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

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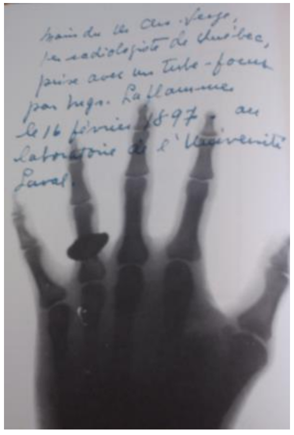
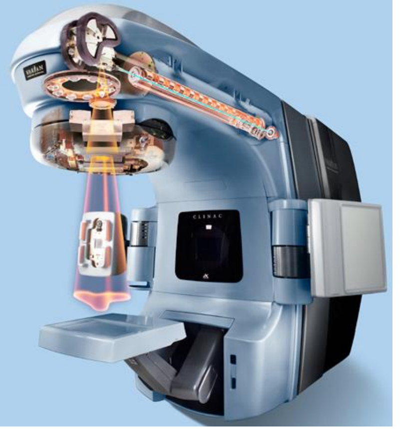
Medical physics

- *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

Medical physics

- 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

Context: radiation oncology (RO)

- Kill (stop) cancer cells with ionizing radiation
  - Most common forms of radiation used:

Particle	Energy range	Production
Photons	200 keV – 20 MeV	Linear accelerator (bremsstrhalung)
Electrons	6 MeV – 20 MeV	Linear accelerator
Proton	70 MeV – 250 MeV	Cyclotron / Synchrotron

  - 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

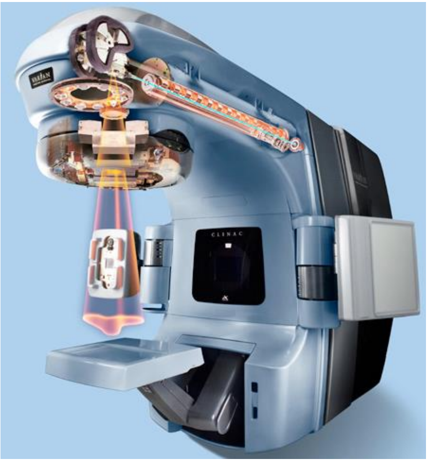
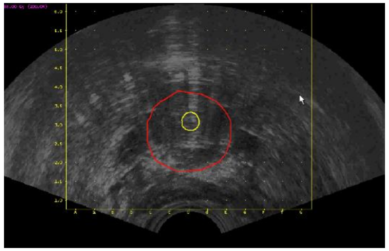
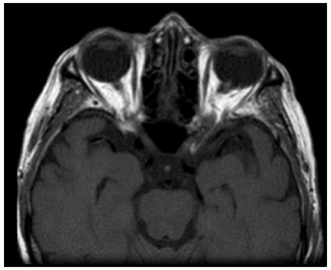


Image from Varian Medical System





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

Large scope

Easier at the academic level

- 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

Focused projects

Easier at the clinical level

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

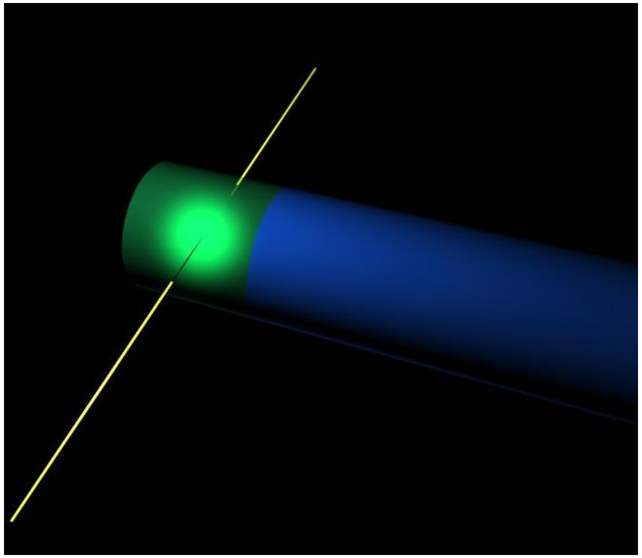
- Three strategies:
  - Development of a new instrument
  - Image processing and data analysis workflow for patient monitoring
  - Retrospective analysis of treatment plan to guide future treatments

