2019).

The Joint Genome Institute helped to sequence human chromosomes for the Human Genome Project.

Chromosome Painting Improves Molecular Diagnostics

Lawrence Livermore National Laboratory

In the late 1980s, LLNL scientists Daniel Pinkel and Joe Gray studied one of the distinguishing effects of radiation damage to DNA: "reciprocal translocation," in which the ends of two chromosomes break off and trade places. These mismatched chromosomes can lead to serious illnesses.

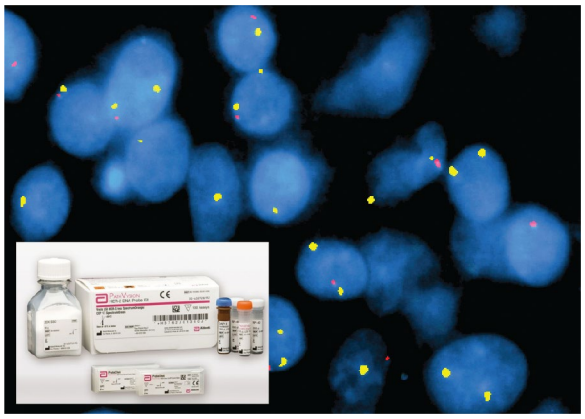
Pinkel and Gray invented a way to identify these translocations by highlighting the desired gene sequence on specific chromosomes with fluorescently labelled probes (short DNA fragments), a technique they dubbed "chromosome painting." Chromosome painting allowed detection of radiation exposure 10 to 100 times more rapidly than other methods available at that time. Chromosome painting, also referred to as fluorescence *in situ* hybridization (FISH), has been widely adopted as an indispensable tool in genetic research.

In 2001, biopharmaceutical giant Abbott acquired Vysis, the company that had licensed the technology and implemented FISH in its products since 1992. Abbott then developed HER-2 gene amplification detection via FISH for a subset of breast cancers. Today, Abbott sells products based on FISH technology for the genomics-based molecular diagnosis of a variety of cancers, as well as other genetic diseases and prenatal genetic abnormalities.

Advantages

Chromosome painting or FISH technology offers the following benefits:

- Highlights desired gene sequences
- Enables more rapid and accurate visualization of chromosomes
- Covers all 23 pairs of human chromosomes



The cell's chromosomes are analyzed using Abbott's Vysis FISH Probe (packaging inset). Image provided by Abbott.

Facts and Figures

Abbott's revenue of FISH products was $185 million in 2015 and accounted for about 85% of the FISH market.

Total sales of the licensed technology exceeded $1 billion, and LLNL accrued more than $47 million in royalties in 2017.

"This technology allows us to identify genetic changes important to the behavior of tumors, but otherwise not apparent. The idea is that one treatment is not best for every patient. It tells us who needs what kind of treatment. It individualizes treatment to the needs of the patient's tumors."

– Dr. Thomas Look, St. Jude's Children's Hospital

Sources: Frost and Sullivan 2019, LLNL 2018, Abbott 2016

1980's: FISH technology invented at LLNL

1992: Vysis' FISH products become available on the market

2001: R&D 100 Award; Abbott acquires Vysis and FISH technology

Today: Chromosome painting is a standard practice for genomics-based diagnosis of cancer and genetic diseases

T7 Protein Expression System

BROOKHAVEN NATIONAL LABORATORY

Proteins are large, complex molecules that carry out the tasks of life. They direct our bodies' activities, organize our thoughts, and defend us against infection; however, in their mutant forms, proteins can threaten our health.

BNL found a way to make a common bacteria produce large quantities of whatever protein is needed for researchers to better understand how that particular protein is involved in disease and how it might be used to target certain biological pathways. Earlier research had shown that the T7 virus can effectively direct E. coli bacterial cells to make T7 proteins. A BNL researcher postulated that T7 genetic elements—even in the absence of the virus—could force cells to produce large amounts of any protein.

By cloning the gene for T7 RNA polymerase, BNL researchers developed an efficient system for engineering common E. coli bacteria to produce nearly any desired protein from a cloned gene. Known as the T7 expression system, this method uses crucial elements of T7 DNA to redirect most of the protein production in a cell toward a single protein specified by a cloned gene. Researchers in academia and industry around the world use the technology to produce proteins within bacterial cells for use in basic biomedical research and practical applications, such as medical diagnostics and treatment.

