Applied physics in the clinic: monitoring radiation doses delivered to cancer patients

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Medical physics

• *Medical physics* is easy to define
  – Application of physics to medicine
• There is a long tradition of using applied physics to improve medicine (both treatments and diagnostics)

From the early radiographs to the modern medical linear accelerator
Medical physics

- However, the clinic is much different from the lab
- Despite numerous opportunities, crossing the *clinical barrier* can be challenging
  – Even for those with a biophysics/biomedical backgrounds
- Nevertheless, several hospitals hire physicists
  – Clinical medical physics is a profession

“The Practice of Medical Physics means the use of principles and accepted protocols of physics to assure the correct quality, quantity, and placement of radiation during the performance of a radiological procedure.”

- American Association of Physicists in Medicine
Medical physics

• Medical physicists background:
  – BSc in physics or engineering physics
  – MS and/or PhD in medical physics
  – Residency
  – Certification (Canadian College of Medical Physicists)

• Most medical physicists have some time for research
  – They can act as:
    • Principal investigators
    • Collaborators
    • Evaluators of new technologies
    • Facilitators for clinical trials
Medical physics

• Where to find clinical medical physicists?
  – Radiation oncology
  – Diagnostic imaging
  – Nuclear medicine
  – Health/radiation protection
Medical physics

• Where to find clinical medical physicists?
  – Radiation oncology (~75%)
  – Diagnostic imaging
  – Nuclear medicine
  – Health/radiation protection
• What do a medical physicist do?
  – Radiation beam calibration and characterization
  – Image quality assessment
  – Consultation and treatment planning with practitioners to determine dose to be delivered
  – Validate the radiation delivery plans of (nearly) every patient
    Acceptance testing and commissioning
  – Radiation shielding design
  – ... and much more

In radiation oncology, the medical physicist’s job is to make sure that the patient receive precisely the intended dose of radiation.
Kill (stop) cancer cells with ionizing radiation

- Most common forms of radiation used:

<table>
<thead>
<tr>
<th>Particle</th>
<th>Energy range</th>
<th>Production</th>
</tr>
</thead>
<tbody>
<tr>
<td>Photons</td>
<td>200 keV – 20 MeV</td>
<td>Linear accelerator (bremsstrhalung)</td>
</tr>
<tr>
<td>Electrons</td>
<td>6 MeV – 20 MeV</td>
<td>Linear accelerator</td>
</tr>
<tr>
<td>Proton</td>
<td>70 MeV – 250 MeV</td>
<td>Cyclotron / Synchrotron</td>
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</tbody>
</table>

- Rarer: Carbon ions, neutrons, pions

Close to 60% of cancer patients will receive some radiation treatments
Context: radiation oncology (RO)

• Main mechanism:

  Physics ➔ Chemistry ➔ Biology

  Ionization ➔ Creation of free radicals H + OH ➔ Damage to DNA
  Simple/double breaks

• Net effect:
  – Prevent cells from dividing

• Treatment objective:
  – Deliver a high dose to a tumor target while minimizing dose to healthy tissues
Advances in radiation oncology

• The basic principles of RO are the same since the 1900s
  – Point a tumor target and ‘shoot’
Advances in radiation oncology

• Most recent advances aim to:
  – Better see the tumor target
  – Better focus radiation doses on small targets
  – Improve sparing of surrounding tissues to reduce side effects

See the presentation by John Schreiner at 13h30 (Botterel B143) for an excellent overview of modern radiation oncology
Ecosystem

• Centered around the medial linac
  – Used in most treatment delivery
  – Also used:
    • Radioactive sources (brachytherapy)
    • Cyclotron / Synchrotron (protons)

• Surrounded by imaging
  – Diagnostic, target definition, treatment assessment
Applied physics research in RO

• Different spectra of research
  – From colossal endeavor to tiny tweak to the clinical workflow
  – From purely academic research to assessment of new products

• Often a collaboration between all the actors:
  – Academia
  – Industry
  – Clinical medical physicists
  – Physicians
  – Clinical professionals (e.g. therapists, dosimetrists, nurses)
Applied physics research in RO

- Combining a linac with a MRI
- Clinically viable ion beam accelerator
  ...

