Medical Physics and the Search for Big Data

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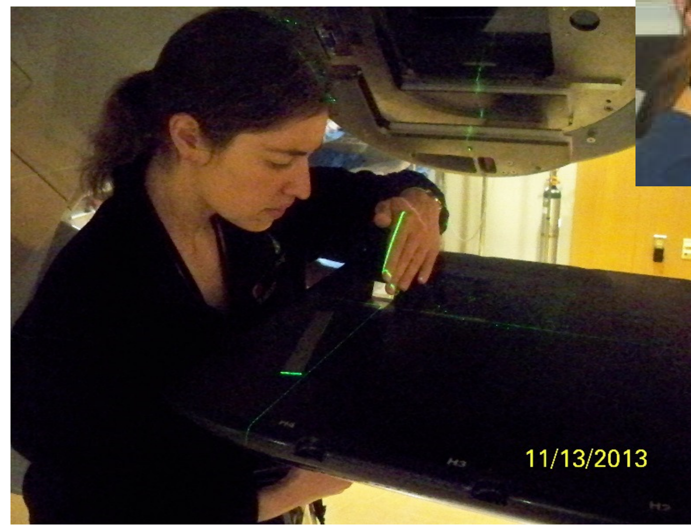
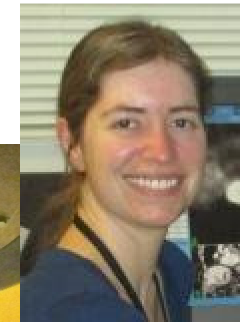
A brief introduction

From the collision hall
…to the hospital





- High-energy physicist on CDF (2002-2010)
  - PhD with Johns Hopkins: B^{**0} and Σ_b searches
  - Postdoc with UW-Madison: Higgs → WW search
- Medical physics residency with Harvard (2010-2013)
  - Clinical medical physicist with MGH (2013-present)

What is medical physics?

- According to the American Association of Physicists in Medicine (www.aapm.org):

AMERICAN ASSOCIATION of PHYSICISTS IN MEDICINE

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Medical Physics

Medical Physics is an applied branch of physics concerned with the application of the concepts and methods of physics to the diagnosis and treatment of human disease. It is allied with medical electronics, bioengineering, and health physics.

Current Issue of Medical Physics

What Is a Medical Physicist?

Medical physicists contribute to the effectiveness of radiological imaging procedures by assuring radiation safety and helping to develop improved imaging techniques (e.g., mammography CT, MR, ultrasound). They contribute to development of therapeutic techniques (e.g., prostate implants, stereotactic radiosurgery), collaborate with radiation oncologists to design treatment plans, and monitor equipment and procedures to ensure that cancer patients receive the prescribed dose of radiation to the correct location.

What do Medical Physicists Do?

Medical physicists are concerned with three areas of activity: clinical service and consultation, research and development, and teaching. On the average their time is distributed equally among these three areas.

What is medical physics?

- Three primary areas of medical physics:
  - Health physics (Radiation safety)
    - Primarily regulatory/governmental
  - Diagnostic (Radiology)
    - Clinical: quality assurance of imaging equipment in Radiology
    - Research: improving image quality or resolution, usually focus on one of CT, PET/Nuclear Medicine, or MRI
  - Therapy (Radiation Oncology) – largest area by far
    - Clinical: designing radiation treatment plans, QA of treatment accelerators, programming and software QA, etc
    - Research: wide-ranging, from improving radiation delivery techniques to modeling biological effects of radiation

Therapeutic medical physics

Core curriculum for MP

- Radiological Physics and Dosimetry
- Radiation Protection and Safety
- Fundamentals of Medical Imaging
- Radiobiology
- Anatomy and Physiology
- Radiation Therapy Physics

- Required knowledge:
  - Graduate-level physics
  - In-depth understanding of particle interactions in matter
    - And how those interactions translate to delivered **Dose**
  - Operating principles of particle accelerators
    - Most centers treat with photons using electron linacs
    - MGH also treats with protons from a cyclotron; more exotic options like neutrons, carbon ions are experimental
  - Radiation protection and safety
  - Imaging principles also important for therapy
  - Knowledge of basic anatomy, and disease/oncology

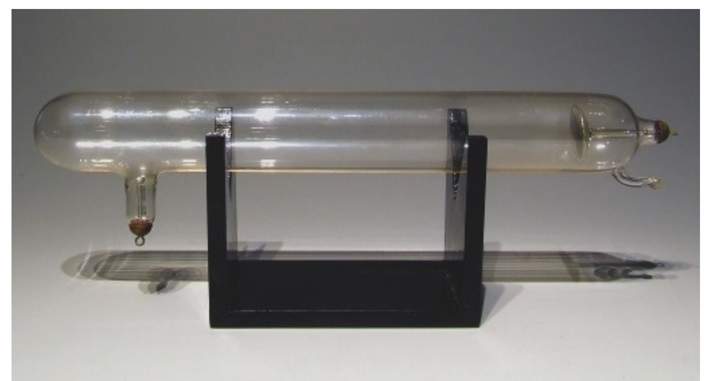
What does a clinical physicist do?

