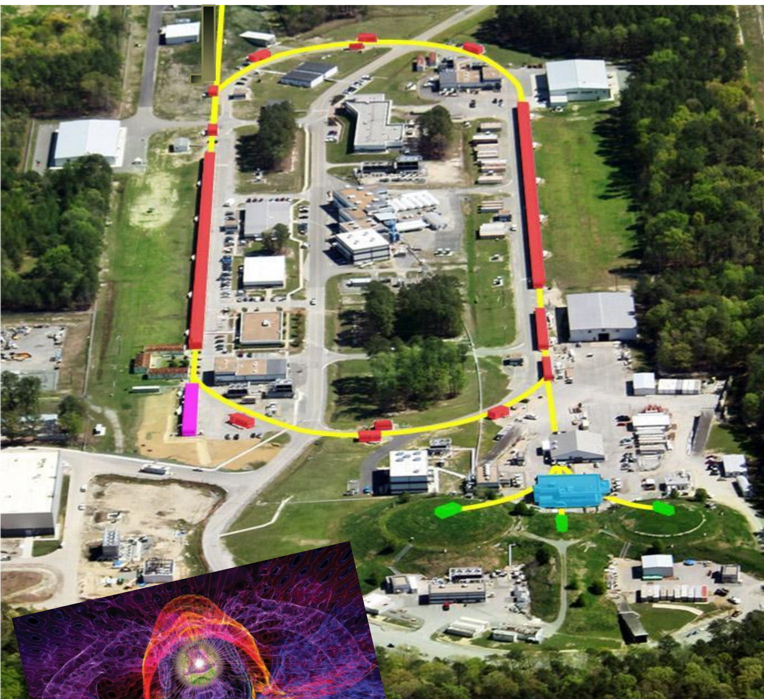
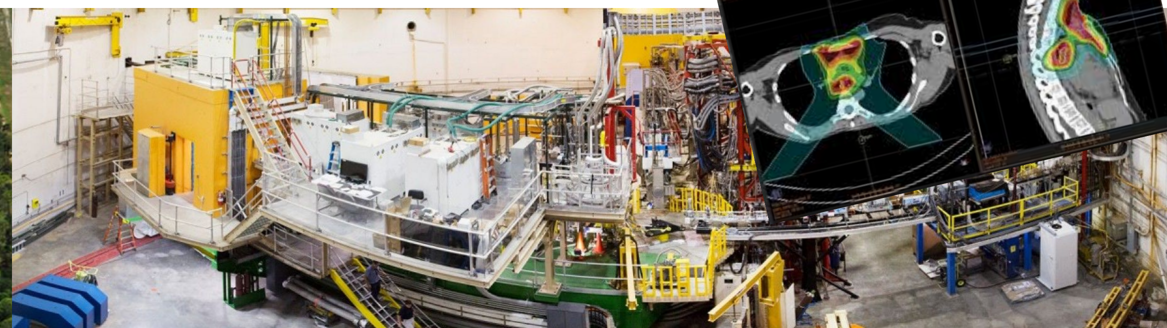
Medical Applications of Nuclear Physics Research

Cynthia Keppel
Thomas Jefferson National Accelerator Facility





DOE/NSF Nuclear Science Advisory Committee Meeting

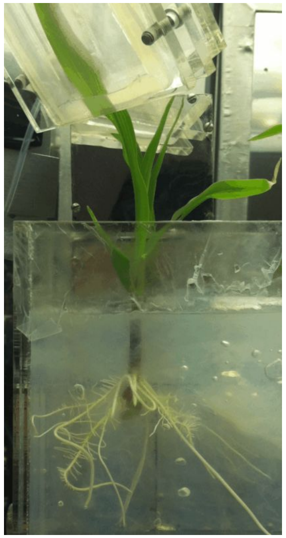
March 18, 2021

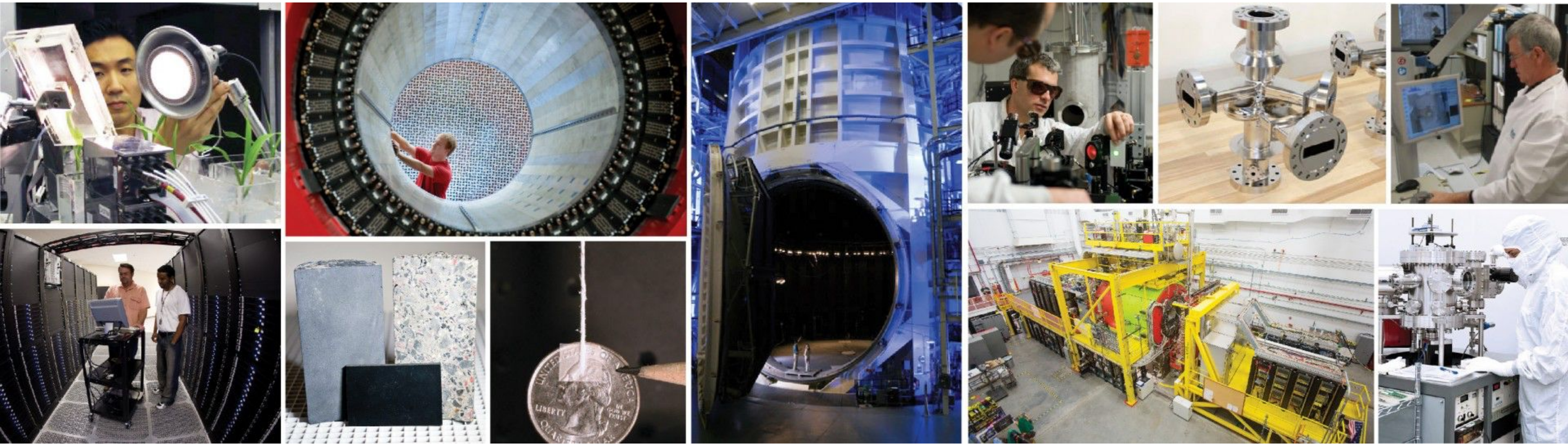
Jefferson Lab
U.S. DEPARTMENT OF ENERGY | Office of Science
JSA

JLab Medical Technology Development

Synergistic Development with Nuclear Science

- Instrumentation and Detection Systems
- Computing, Software and Data Management
- Particle Accelerator Technology





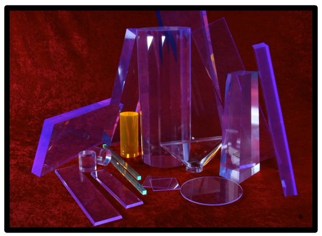
Jefferson Lab

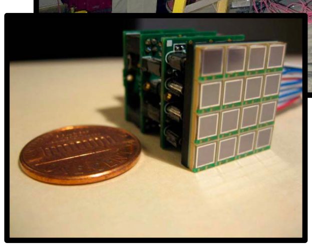
Instrumentation and Detection Systems: *Medical Applications*

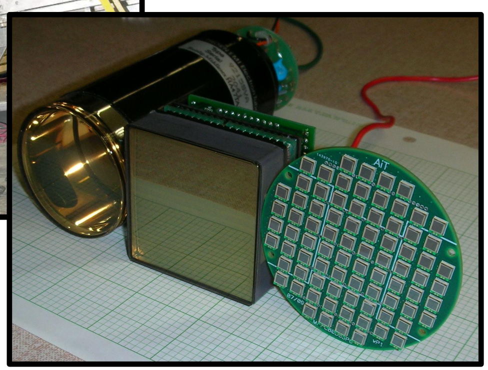
Particle Detector Spin-Off Advances Patient Care

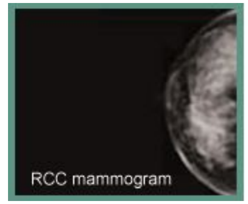
Nuclear physics detector technology developed to explore the structure of matter at Jefferson Lab leads to new and advanced tools for better patient care.