Advantages

- T7 RNA polymerase is a very active, selective enzyme that can produce almost any RNA.
- This inducible protein expression system has been used to produce a wide range of proteins from various species, including humans.

F. William Studier and colleagues developed the T7 protein expression system.

Facts and Figures

~800 Licensees

~$72 million in royalty revenue

"The new autoinduction system is very convenient. Instead of spending much of the day monitoring the growth of many different cultures to get optimum conditions for producing proteins, we simply inoculate cultures late in the day, let autoinduction do the work for us, and collect our proteins the next morning."

– F. William Studier, Biophysicist at BNL

Sources: Greenberg 2004, BNL 2018

1970: Demonstration of stringent specificity of T7 RNA polymerase to its promoter

1981: Demonstration that T7 RNA polymerase can transcribe any DNA linked to a T7 promoter

1984: T7 RNA polymerase used to direct selective, high-level expression of cloned genes, and BNL files the first patent related to the T7 expression

2004: R&D 100 Award

Multiplexed Capillary Electrophoresis

Used in mapping the human genome, multiplexed capillary electrophoresis (MCE) can rapidly and quantitatively analyze the chemical content of a single red blood cell. This technology is now the standard analysis tool used for DNA sequencing.

Key innovations include highly parallel optical designs to detect fluorescence and novel, high-speed separation schemes that are simultaneously simple, rugged, sensitive, lower-cost, and broadly applicable. Highly multiplexed capillary electrophoresis allows hundreds or thousands of parallel sequencing runs, enabling far greater throughput than prior DNA sequencing instrumentation.

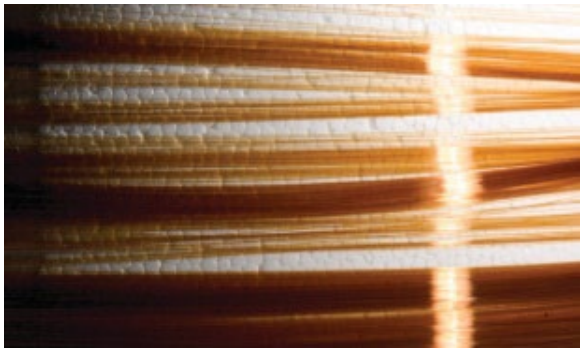
Ames scientist Edward Yeung developed MCE in 1995, prompting a series of publications and patents. SpectruMedix, Inc. and Applied Biosystems (now Thermo-Fisher Scientific) first marketed the technology for MCE. SpectruMedix and another spin-off company CombiSep (now Agilent) developed, manufactured, and marketed high-throughput, fully automated nucleic acid analysis systems out of Ankeny, Iowa. In both commercial and research applications, these products are designed to improve processes in the molecular diagnostics, pharmaceutical, life science, agricultural, and biofuels industries.

Advantages

MCE technology offers the following benefits:

- High-speed, high-throughput characterization of proteins, metabolites, and pharmaceuticals
- Supporting technology for combinatorial drug development and personalized medicine
- Uses less solvent
- Shorter time for sample analysis
- Reduced environmental risk and related costs relative to competing technology

AMES LABORATORY
Creating Materials & Energy Solutions
U.S. DEPARTMENT OF ENERGY



Fine glass capillaries (shown) allow for quick, accurate chemical analysis of substances using multiplexed capillary electrophoresis, which was developed at Ames Laboratory.

Facts and Figures

Four R&D 100 Awards

The core IP developed at Ames is used in 82% of commercially available capillary electrophoresis instruments on the market today.

Patent licensing brought in revenue well in excess of $5 million.

"Any kind of chemical measurements that involve separation can, in principle, be fitted to use this technology."

– Ed Yeung, Distinguished Professor in Liberal Arts and Sciences at Iowa State University

Sources: Ames 2019; Ames 2012; Johnston, Saren 2001; Mills, Bob 2001

1995: Ames scientist Edward Yeung patents the MCE technology

1997: Ames licenses the patent to SpectruMedix, and in 1999 sublicenses it to Applied Biosystems (now Thermo-Fisher Scientific)

2000: SpectruMedix receives NIH grant to develop its DNA sequencing instrument

2001: Edward Yeung forms spin-off company CombiSep (now Agilent), after developing a unique absorbance-based detection system