- Many answers, and much depends on where you work
  - Small community hospital: keep the linac running (QA and testing, coordinating repairs), check treatment plans for completeness and safety, design safe procedures, train staff
  - Large academic hospital: have on-site engineering support, split QA duties with other physicists, specialize in specific advanced procedures, participate in research & development, some teaching load
- My day as a clinical physicist at MGH:
  - Clinical duties: care for one linac, standard QA duties (plan checks)
    - Special procedures: brachytherapy, intra-operative therapy
  - Teaching: mentoring residents; courses in Radiology & Physics
  - Research? Some small projects, no external grant funding

A brief history of radiation oncology…

- It all started with Roentgen:
  - Discovery of x-rays: Nov 8, 1895
    - Benefits of x-ray radiography immediately apparently
  - Within a year, attempts made to use x-rays to treat cancer
    - But initially had only very low energy x-rays, treatment limited to superficial lesions (skin, breast)

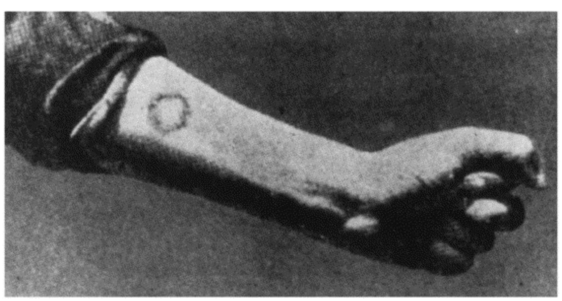

Wilhelm Conrad Roentgen (1845-1923). The first medical X-ray of the hand of Anna Roentgen, taken in 1895 by Wilhelm Conrad Roentgen (1845-1923).

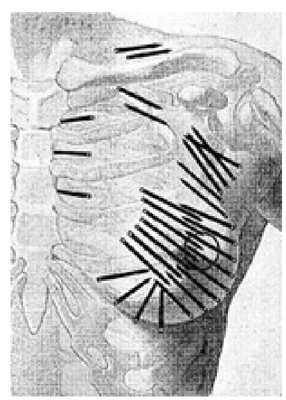


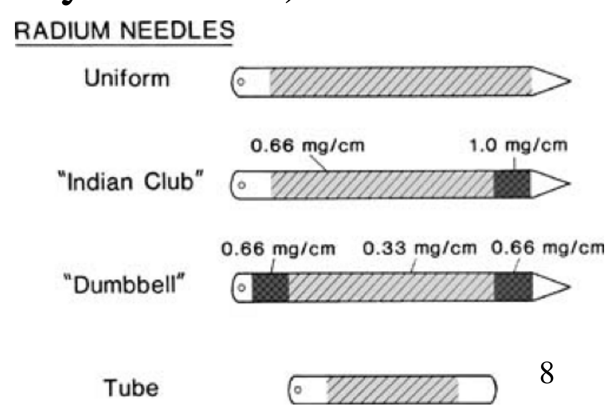
The Cathode Ray Tube site, www.crtsite.com, and the German Roentgen-Museum

Advent of Radium

- Becquerel discovered radioactivity
- Marie & Pierre Curie discovered Radium and isolated radioactive isotopes
  - 1901: Pierre Curie notes a burn from contact with Radium
  - Paved the way for Brachytherapy (short-distance therapy)
    - Placing radioactive sources on the skin, or inserting in body cavities or in needles placed in the tumor
    - Dose was prescribed in mg-Ra-hours (activity and time)





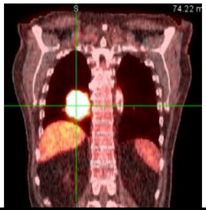


Advent of medical physics

- By 1910, x-ray imaging and Radium radiotherapy well established
  - Physicists heavily involved in technology development
    - Coolidge developed more reliable x-ray tubes; Sievert standardized radiation measurement
- But finally physicists became involved in the clinic also
  - Charles Phillips, honorary physicist to the Royal Cancer Hospital in Longond (1892-1927)
  - First formally appointed physicists around 1912-1913
  - Supported development of equipment, radiation protection and dosimetry, and new treatment techniques

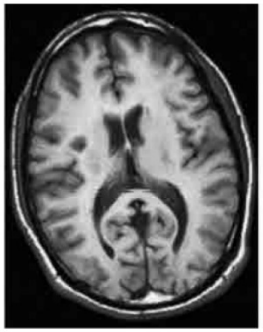
Development of medical imaging

- Late 1930s: Manhattan project lead to developments in nuclear physics technology & radioisotope production
  - Made into radiotracers for nuclear medicine imaging

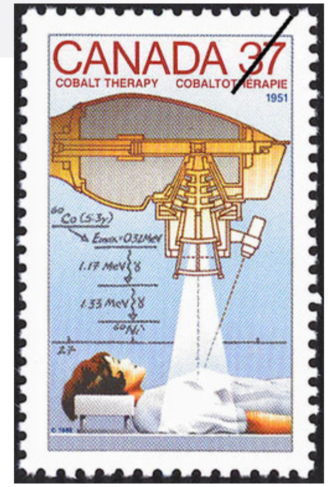


- Also late 1930s: ultrasound imaging introduced
- Rapid improvements in x-ray detectors, from single Geiger-Muller tube to arrays of detectors
  - Scintillators + PMTs → amorphous silicon + TFT arrays