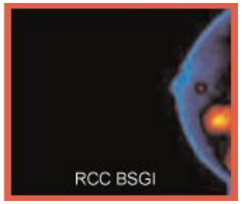
Tools for nuclear physics research
photomultiplier tubes, silicon photo multipliers, scintillator and detector electronics.











Compact gamma camera for breast cancer detection

- Led to several Jefferson Lab **patents and a start-up company**

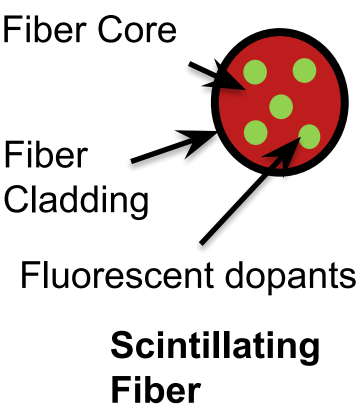
Tools for better patient care

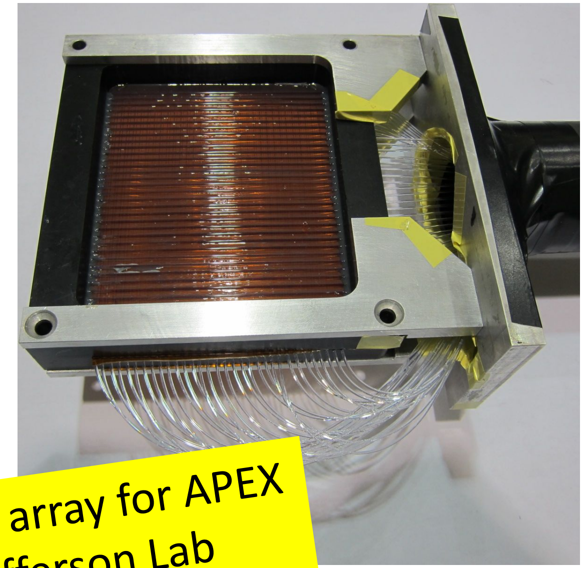
Hand held gamma camera to guide surgeons

- **Silicon photo multipliers** provide precise imaging at low voltages
- Now also **wireless**, to give flexible motion without tethering
- Working on on-board display

“Active Catheter” Development for Brachytherapy

- ”Brachy” = near, short distance: **Internal**
  - Radioactive seeds or sources are placed near tumor, delivering a high radiation dose to the tumor while reducing exposure to surrounding healthy tissue
- *NO real time dose distribution feedback!*
  - AAPM’s TG56: *"no practical and validated dose measurement technology is available to the hospital physicist”.*
- *In-vivo dose measurements would allow for real time evaluation of dose delivered to patient.*
- Increase patient safety since the detector may be used for dose-at-a-point confirmation or to monitor dose absorbed by critical organs.
- ***Idea:** What about scintillating fibers (used in nuclear physics) placed INSIDE the brachytherapy catheters?*



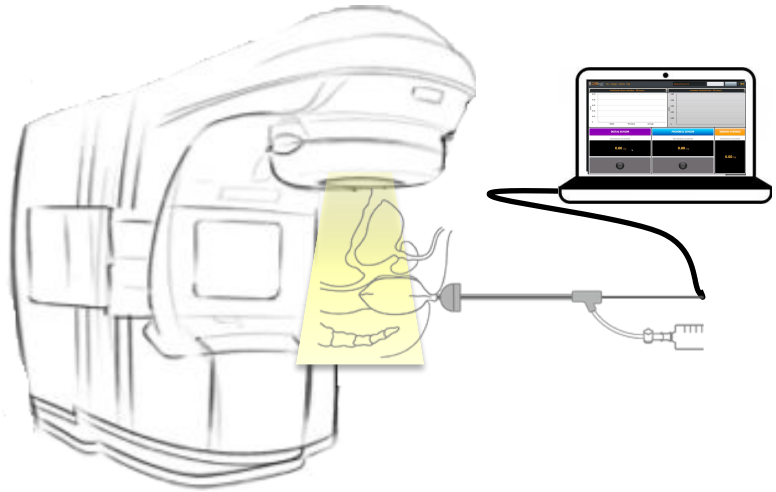


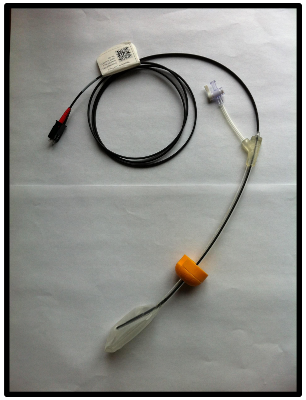
Scintillating fiber array for APEX experiment at Jefferson Lab

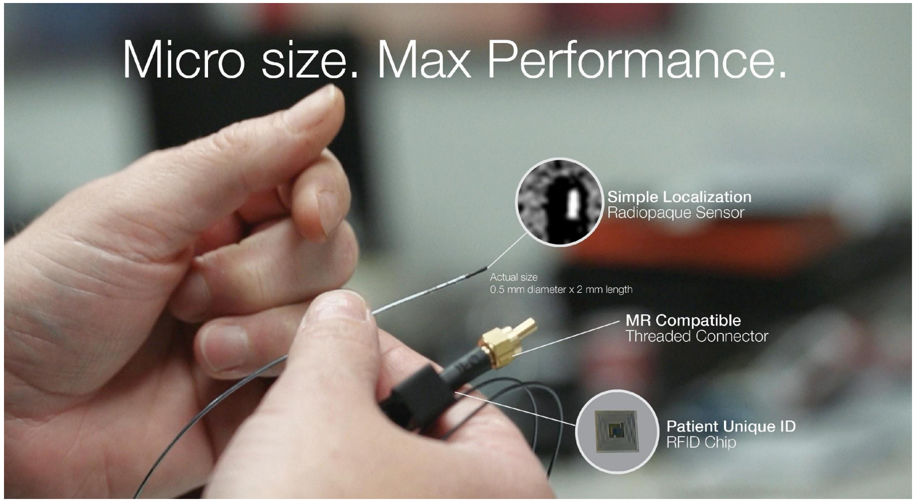
Enabling Real Time Radiation Treatment Dosimetry

Nuclear physics detector technology for real time dosimetry monitoring into radiotherapy cancer treatment procedures.

- Radiation treatment dose uncertainties can affect tumor control and may increase complications to surrounding normal tissues.
- The current standard of practice does not provide information on actual delivered dose to the tumor.
- **Nuclear scientists at Jefferson Lab and Hampton University developed real-time, in vivo, dosimetry technology (3 patents)**
- Licensed to Radiadyne, created OARtrac







MEDTECH BREAKTHROUGH AWARDS

2018 Awards

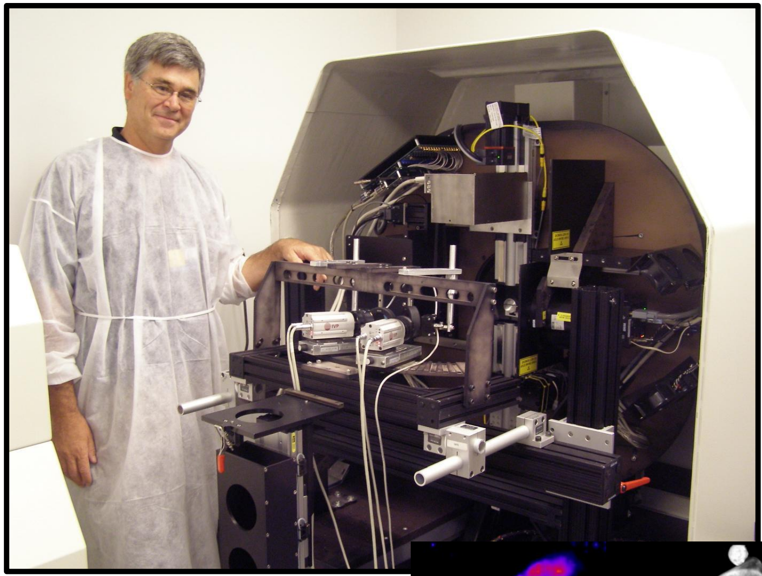
Jefferson Lab

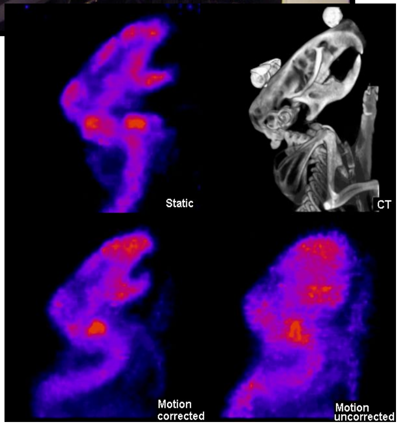
Advancing Brain Imaging Technologies

Methods based upon anesthesia inhibit/complicate brain based studies. Scientists work towards imaging methodology in awake humans to study neurological based diseases.