M3 Emitters

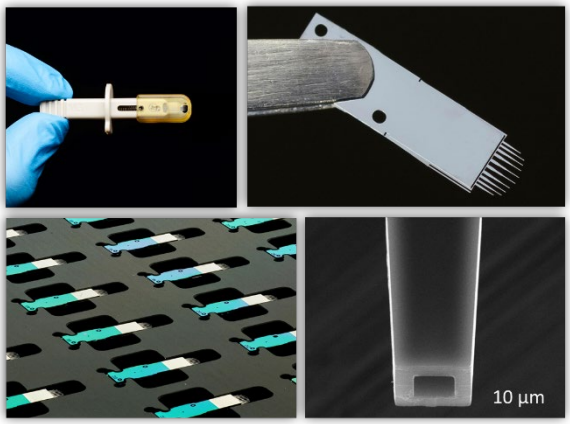
Researchers seeking to cure disease or address environmental and food safety hazards faced a bottleneck when using electrospray ionization mass spectrometry (ESI-MS). This process required each biospecimen to be loaded and delivered individually to the instrument. LBNL researchers set out to clear that expensive, time-consuming bottleneck with a multi-nozzle emitter array. This device creates smaller sample droplets, improving the sensitivity of mass spectrometry more than 10 times over conventional emitters—while also speeding the process. Work funded by an LBNL technology maturation grant demonstrated the device's use for bioimaging and high-throughput ESI-MS. The startup Newomics then received $12 million in NIH SBIR awards to develop the commercial product and follow-up product pipelines.

Newomics released the market-ready version of the multi-nozzle emitter array—the M3—in 2019 and developed integrated, precision medicine platforms that require very small amounts of blood. Among the startup's products are blood-based assays for diabetes diagnosis and for managing and monitoring man-made chemicals in the environment, such as potentially harmful perfluorinated chemicals (PFCs). Newomics also uses its proprietary technologies to provide industry and research organizations with services such as environmental biomonitoring, biomarker discovery, and drug screening.

Advantages

- Extremely sensitive, clog-resistant device for faster, more accurate biospecimen analysis
- Identification of over 3,000 proteins and 300 lipid species for monitoring disease starting from as little as five microliters of blood
- Used in biopharma, clinical, environmental, food, and forensic applications

Sources: LBNL 2019; Genomeweb 2014; Kim et al. 2007; Mao et al. 2011



Clockwise from top left: Plug-and-Play M3 emitter, a 10-nozzle M3 emitter, the cross-section of a 10 µm inner diameter nozzle, and multiple M3 emitters made from one silicon wafer. Images provided by Newomics.

Facts and Figures

Newomics was awarded $12M in NIH SBIR funding before securing $3.9M Series A funding toward commercialization.

One year after its global launch, Newomics now supplies the M3 emitter to 60 leading R&D laboratories including Merck, Genentech, Regeneron, and the CDC.

"If someone wants to look at low-abundant species by mass spectrometry, they can utilize our devices. Improved robustness means the results are more reproducible and reliable."

– Daojing Wang, Newomics Founder and CEO

2007: First of three M3 emitter manuscripts published in *Analytical Chemistry*

2011: M3 emitter patent granted

2012: R&D 100 Award

2012-16: SBIR funding

2017: Technology licensed to inventor startup

2019: The M3 is commercially launched

Lab on a Chip: Microfluidic Technology Speeds DNA Analysis

In 1987, ORNL scientist Mike Ramsey proposed using "microfluidic structures" to separate and identify chemicals inside very small volumes of liquid. His Lab on a Chip concept called for injecting a few drops of liquid into a winding, hair-like channel etched into a postage-stamp-sized glass microchip, then guiding the liquid through the channel using an electric field.

This microfluidic technology can analyze a volume of liquid 10,000+ times smaller than traditional methods, minimizing the amount of needed material, which can be expensive or hard to acquire, such as DNA. In addition, Lab on a Chip's computer-controlled design requires less labor and generates results much faster. For example, it uses enzymes to perform a DNA analysis in only five minutes instead of the hour required by the conventional technique.

Caliper Technologies recognized the beneficial applications for ORNL's Lab on a Chip and licensed the technology in 1995. Caliper, with Agilent Technologies, Inc., then introduced the 2100 Bioanalyzer in 1999 as the first commercially available instrument to use microfluidic technology for the analysis of biological samples. The success of the technology contributed to PerkinElmer's decision to buy Caliper in 2011 for $600 million.