- Late 1960s: development of Computed Tomography
- 1970s: Nuclear magnetic resonance imaging (MRI)
- Continue to improve resolution and contrast



Development of teletherapy



- Brachytherapy dominated for decades
  - Primary isotopes: ^{226}Ra, ^{137}Cs, ^{192}Ir
- Late 1940s: ^{60}Co used in teletherapy units (long-distance)
  - Gamma rays of 1.2 and 1.3 MeV; 5 year half-life
- 1950s: wartime efforts for radar turned into development of electron linacs for delivery of megavoltage x-rays
  - Achieve higher energies and dose rates than available with radioisotopes, with fewer radiation safety concerns
  - Linacs developed with energies ranging from 4 to 30 MV
- Proton accelerators proposed around this time (R. Wilson)

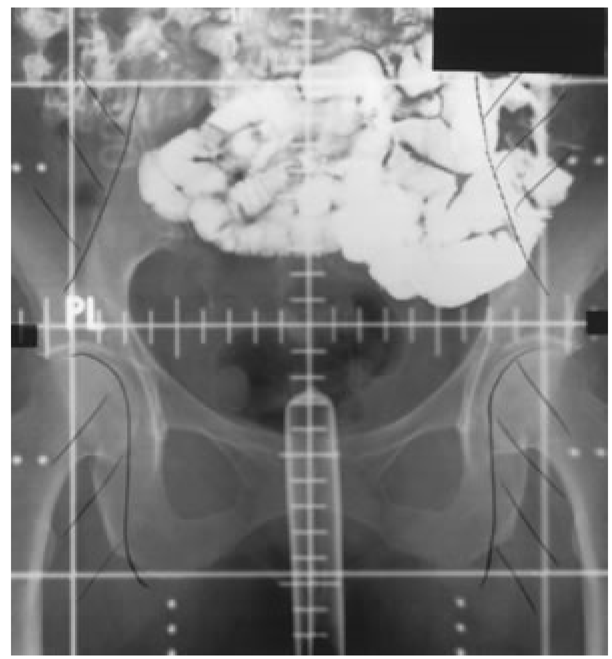
The modern linac

- Commercial products with vendor support
  - Primarily two vendors: Elekta & Varian
  - Different designs, same functionality

- Linacs provide photon or electron beams
  - Photon energies: 6, 10, and/or 15 MV
  - Electron energies: 6 MeV up to 20 MeV
- Orthogonally mounted imaging x-ray tube and detector
- Linac and treatment couch rotate around a single axis point called the isocenter
  - Radiation beam directed towards patient from many possible angles