AwakeSPECT System is **based on technology developed by Jefferson Lab**, with contributions from ORNL, Johns Hopkins University and University of Maryland.

- Utilizes custom-built gamma cameras, image processing system, infrared camera motion tracking system and commercial x-ray CT system.
- Acquires functional brain images of conscious, unrestrained, and un-anesthetized mice.
- Can aid research into Alzheimer's, dementia, Parkinson's, brain cancers, traumatic brain injury and drug addiction.



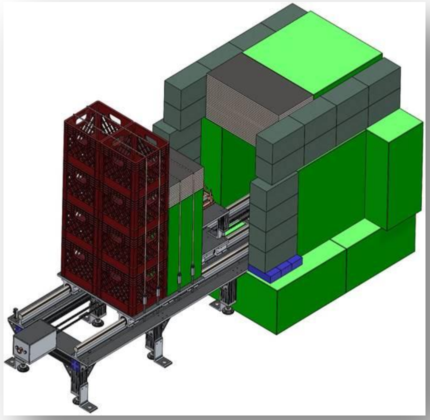


Gamma cameras based on nuclear physics detector technology.

Three IR markers attached to the head of a mouse enable the AwakeSPECT system to obtain detailed, functional images of the brain of a conscious mouse as it moves around inside a clear burrow.

Accelerator Based Radioisotope Production

Low Energy Recirculator Facility (LERF) accelerator at JLab used for (^{67}Cu) production experiment via photo-production using bremsstrahlung photons from Gallium target

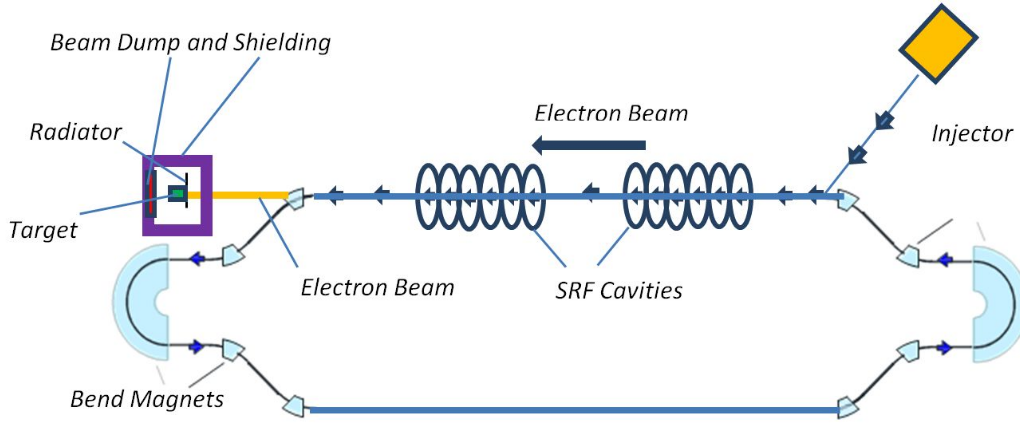


Isotope Target Hot Cell and Shielding

"Theranostic" radionuclide for Targeted Radiotherapy:

- 141 keV mean energy β- for therapy (~cell diameter range in tissue)
- 185 keV energy gamma for SPECT imaging
- Half-life of 61.8 hours convenient for production, transportation, and delivery to patient
- Favorable biochemistry

JLab LERF



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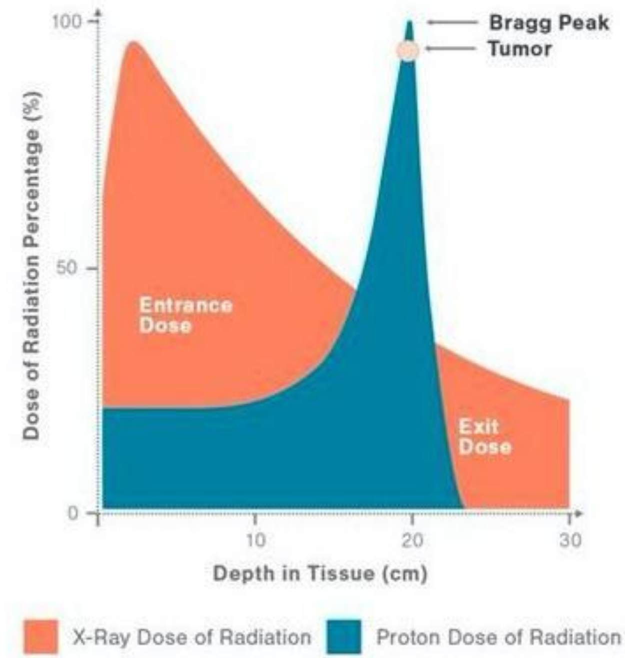
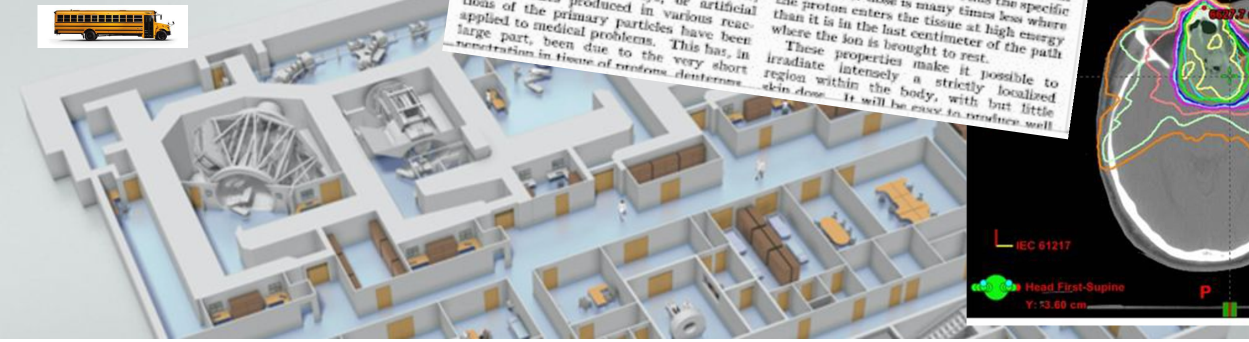
Proton Therapy for Cancer Treatment

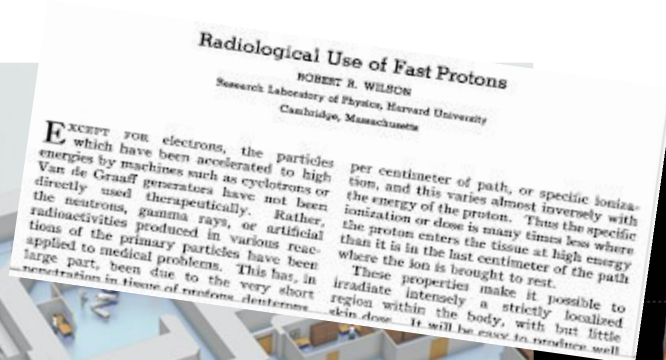
Radiotherapy with a **proton accelerator** (up to 250 MeV) allows oncologists to design fine-tuned three-dimensional cancer treatment plans.