- Multi-institution, big data initiatives
- Developing new dose detectors
- Better imaging modalities
- Better treatment planning system
  ...

- Efficient quality assurance
- Clinical trials to quantify treatment efficiency
  ...

- Better interoperability between clinical tools
Current challenges in RO

• Treatments are increasingly complex
  – More taxing for the delivery equipment
  – Less intuitive -> harder to QA

• How can we integrate online imaging capabilities
  – Balancing potential benefits with increased costs and time
    • A daily radiation treatment = 15 minutes
  – Target segmentation
  – How to account for daily morphological variations
Illustration through an example

• **Goal**: Illustrate how physics research can help answer clinical needs

• One central theme

  How can we guarantee that the patient receives the exact dose prescribed by a physician

• Three strategies:
  – Development of a new instrument
  – Image processing and data analysis workflow for patient monitoring
  – Retrospective analysis of treatment plan to guide future treatments
Development of a new instrument

A multipoint scintillation detector
Plastic scintillation detectors (PSD)

• Plastic scintillators have interesting properties for RO
  – Attenuation properties nearly identical to tissues in the MeV
    • Dose in scintillator = dose in tissues
  – *Good* response
    • Independent to photon/electron energies above ~100 keV
    • Independent of dose rate
  – Online capability
    • Scintillation emitted in a few ns
  – Potential for high spatial resolution
    • < 1 mm is ideal for RO
Overview of a medical PSD

• Simple design: scintillator + optical fiber + photodetector
  – Reflective coating, coupling agent ...

• Integrate the signal over a given irradiation
  – Photon counting nearly impossible due to high dose rate
  – Scintillation light is proportional to dose
  – Cherenkov is an important source of noise
PSD: industry-academia collaboration

• Brief history:
  – 1990s: proof of principle
  – 2000s: demonstration of clinical potential (patent)
  – 2010s: licensing and commercial development

• A commercial prototype was released in 2012
  – Exradin W1 from Standard Imaging
  – A simple but robust device
    • ~ 2 mm$^3$ sensitive volume
    • Readout with photodiodes
Moving forward: multi-points

• Single point PSD is good, but a detector array would be better
  – e.g. monitor dose to the target **and** to organs at risk

• Arrays can be difficult to use clinically
  – Especially for in vivo applications
Multi-points PSD

• To build efficient arrays, we can’t simply stack more detectors together

• Alternative:
  – Multiple scintillating element along a single optical fiber
  – If we can decouple scintillation and Cherenkov, we can decouple multiple scintillation signal
    • Thus, spatial information can be encoded in the emission spectrum of the scintillating elements
Multi-points PSD

• The fun thing with applied science: scavenging ideas from other fields
• Hyperspectral imaging has tackled a far more complex problem:

Kesheva 2003
Hyperspectral PSD

• Concepts to adapt to PSD
  – Spectral unmixing
    • Determine the fractional amount of source composing the signal
  – Dimensional reduction
    • Determine the best wavebands to use for an optimal unmixing

Bringing hyperspectral PSD to the clinic

- What remain to be done to bring this new instrument in the clinic?
  - Optimize the design to improve precision
    - Uncertainty < 2% ideal for a clinical dosimeter
  - Demonstrate clinical benefits
  - Commercialize
    - Partnership with the industry or with a new ‘startup’
Patient classification during radiotherapy
During radiation therapy (RT)

• RT is a long process (up to 6-8 weeks of treatments)
  – Treatment fractionation let us exploit biological differences between cancer and healthy cells

• Morphological changes are frequent during RT
  – However, patients often have a single treatment plan
    • Based on the anatomy at the beginning of RT
    • For the rest of treatment:
Morphological changes
Morphological changes
Adaptive RT

• Adaptive RT: treating the anatomy of the day
  – Desirable, but resource intensive
  – Clinically impossible to implement in most cases

• Shortcuts must be developed
  – Algorithms must do some of the work
    • Add an additional layer of complexity to RT

• However, not all patient changes
  – Can we spot those most at risk?
Automated patient monitoring

- Our goal: deploy an automated *patient safety net*
  - Using exit (i.e. portal) dose (EPID)
  - EPID contains information on the dose delivered *and* the anatomy