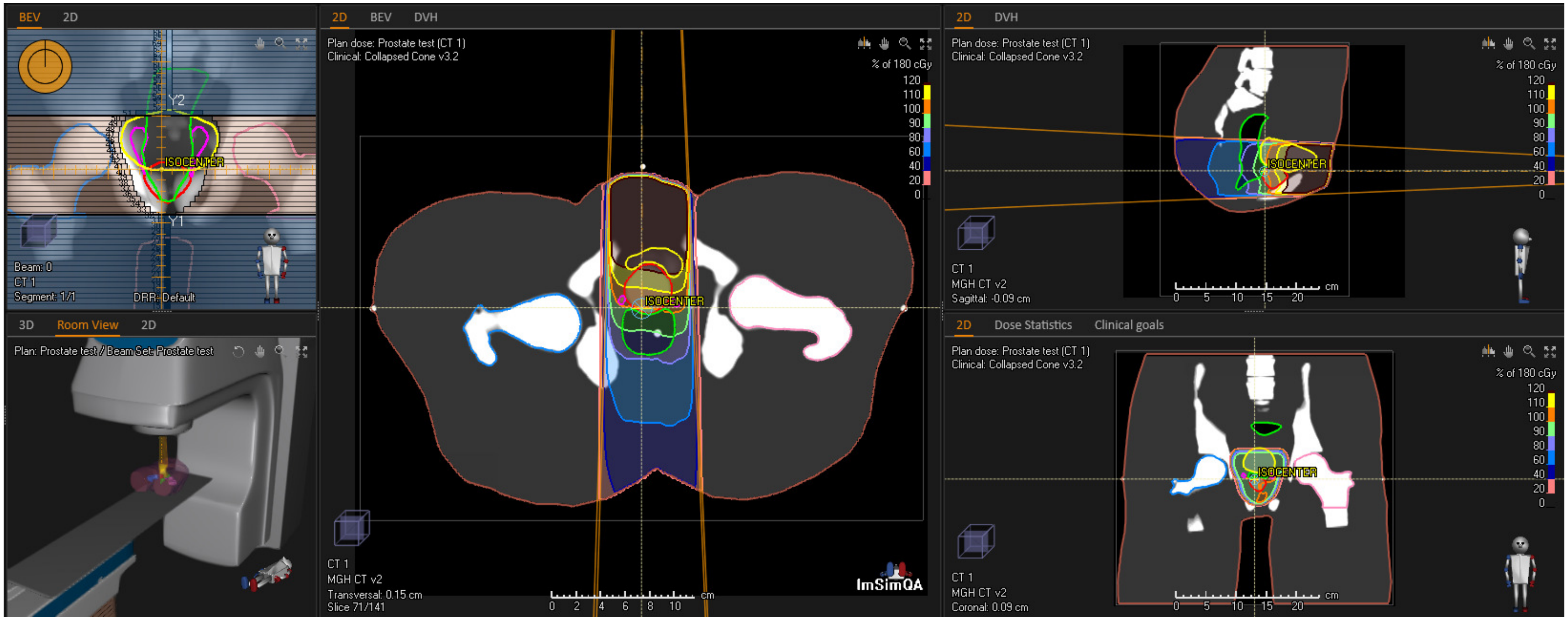
Evolution of treatment planning

- Physician outlines disease to be treated
  - Includes tumor and surrounding area that may be infiltrated by tumor cells, especially around lymphatic drainage
- With only 2D imaging, no soft tissue visualization
  - Treatment based on bony anatomy
  - No control of or visualization of dose delivered to tumor or nearby organs
- Computers and 3D imaging revolutionized treatment planning
  - Digital linacs, multi-leaf collimators



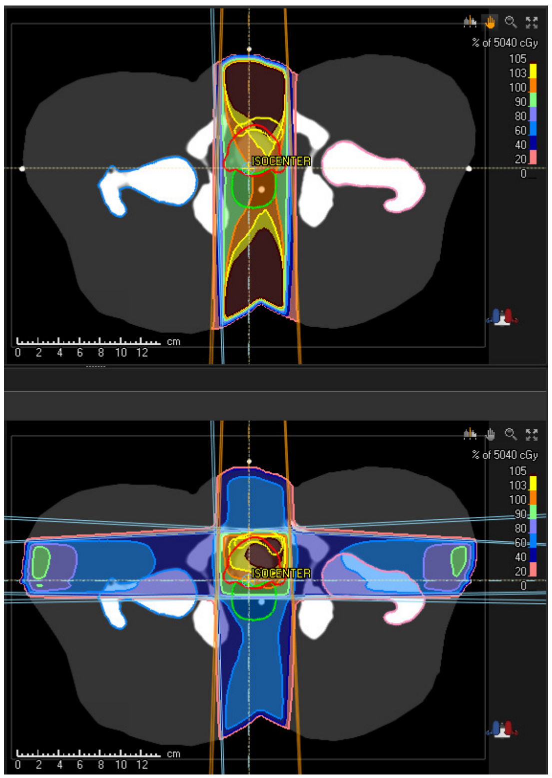
Evolution of treatment planning

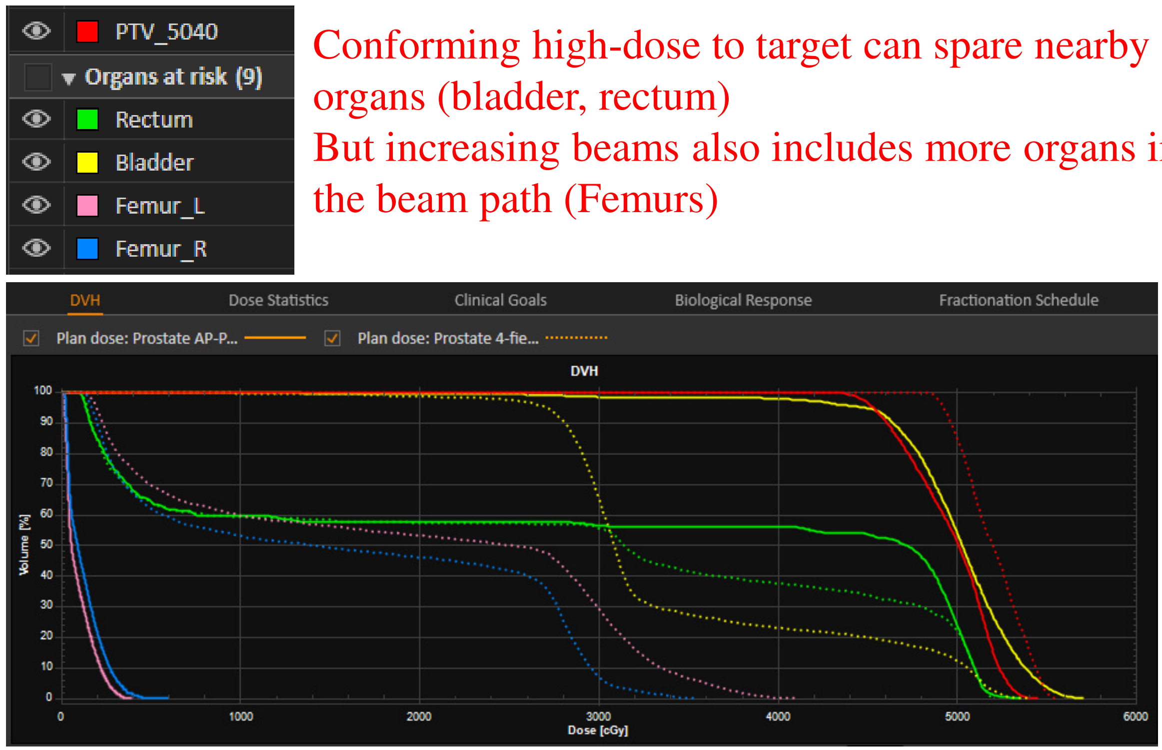
- Analytical models of photon beams and material interactions allow calculating and displaying dose in 3D
  - Monte Carlo modeling of interactions is gold standard, but calculations take too long for clinical use