Fundamental nuclear physics: *Bragg peak determines proton energy loss = dose to patient*

- Enables higher precision localized treatment
- Associated with fewer side effects due to reduced stray radiation outside the tumor region
- Nuclear physics technology to enable this includes **simulation, beam transport, acceleration, dose monitoring**, *and more….*







Radiological Use of Fast Protons

ROBERT R. WILSON

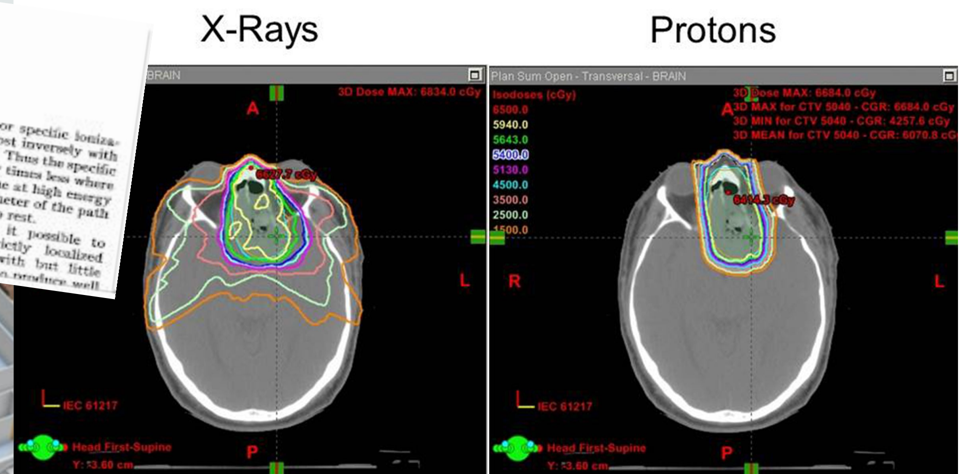
Research Laboratory of Physics, Harvard University

Cambridge, Massachusetts

EXCEPT FOR electrons, the particles which have been accelerated to high energies by machines such as cyclotrons or Van de Graaff generators have not been directly used therapeutically. Rather, the neutrons, gamma rays, or artificial radioactivities produced in various reactions of the primary particles have been applied to medical problems. This has, in large part, been due to the very short penetration in tissue of protons, deuterons ...

per centimeter of path, or specific ionization, and this varies almost inversely with the energy of the proton. Thus the specific ionization or dose is many times less where the proton enters the tissue at high energy than it is in the last centimeter of the path where the ion is brought to rest.

These properties make it possible to irradiate intensely a strictly localized region within the body, with but little skin dose. It will be easy to produce well ...



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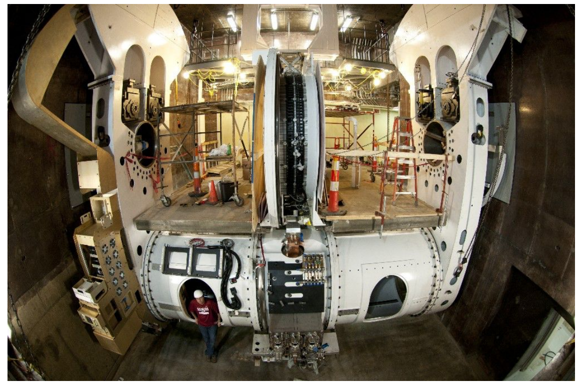
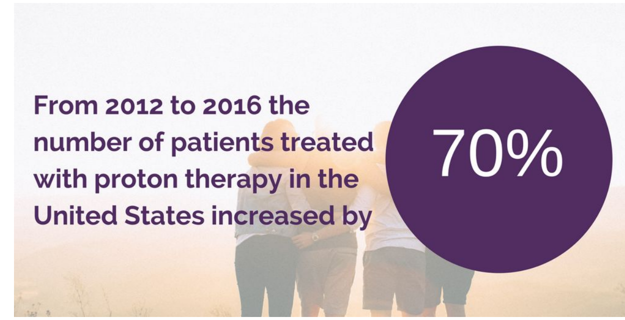
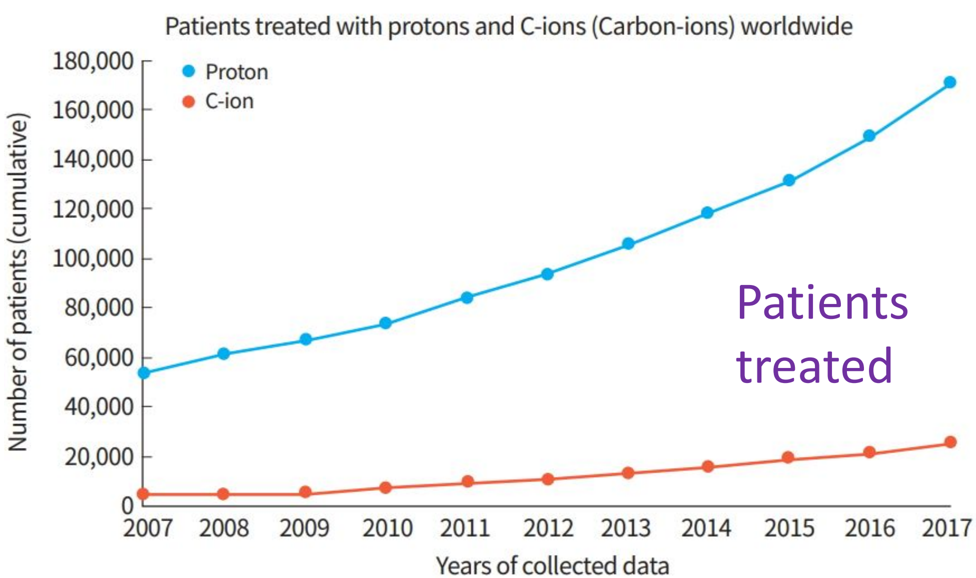
Proton Therapy for Cancer Treatment

- >250,000 patients have been treated with particle therapy worldwide from 1954 to 2020.
- Current average ~15,000 patients treated annually.