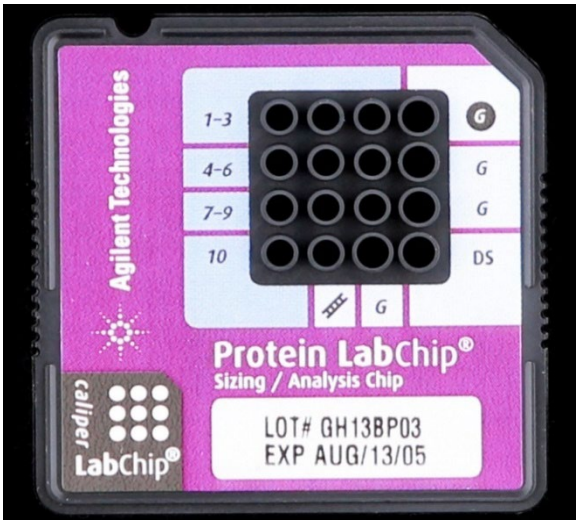
The introduction of microfluidics to Lab on a Chip technology seeded the expansion of the technology into medical diagnostics, manufacturing, biomedical research, personalized medicine, and *in vitro* diagnostics applications.

Advantages

- Analyzes liquid samples 10,000+ times smaller
- Saves money by requiring smaller samples
- Speeds results with faster, computer-controlled analysis
- Performs a DNA analysis in five minutes

Sources: Lab-on-a-chip 2004; PerkinElmer 2011

OAK RIDGE National Laboratory



Caliper Life Sciences commercialized ORNL's Lab on a Chip, which can analyze tiny samples of RNA, DNA, proteins, and other compounds—as small as a few millionths of a liter.

Facts and Figures

Required 10,000 times smaller sample than traditional methods

Caliper sold over 500,000 microfluidic Lab Chips in a year (2004).

PerkinElmer bought Caliper, the original license holder, for $600 million in 2011.

"ORNL's Lab on a Chip technology is a great example of how national laboratory research can provide innovations that help launch entirely new industries that touch the lives of people everywhere."

– Mike Paulus, ORNL's Director of Technology Transfer

1987: ORNL scientist Mike Ramsay proposes microfluidic Lab on a Chip design

1995: ORNL files patent; Ramsey cofounds Caliper Technologies, which licenses Lab on a Chip in the same year

1996: R&D 100 Award

1999: Caliper and Agilent launch the first commercial product

2011: PerkinElmer acquires Caliper for $600 million

Summary

This document highlights 12 technologies that represent only a fraction of the technological advancements originating from research at the DOE National Laboratories.

Outcomes of the 12 technologies by category:

Health Outcomes

25 million patients

- 1.8 million yearly FDG PET scans
- 250,000 patients have been screened with BSGI/MBI worldwide
- 15 million Wavefront guided Lasik procedures
- 600,000 successful proton treatments delivered
- 20,000+ melanoma patients treated with Zelboraf® worldwide
- 8 million stents implanted into heart patients worldwide

Economic Outcomes

Billions in domestic sales

- $299 million in yearly sales of the ^{18}F-FDG tracer (2010)
- $643 million in yearly sales revenue for Bio-Rad's ddPCR instrument (2018)
- $4+ billion in sales for Boston Scientific's radiopaque alloy stents
- $185 million in yearly sales revenue for Abbott's FISH products, accounting for 85% of the market (2015)
- $47+ million in licensing royalties for LLNL from total sales of $1 billion for FISH technology
- $72 million in royalty revenue from T7 protein expression licensing
- $14+ million in royalty revenue from multiplexed capillary electrophoresis (MCE) licensing