Multiple beam angles

- Every beam deposits the most dose near the surface
  - Use multiple beam angles to reduce surface dose and make high-dose region conform to target



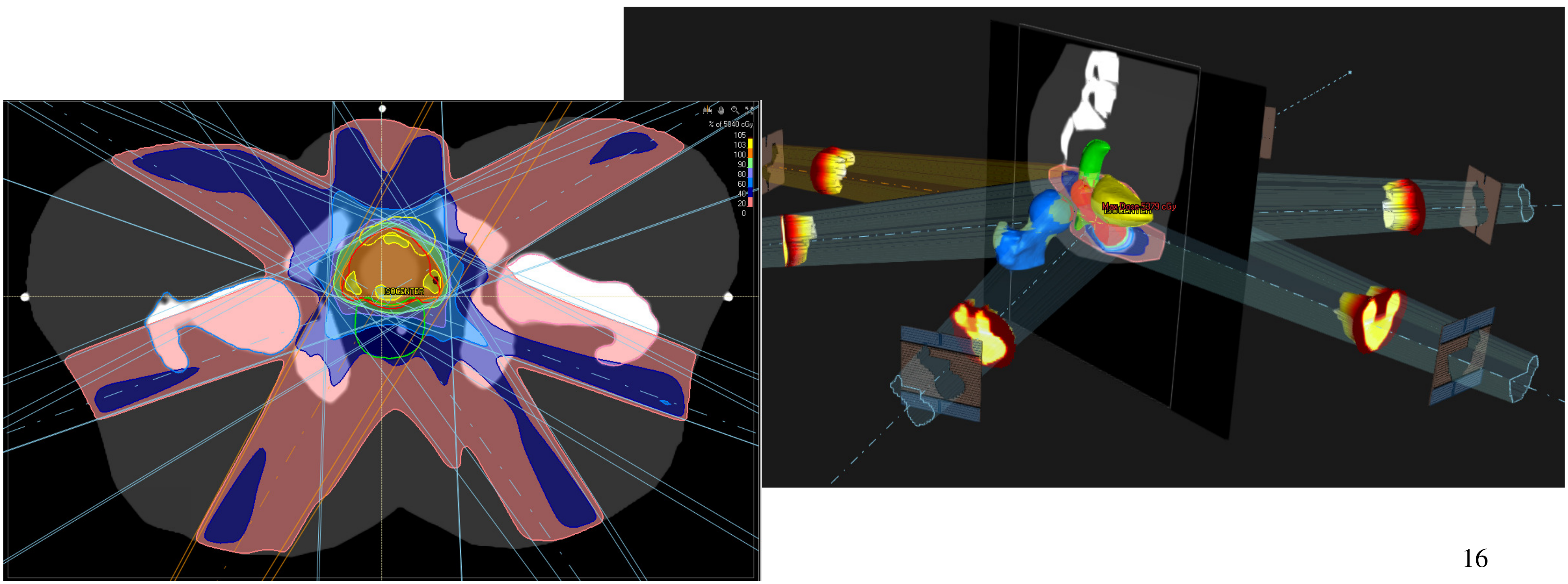


Conforming high-dose to target can spare nearby organs (bladder, rectum)

But increasing beams also includes more organs in the beam path (Femurs)