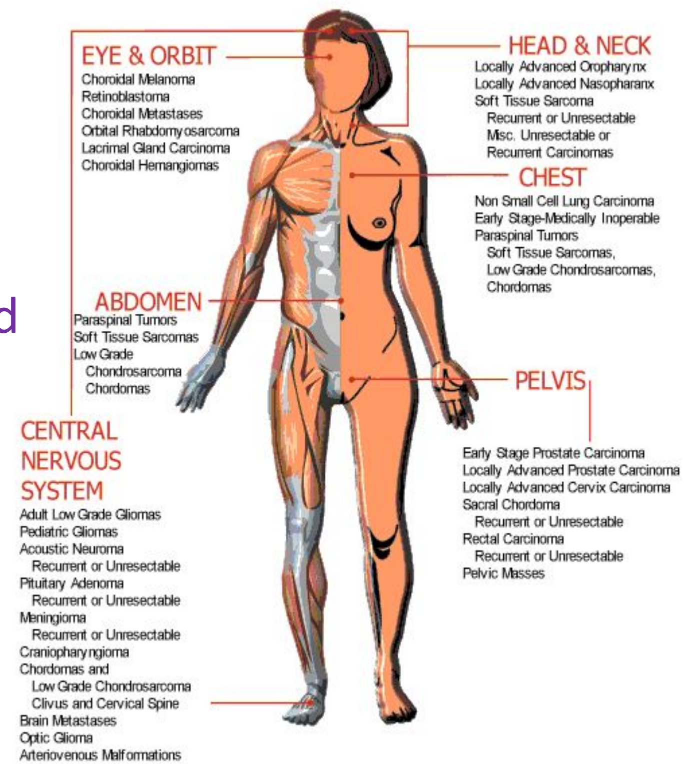






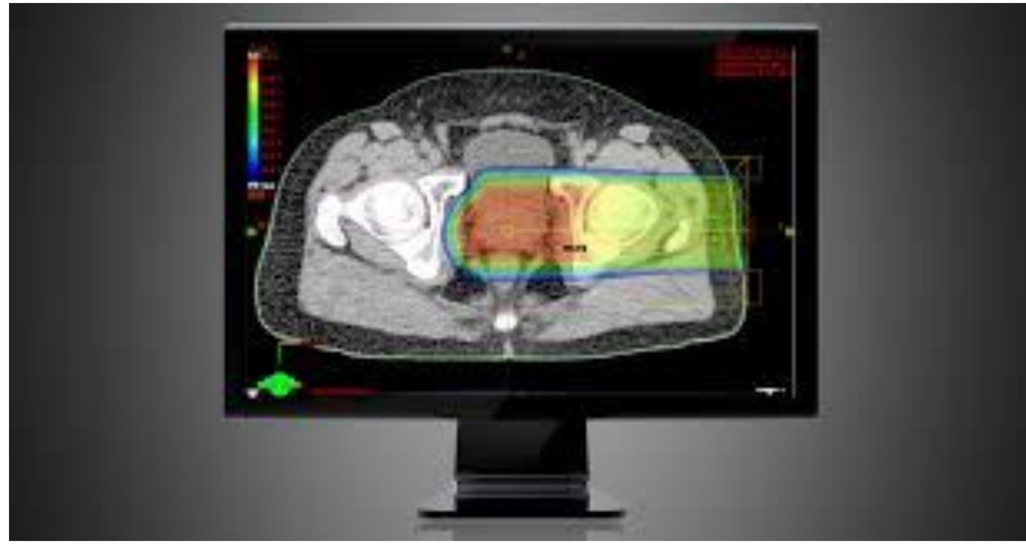
Patients treated

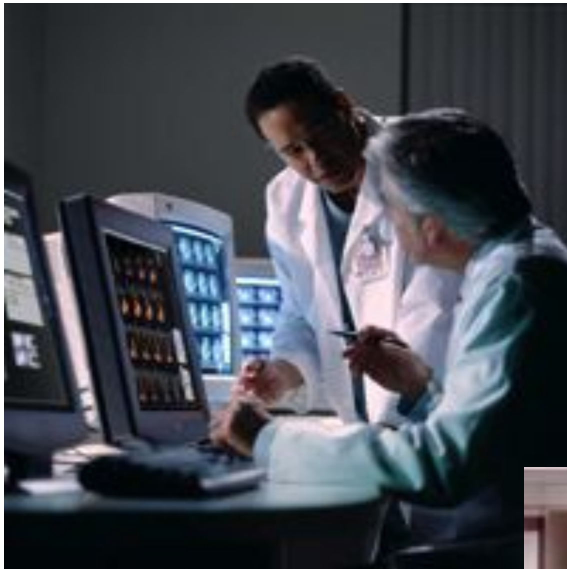
Tumor sites treated



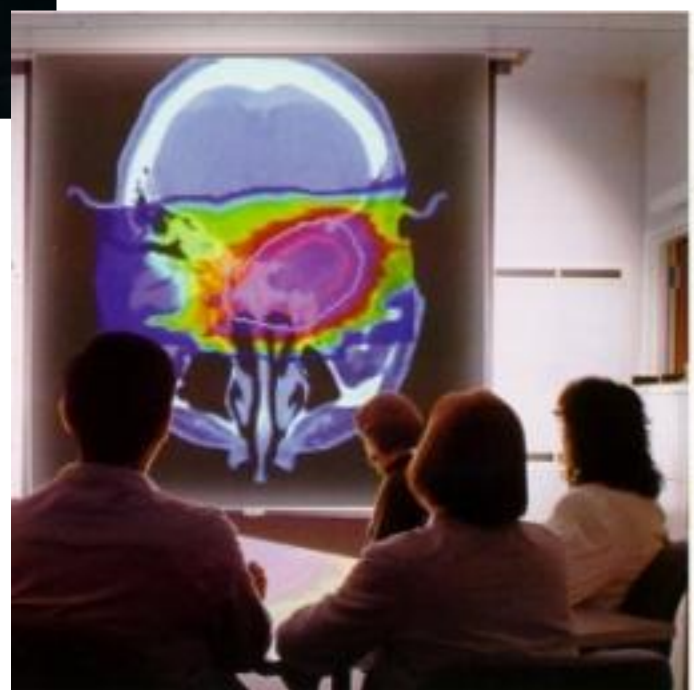
Proton Beam Simulation

Varian Medical Systems "Eclipse" software product





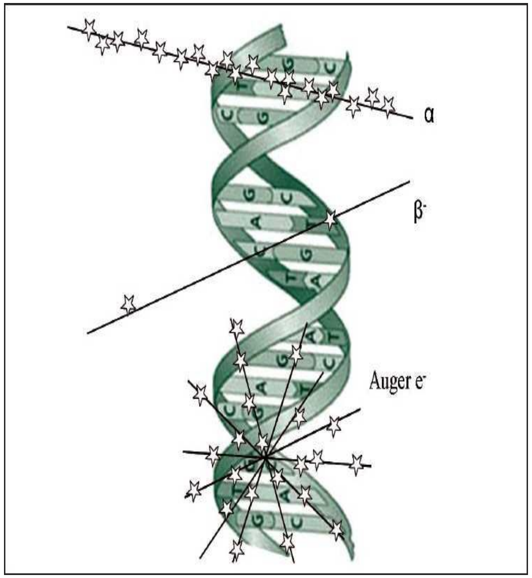
Doctors prescribe dose based on (CT) images of tumor volume and location

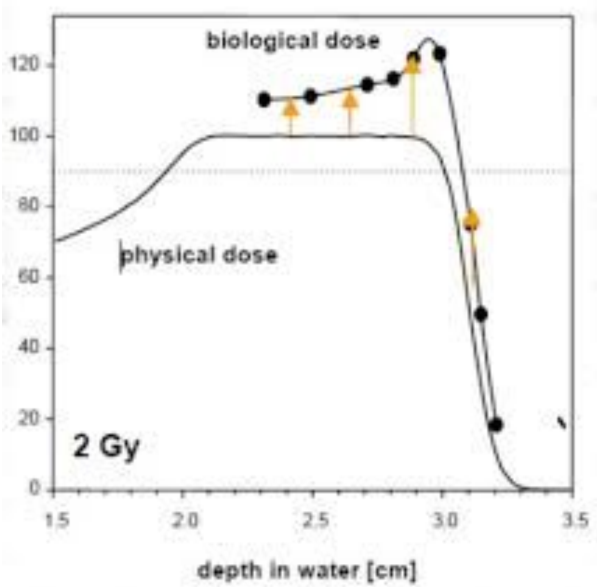


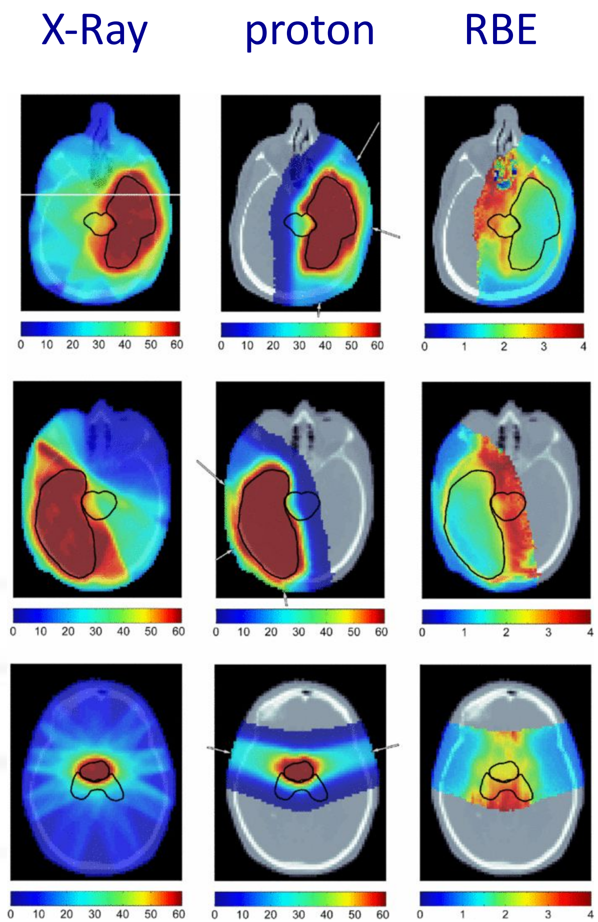
Physics team *simulates radiation transport through patient* using beam angles, energies, devices, etc. in patient to achieve desired dose