- Our strategy
  - Track relative changes
  - Classify treatment fractions through machine learning
  - Flag patients for more careful evaluation by a clinical physicist
Tracking patients

- Daily EPID
- Automated image collection
- Comparison to a reference
  - Validate reference with CBCT

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<th>Fraction 3</th>
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PhD student: O. Piron
**Tracking patients**

- Daily EPID
- Automated image collection
- Comparison to a reference
  - Validate reference with CBCT
  - Relative gamma analysis
- Track image features over time

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Only 3 out of 5 gantry angle shown for clarity

PhD student: O. Piron
Patient time series

- Each patient is a time series
Time series

- Time series are omnipresent in many fields

- Stock market analysis
- Speech recognition

- Environment
- Climate science
- Gene expression
- ...

- Again, we can get inspiration from others:
  - In this case, we used hidden Markov models
Hidden Markov models (HMM)

• Unsupervised machine learning approach
• Assume a system is composed of $N$ hidden states
  – Each state is a Markov process
  – $N$ given as an input
• Useful for time series
  – Markov process: step $k+1$ transition determined by step $k$
  – Used to classify each fraction
Hidden Markov models (HMM)

- $S_1$: stable patient, remain close to the reference
- $S_2$: light drift, patient is slowly deviating from reference
- $S_3$: strong drift, large fluctuations from reference
- $S_4$: offset, patient is systematically different from reference
Tracking patients

- EPID is a rich (and mostly free) source of information
- Machine learning models can be trained to:
  - Classify patient states
  - Flag patients likely to deviate from their plan
- Thus automated and unbiased tracking of patient appears feasible
- A prospective trial is underway to validate this workflow
A stochastic frontier analysis to improve treatment planning
Treatment planning

Once a physician decide to treat a patient:

- CT imaging for treatment planning
- Tumor and organs at risk segmentation (contours)
  - Manually by the physician and dosimetrists
- Selection of a treatment modality
  - Photon or electron, static or dynamic ...
- Dose optimization
  - Try to find the best possible dose distribution
- Final dose calculation

This whole process typically takes 1 to 2 weeks
Finding the best dose distribution

• **Hypothesis**: the best achievable dose distribution is defined by the patient morphology

• If true:
  – Dose/geometry relationship of past patients can predict dose distribution of future patient
Stochastic frontier analysis (SFA)

• This time, we get our inspiration from economy:
  – The stochastic frontier analysis is used to model the productivity of enterprises
• In SFA, the output of an enterprise is a combination of
  – Technical efficiency
  – Random ‘shocks’
• Can be used to model outputs or costs
Stochastic frontier analysis (SFA)

Each point represents an enterprise

\( \varepsilon \to \text{degradation} \)

\( \varepsilon \)

Frontier

Technical efficiency

Random variations

\( \varepsilon_i = \nu_i + \mu_i \)
Stochastic frontier analysis (SFA)

- The SFA concept can be adapted to treatment planning
  - Cost frontier = protection of organs at risk
  - Production frontier = optimization of target dose
Geometric parameters

- We extract parameters from the contours
  - Overlap, Hausdorff distance, gradient of overlap ...

- These serves as ‘inputs’
Computing the frontier

- The degradation, technical efficiency and random variations are optimized by likelihood maximization

Rectum dose in prostate treatment

PhD student: A. Kroshko
Computing the frontier

• It thus possible to find the frontier
  – Then use this frontier to guide future plans

Rectum dose in prostate treatment

PhD student: A. Kroshko
How to use the frontier

• Using SFA, it is possible to harness information from past plans to improve current treatment quality
  – Help make sure patients receive the best possible dose distribution
  – Planning guidance saves valuable time in the clinic

• Falls in the family of ‘knowledge-based planning’
  – However our approach is not dependent on initial plan selection
Conclusion
Conclusion

• Technology in RO is rapidly evolving (and complexifying)
  – Several opportunity for research

• I hope these 3 brief examples showed the diversity of applied physics in the clinic
  – Hardware, imaging, software
  – Feel free to adapt great ideas from other fields

• Clinical medical physicists can help you
  – Explain the needs for new tools and methods
  – They are often eager to contribute to research