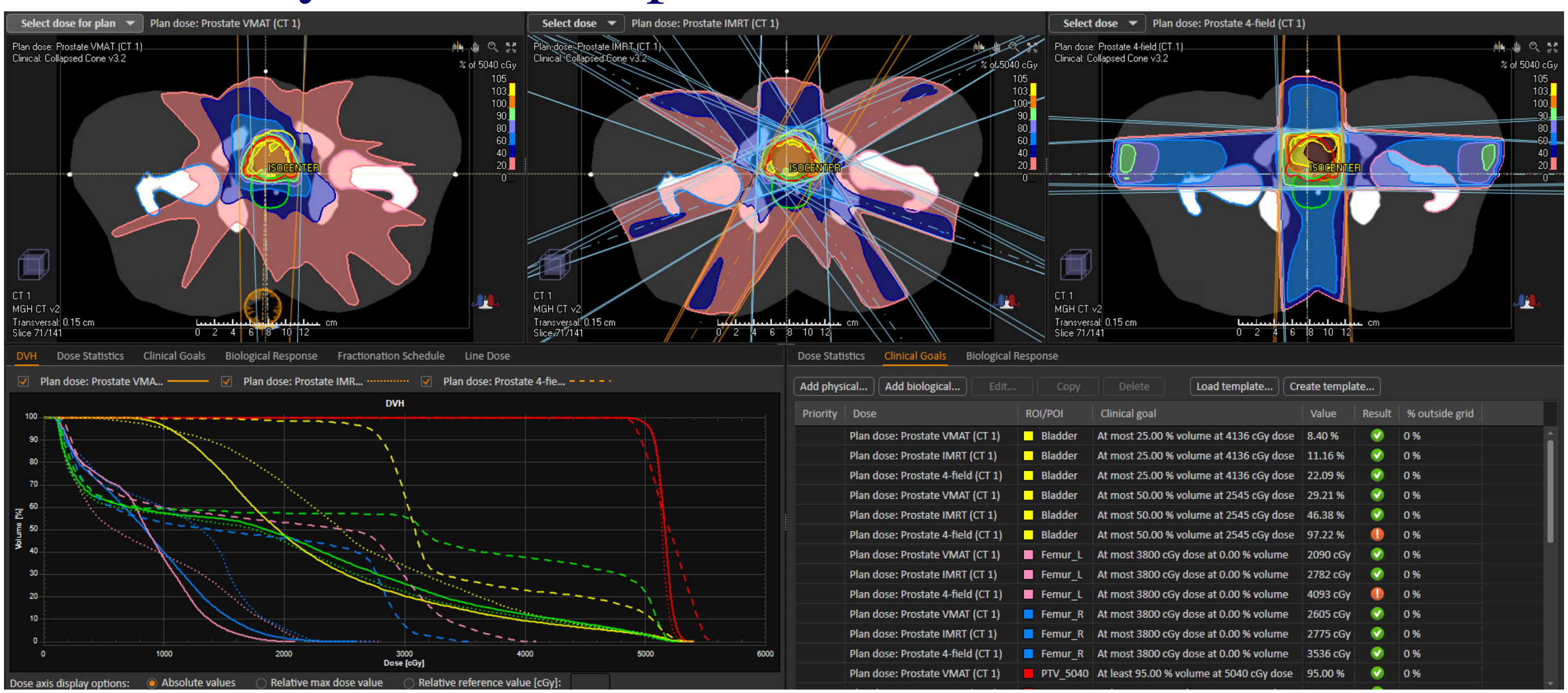
Intensity modulation (IMRT)

- Why deliver radiation with a static open field?
  - Multi-leaf collimators move across the field while the beam is being delivered to create modulated photon intensity
- Initially used static gantry angles:



Arc intensity modulation (VMAT)

- Current state-of-the-art: gantry rotates continuously
  - Modulate gantry speed, dose rate, and multi-leaf collimator positions simultaneously
- Extremely conformal plans with low surface dose



Pushing the limits

- What can we do right now?
  - Linac imaging technology allows us to set patients up for treatment within 1-2 mm of accuracy
  - Treatment planning technology allows us to deliver high dose with sharp dose falloff within 2-5 mm
  - Advanced techniques allow us to control for patient breathing motion, other internal or external motions
- So what’s left to improve radiation therapy?
  - We can already deliver treatment more accurately than physicians can define areas that need to be treated…

Technological developments

- Real-time imaging during treatment
  - X-ray imaging gives too much dose, MRI preferred
  - Technical challenges of MRI-linac being overcome:

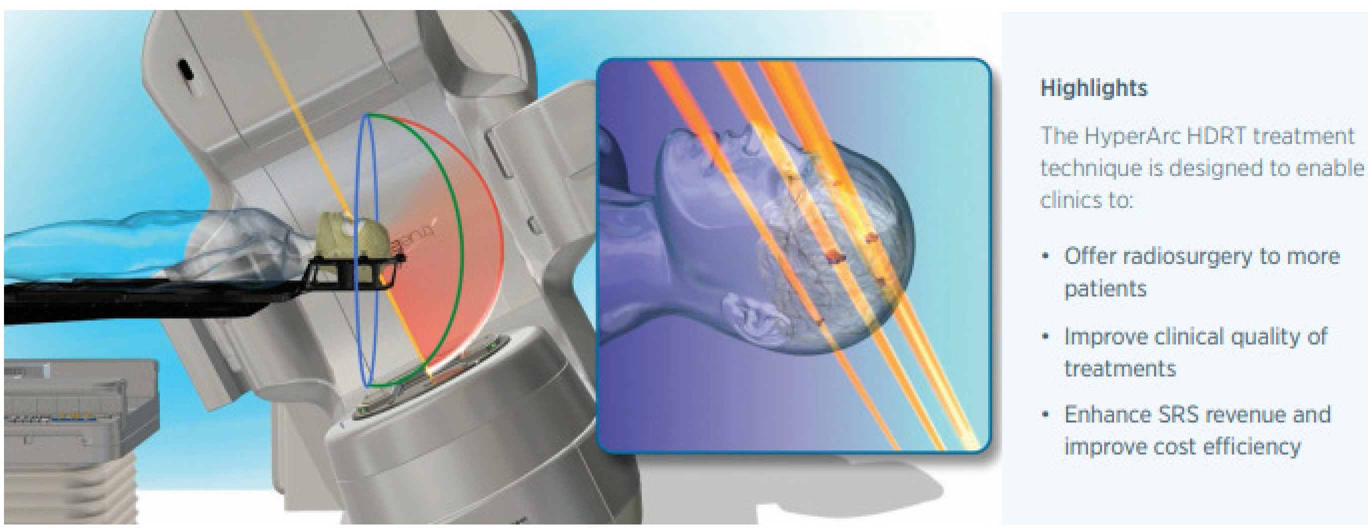
ViewRay MR-linac

Elekta MR-linac

Technological developments

- Real-time imaging during treatment
- Even more conformal treatments
  - Better avoid organs by simulating “4π” delivery
  - Allow simultaneous motions of: gantry, collimator, couch, modulating the velocity of each, along with MLCs