Proton Beam Simulation – "BioEclipse" Development

VARIAN medical systems







Effect of RBE-weighted treatment planning on brain tumor dose distributions

JLab, Eastern Virginia Medical School, HUPTI

- *"Relative Biological Effectiveness"* (RBE) factor allows comparison between the killing power of radiation of type *R* to that of X-rays.
- A *single (RBE) value* is currently applied to all proton patient treatment plans, RBE=1.1
- We were able to show that RBE's at the *far side* of the treatment volume can be significantly higher

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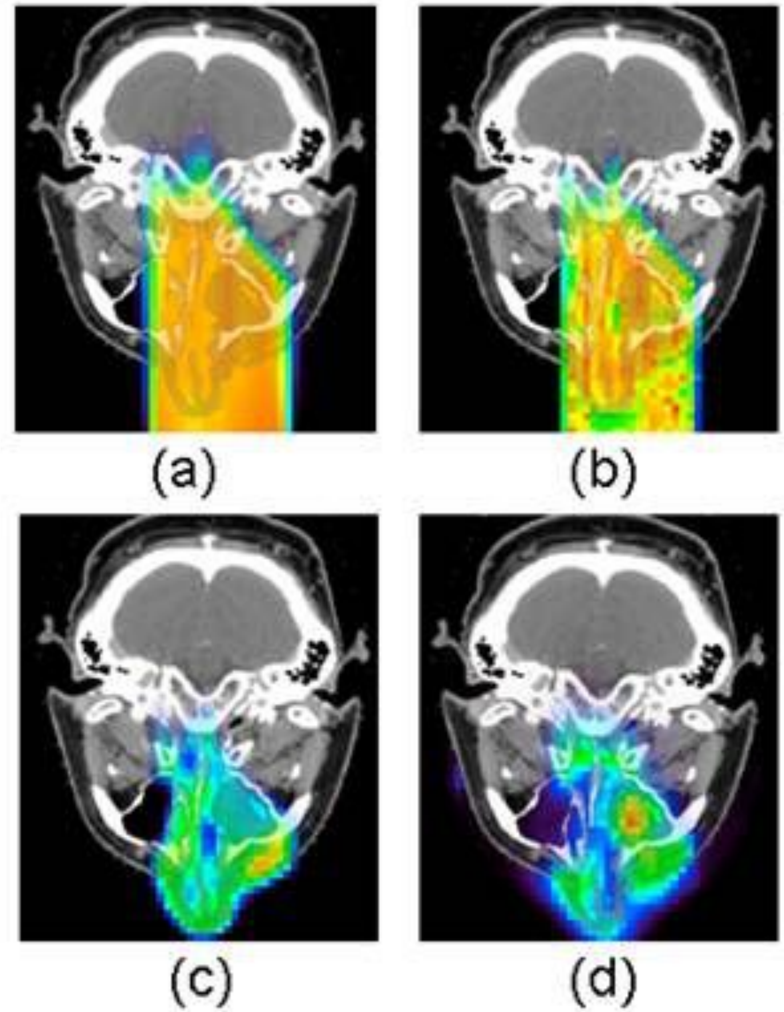
PET Imaging of Proton Beam Delivery

nasal cavity melanoma

Radionuclide	Half life (min)	Nuclear reaction channels Threshold energies (MeV)
^{15}O	2.037	$^{16}O(p,pn)^{15}O$/16.79
^{11}C	20.385	$^{12}C(p,pn)^{11}C$/20.61,
		$^{14}N(p,2p2n)^{11}C$/3.22,
		$^{16}O(p,3p3n)^{11}C$/59.64
^{13}N	9.965	$^{16}O(p,2p2n)^{13}N$/5.66,

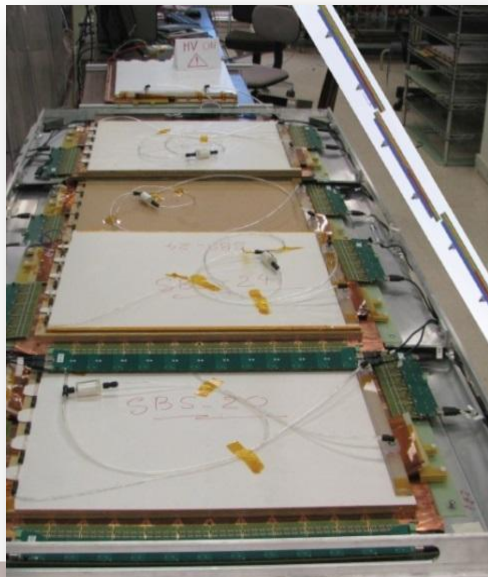


- Promising for range verification
- Develop into dose verification?
- Or, try using ^{11}C beam for treatment and imaging?

Zhu X, Fakhri GE. Proton Therapy Verification with PET Imaging. *Theranostics* 2013; 3(10):731-740

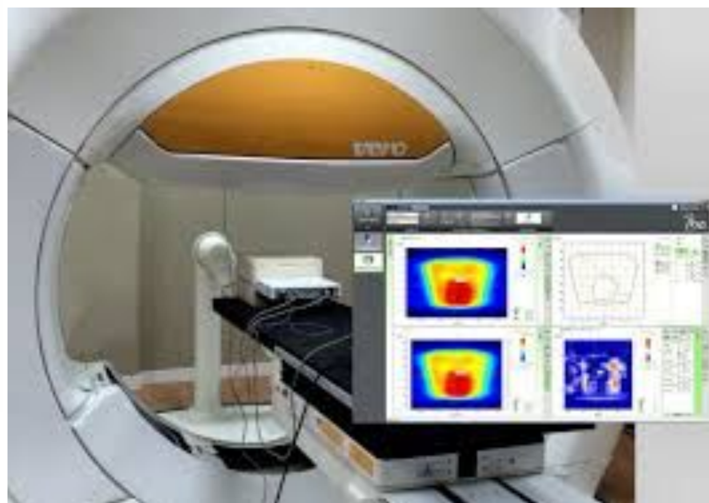
Proton Beam Characterization and Dosimetry

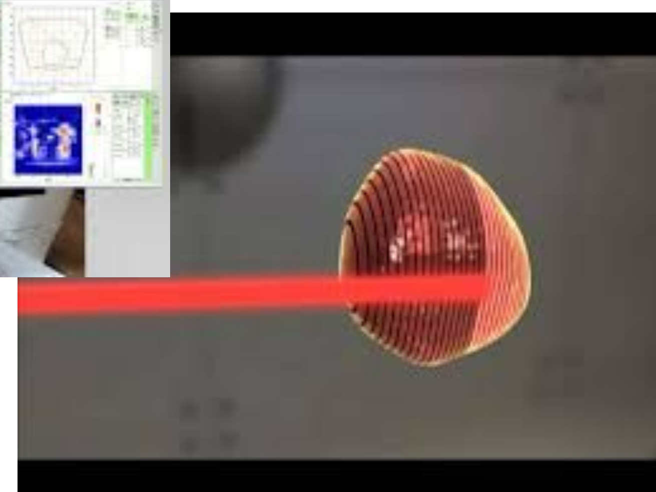
Gas Electron Multiplier
Detectors for Jefferson Lab Hall
A Super Bigbite Spectrometer