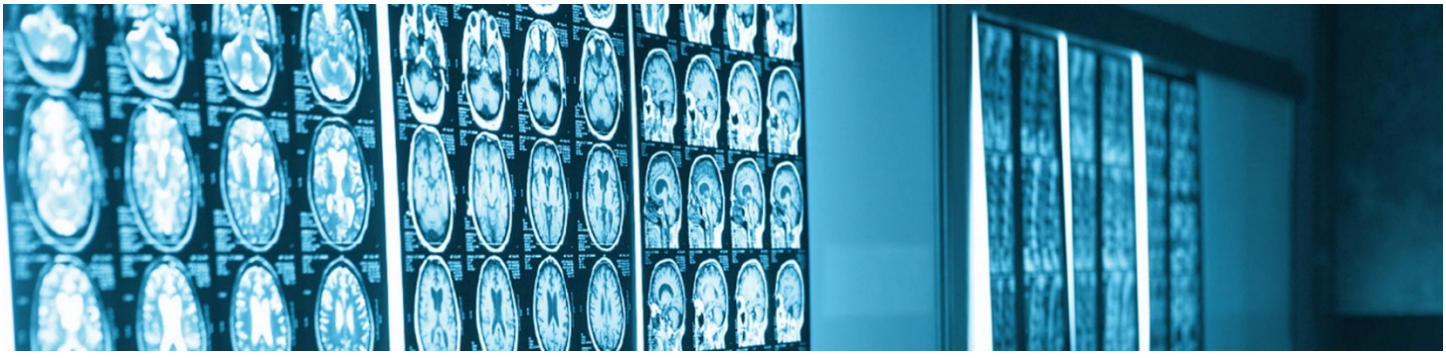
Knowledge Outcomes

Shaping our future

- National Medal of Science
- Nobel Prize
- 9 R&D 100 awards
- Scrip Award for Best New Drug (Zelboraf®)
- 800+ patent licenses sold
- 200,000+ academic journal citations
- Human Genome Project (HGP)

"The HGP is arguably the single most influential investment to have been made in modern science and a foundation for progress in the biological sciences moving forward."

– Economic impact of the human genome project (Battelle, 2011)



Technology Outlook Beyond 2020

The DOE National Laboratories have developed many technologies that have not yet entered the commercial sector. Some selected technologies in the pipeline are listed below:

HIV Vaccine (LANL) A research team at LANL explored the history, structure, and complexity of the HIV virus, then used that information to assemble a mosaic of vaccine antigens to elicit a broader immune response. Janssen, a subsidiary of Johnson & Johnson, further developed the vaccine and is now testing it in the HTVN705/Imbokodo clinical trial in South Africa and neighboring countries; the results are expected in 2021.

Potential Outcome: Curb the worldwide HIV/AIDS pandemic.

Universal Bacterial Sensor (LANL) This sensor is designed to mimic the body's biological recognition of bacterial pathogens to enable the detection of bacterial infections even before the onset of symptoms. The technology, which received a 2018 R&D 100 Award, is currently being validated for use in clinically relevant samples.

Potential Outcome: Portable diagnostic tool for early detection of infectious diseases.

Accelerating Therapeutics for Opportunities in Medicine (ATOM) Consortium (LLNL, ANL, industry and university partners) The ATOM consortium is a public-private partnership building a pre-competitive drug discovery platform to swiftly design and identify drug candidates for more effectively and safely treating disease. By pairing high-performance computing, diverse biological data, advanced machine learning, and human-relevant experimentation, ATOM aims to give researchers the ability to rapidly evaluate billions of drug candidates.

Potential Outcome: A streamlined, patient-centric drug discovery process.

Cancer Distributed Learning Environment (CANDLE) This initiative by DOE and the National Cancer Institute taps unique capabilities at ANL, ORNL, LLNL, LANL, and the NIH Frederick National Laboratory for Cancer Research to better understand cancer. CANDLE is using DOE's high-performance computing and deep learning to build predictive models from massive amounts of cancer data in order to guide effective treatments. This project will take advantage of the exa-scale computers to be installed at DOE beginning in 2021.

Potential Outcome Improved understanding and treatment of Cancer resulting in better patient outcomes.

"Flash" Radiotherapy (SLAC) In 2018, researchers at SLAC and Stanford University secured funding to begin building a new linear accelerator-based technology prototypes. The technology uses high-intensity radiation to deliver an entire therapy session within a single flash that lasts less than a second. This flash of radiation is expected to markedly reduce the radiation toxicity side effects usually caused by movement of healthy tissue and organs during exposure.

Potential Outcome: Reduction in toxic side effects from cancer radiation therapy.

Genome Editing to Explore Viral Infection (SNL) Researchers from both SNL and UCLA worked together on a cooperative agreement to determine mechanisms for viral infection using CRISPR (clustered regularly interspaced short palindromic repeats). CRISPR allows researchers to remove specific gene sequences to help determine which host cell genes must be present for viral infection to occur. Because this process can be inexact and time intensive, this joint research seeks to improve the CRISPR library—making it easier to map the pathway for viral infection.

Potential Outcome: Better detection and treatment of breast cancer and potentially many other types of cancer.

References

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