Varian HyperArc for cranial treatments



Technological developments

- Real-time imaging during treatment
- Even more conformal treatments
- Real-time adaptive planning
  - Organs move, closer to or farther from target
  - Optimize radiation delivery on the daily image

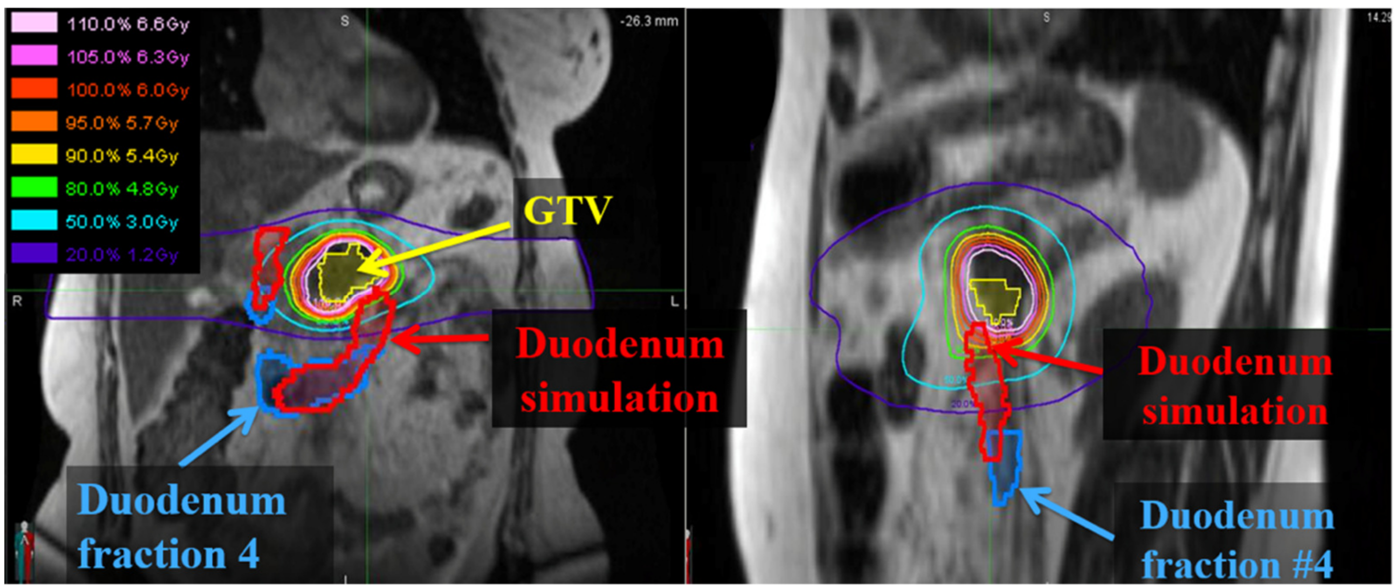
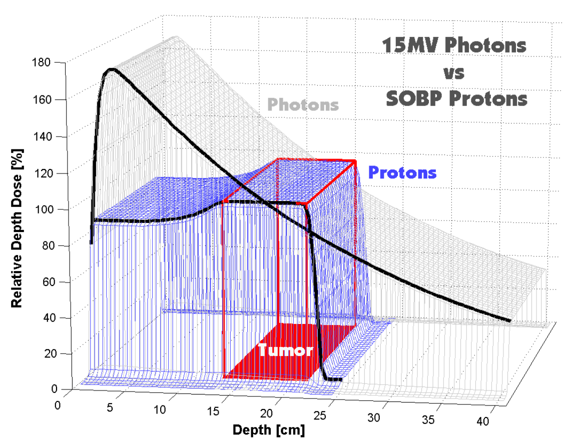
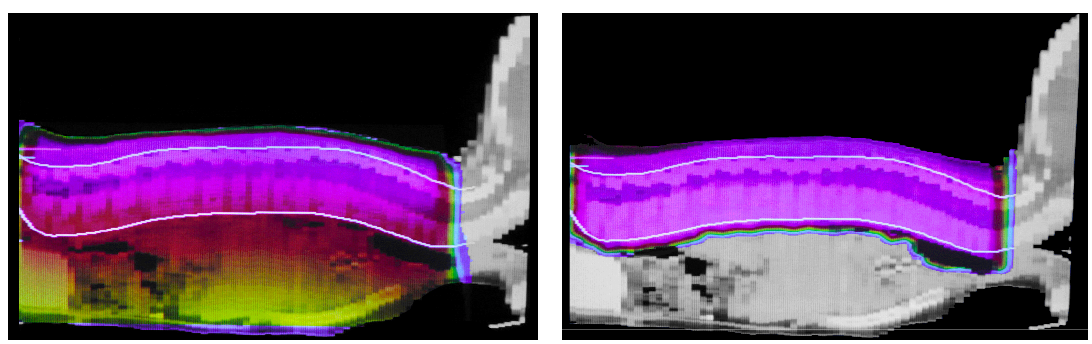