70 (50) **micron**
resolution

7 **mm**
resolution

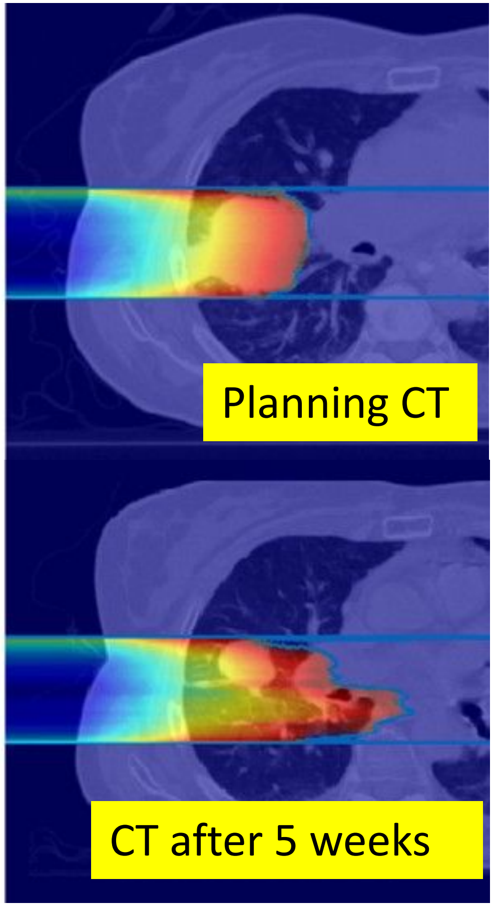




Potentially excellent
tool for (new) pencil
beam scanning delivery

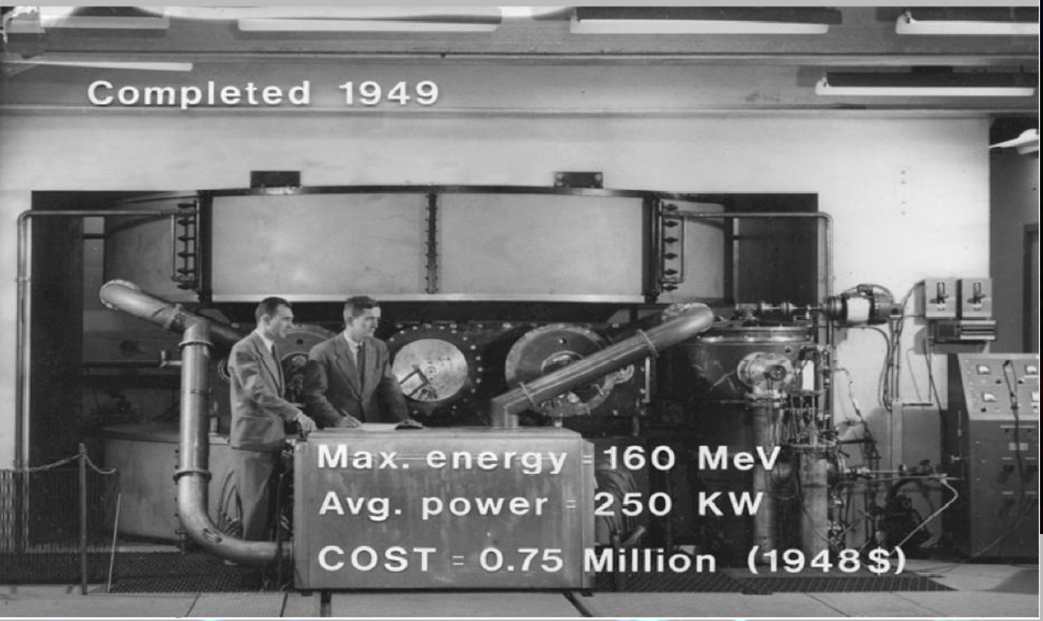
Towards real time 3D imaging, *proton* Computed Tomography

- Range uncertainty in proton therapy
  - (Photon) CT conversion to proton stopping power
  - Anatomy/setup variation
  - Anatomical changes during treatment
- Proton CT can reduce target volume in proton therapy
  - reduce planning "margins"
  - important when treating tumors close to critical structures (brain stem, optic chiasm, spinal cord…)
- pCT imaging could replace x-ray imaging for patient alignment verification before treatment
  - facilitate adaptive planning
- Thin tracking detectors needed
  - GEM spatial resolution a plus
  - < 1 mm water equivalence per plane
  - exiting proton energy as low as 50 MeV, Coulomb scattering a challenge



Lomax, Oxford

We've come a long way!



Patient Treatments 1974-2002

Patient Treatments Today in 29 US clinics and 40+ more around the world

But, we can go further…

- Continue trend toward less expensive, compact equipment
- *Monte Carlo based* treatment planning, full and fast dose simulation
  - *Implement variable RBEs into planning*
- Prompt gamma detection for range verification
- On-board PET for prompt gamma imaging
- Proton tomography – on gantry
- Adaptive planning
- Integrated gating techniques
- Improve immobilization
- More cost-effective building construction, radiation shielding

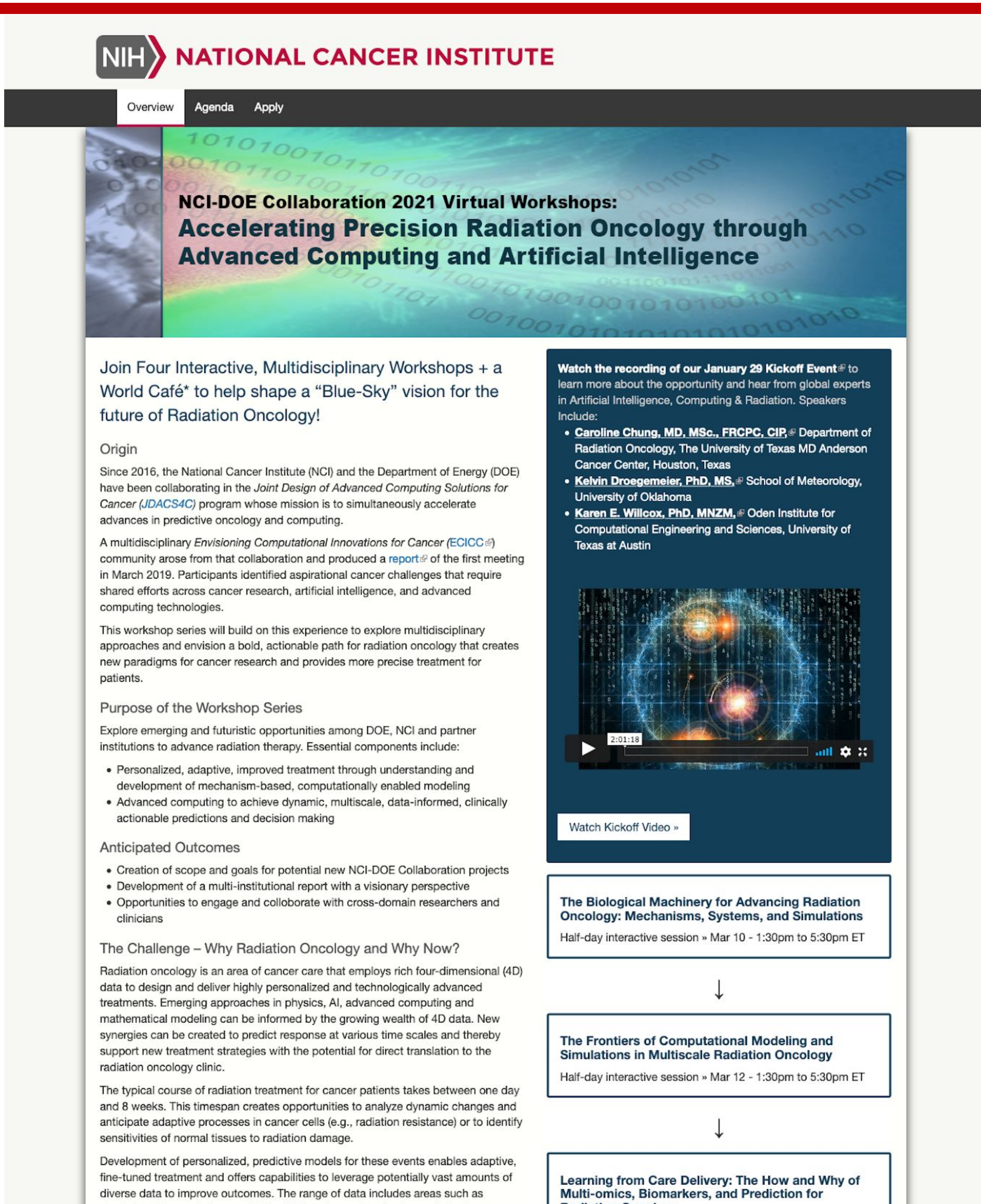
Summary

- Jefferson Lab (like much of the nuclear physics community) has multiple facilities spanning a broad range of expertise to support research activities

- Nuclear facilities and expertise can be leveraged for medical and other technology development

[*Getting attention….*]

JOINT DOE/NIH WORKSHOPS



NIH NATIONAL CANCER INSTITUTE

Overview | Agenda | Apply

NCI-DOE Collaboration 2021 Virtual Workshops:
Accelerating Precision Radiation Oncology through Advanced Computing and Artificial Intelligence

Join Four Interactive, Multidisciplinary Workshops + a World Café* to help shape a "Blue-Sky" vision for the future of Radiation Oncology!

Origin

Since 2016, the National Cancer Institute (NCI) and the Department of Energy (DOE) have been collaborating in the *Joint Design of Advanced Computing Solutions for Cancer* (*JDACS4C*) program whose mission is to simultaneously accelerate advances in predictive oncology and computing.

A multidisciplinary *Envisioning Computational Innovations for Cancer* (ECICC) community arose from that collaboration and produced a report of the first meeting in March 2019. Participants identified aspirational cancer challenges that require shared efforts across cancer research, artificial intelligence, and advanced computing technologies.

This workshop series will build on this experience to explore multidisciplinary approaches and envision a bold, actionable path for radiation oncology that creates new paradigms for cancer research and provides more precise treatment for patients.

Purpose of the Workshop Series

Explore emerging and futuristic opportunities among DOE, NCI and partner institutions to advance radiation therapy. Essential components include:

- Personalized, adaptive, improved treatment through understanding and development of mechanism-based, computationally enabled modeling
- Advanced computing to achieve dynamic, multiscale, data-informed, clinically actionable predictions and decision making

Anticipated Outcomes

- Creation of scope and goals for potential new NCI-DOE Collaboration projects
- Development of a multi-institutional report with a visionary perspective
- Opportunities to engage and colloborate with cross-domain researchers and clinicians

The Challenge – Why Radiation Oncology and Why Now?

Radiation oncology is an area of cancer care that employs rich four-dimensional (4D) data to design and deliver highly personalized and technologically advanced treatments. Emerging approaches in physics, AI, advanced computing and mathematical modeling can be informed by the growing wealth of 4D data. New synergies can be created to predict response at various time scales and thereby support new treatment strategies with the potential for direct translation to the radiation oncology clinic.

The typical course of radiation treatment for cancer patients takes between one day and 8 weeks. This timespan creates opportunities to analyze dynamic changes and anticipate adaptive processes in cancer cells (e.g., radiation resistance) or to identify sensitivities of normal tissues to radiation damage.

Development of personalized, predictive models for these events enables adaptive, fine-tuned treatment and offers capabilities to leverage potentially vast amounts of diverse data to improve outcomes. The range of data includes areas such as

Watch the recording of our January 29 Kickoff Event to learn more about the opportunity and hear from global experts in Artificial Intelligence, Computing & Radiation. Speakers Include:

- **Caroline Chung, MD, MSc., FRCPC, CIP,** Department of Radiation Oncology, The University of Texas MD Anderson Cancer Center, Houston, Texas
- **Kelvin Droegemeier, PhD, MS,** School of Meteorology, University of Oklahoma
- **Karen E. Willcox, PhD, MNZM,** Oden Institute for Computational Engineering and Sciences, University of Texas at Austin

2:01:18

Watch Kickoff Video »

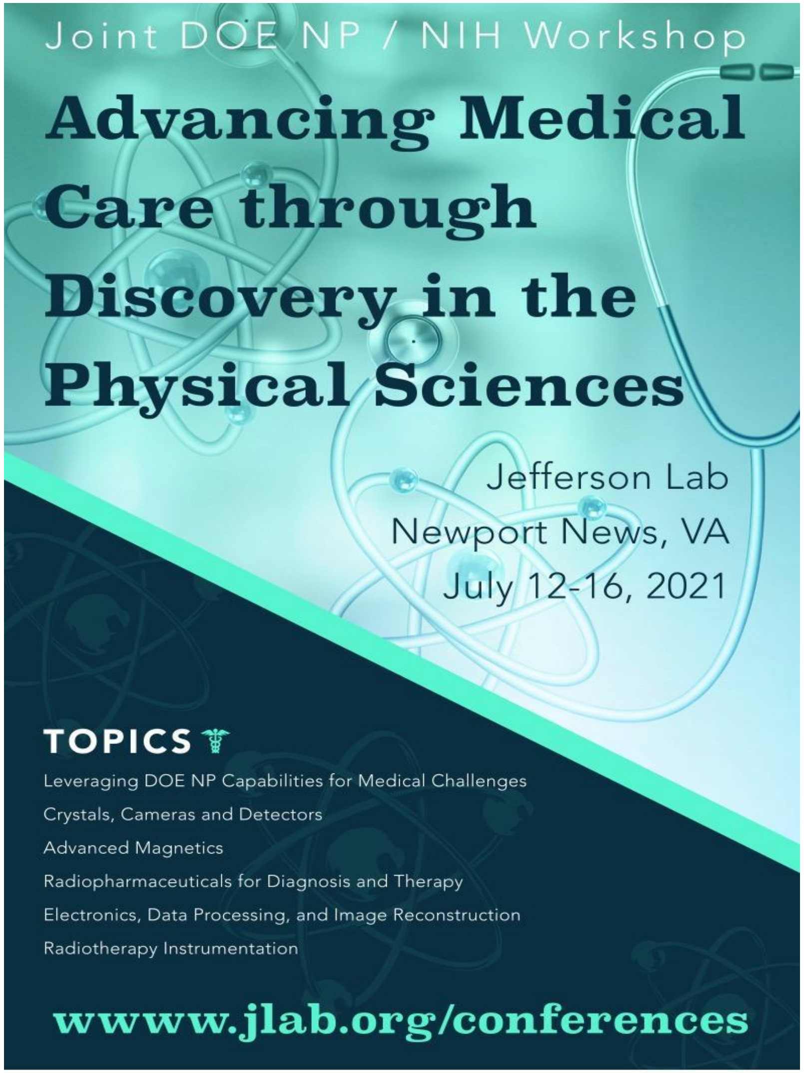
The Biological Machinery for Advancing Radiation Oncology: Mechanisms, Systems, and Simulations
Half-day interactive session » Mar 10 - 1:30pm to 5:30pm ET

↓

The Frontiers of Computational Modeling and Simulations in Multiscale Radiation Oncology
Half-day interactive session » Mar 12 - 1:30pm to 5:30pm ET

↓

Learning from Care Delivery: The How and Why of Multi-omics, Biomarkers, and Prediction for



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- *Thank you!*