Image from University of Wisconsin Dept of Human Oncology, Medical Physics Research

Technological developments

- Real-time imaging during treatment
- Even more conformal treatments
- Real-time adaptive planning
- Heavy charged particle treatments: protons, carbon…
  - Advantages: Bragg peak – deposit most dose at end range
  - Barriers: cost; radiobiology not as well studied





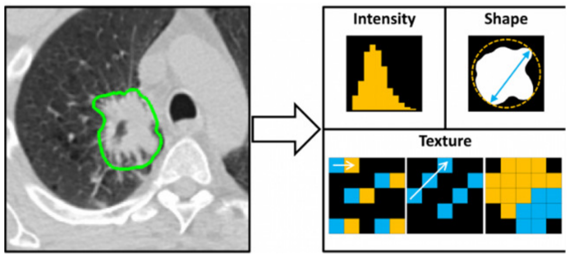
Photons vs Protons

Biological developments

- Optimize radiation delivery dose and timing
  - Total dose and dose per day based on historical practice
  - Many alternate options: fewer, larger doses? every other day? or twice per day instead of once per day?
- Model radiation response of tumors and normal organs
  - Can't optimize delivery without a realistic model
  - How much radiation causes damage? When is function lost? Will sparing one part of an organ preserve function?
- Immunotherapy: role for radiotherapy?
  - Kick-start the immune system? Shrink large solid tumors?

AI/machine learning developments

- Computer Aided Diagnosis (CAD), Pathology
  - Machine learning to identify disease in images
- Automation in contouring and treatment planning
  - Save time with automated contouring of normal organs
  - Also many treatment plans look similar, adapt for individual patient's anatomy
- Radiomics/"Quantitative Imaging"
  - Feature extraction from medical images
  - Correlate features with outcome



www.radiomics.world

- Most are task-based implementations… can we do more?

The Search for Big Data

- Define: extremely large datasets that can be analyzed computationally to reveal patterns, trends, & associations
- National Cancer Institute (NCI) estimates:
  - 1.7 million new cases of cancer in the US in 2018
  - In 2016, 15.5 million cancer survivors in the US
- Can we use computational techniques and data from treated patients to devise better treatments?
  - Well… there are complications
  - One is patient consent for research use (privacy/ethical considerations, knowledge of how data will be used)

What does the data look like?

- Cancer patient diagnosis, treatment, and outcome data is in a wide variety of formats
  - Imaging scans of different modality
  - Lab results, blood work, genetic testing
  - Textual report formats
  - Every hospital has different electronic formats and systems
- Many possibly relevant details not captured at all
  - Environmental and nutritional factors
  - Support systems, emotional resilience
  - Access to care and affordability of care

Database efforts – SEER

- NCI SEER database (Surveillance, Epidemiology, and End Results)
  - Collect and publish data from state cancer registries, covers ~28% of all US cancer incidences
  - Data is in aggregate (no personal identifiable details)
  - Frequently used for retrospective studies for lack of better data

Illinois Cancer Registry Data for Chicago Community Areas:

Readme file:

File layout for Chicago Community Areas CA0615.DAT
(Number of records 118,447)

Record Format (all fields are numeric)

Data Field	Positions	Length
Chicago Community Areas	1-2	2
Diagnosis year group	3-3	1
Cancer site group	4-5	2
Age at diagnosis group code	6-6	1
Sex code	7-7	1
Race group code	8-8	1
Stage of disease at diagnosis	9-9	1
Hispanic code	10-10	1
Geocode precision	11-11	1

Data file snippet:

```
562 6621211
 12 4422101
322 1522101
412 6112301
431 6222111
 81 6521301
121 1721101
161 3621201
 71 6313101
121 5711101
 21 6611201
 91 7521001
641 6711101
 61 6321101
641 6621101
```

Rad Onc community database efforts

- EuroCAT (www.eurocat.info): distributed learning
  - Rather than building a shared database, build a model and ship it to institutions to run over their data, compile results
  - Patient data not shared, can use imaging and radiation data
- Johns Hopkins Oncospace: informatics program
  - Database design promotes structured data collection for radiation treatment and outcomes reporting
  - Primary goal: establish database for efficient access to clinical data to evaluate toxicity and outcome trends
  - Data is anonymized but still shared, so single-institution

Roadblocks to using big data

- Databases to hold relevant info
  - Difficult to capture and query such diverse data
  - Increasing workload on patients or physicians decreases participation
- Privacy/data sharing concerns
  - Prevents institutions from combining their data
- Lack of expertise in modeling among medical physicists
  - Divide between research and clinical physicists
  - Clinical physicists understand the data but don’t have the time or expertise to design the best model

In summary…

- Thanks to physicists, huge technological advances in imaging and radiation treatment in the past century
- Next advances likely to be focused on biology
  - Role of genetics; how disease spreads through the body
  - How to best kill tumor cells (dose and fractionation) and spare normal organs
  - Individual-specific responses to drugs or radiation
- But physics techniques crucial to biological advances
  - AI/machine learning, modeling, knowledge-based
  - Bringing data together in a machine-readable format