Development of a new instrument

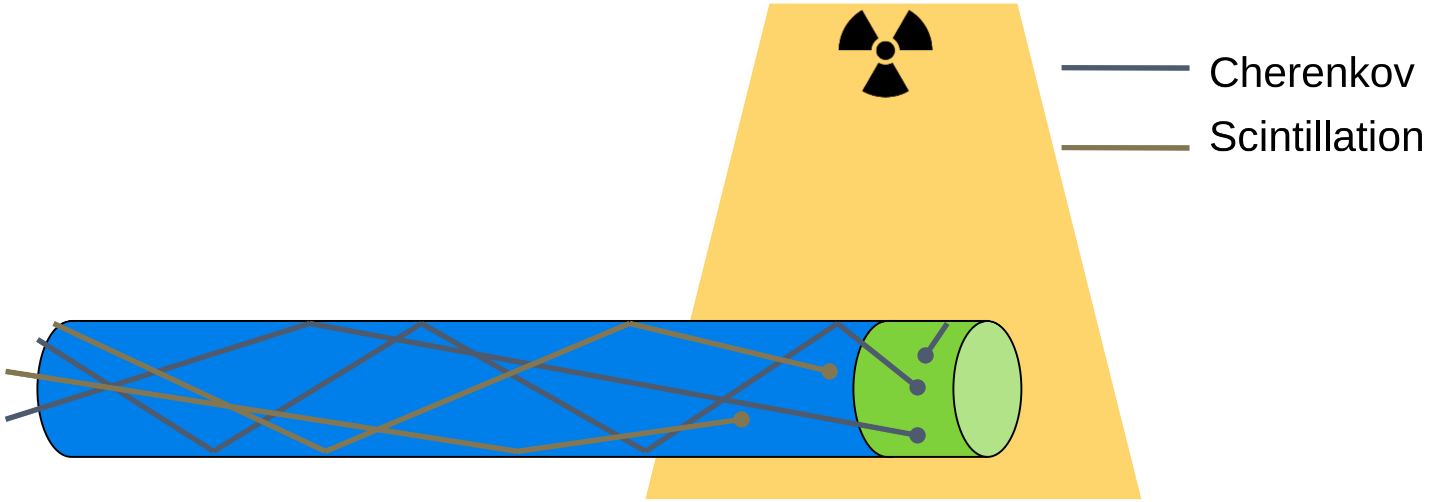
A multipoint scintillation detector

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



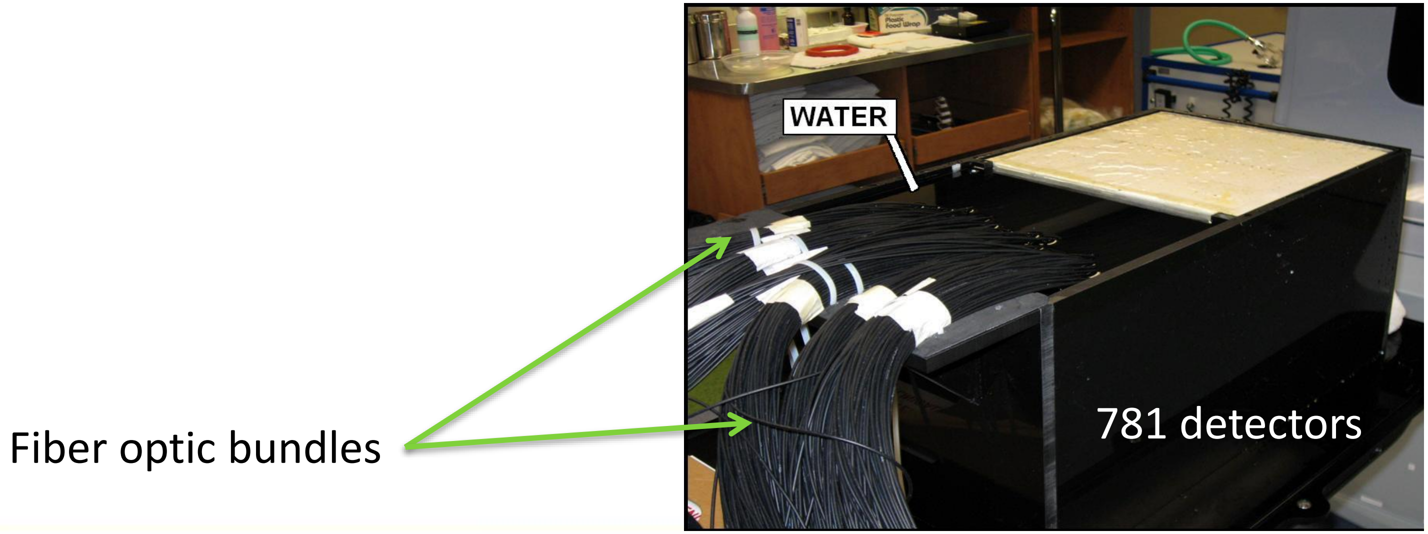
- Simple design: scintillator + optical fiber + photodetector
  - Reflective coating, coupling agent …
- Integrate the signal over a given irradiation
  - Photon counting nearly impossible due to high dose rate
  - Scintillation light is proportional to dose
  - Cherenkov is an important source of noise

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

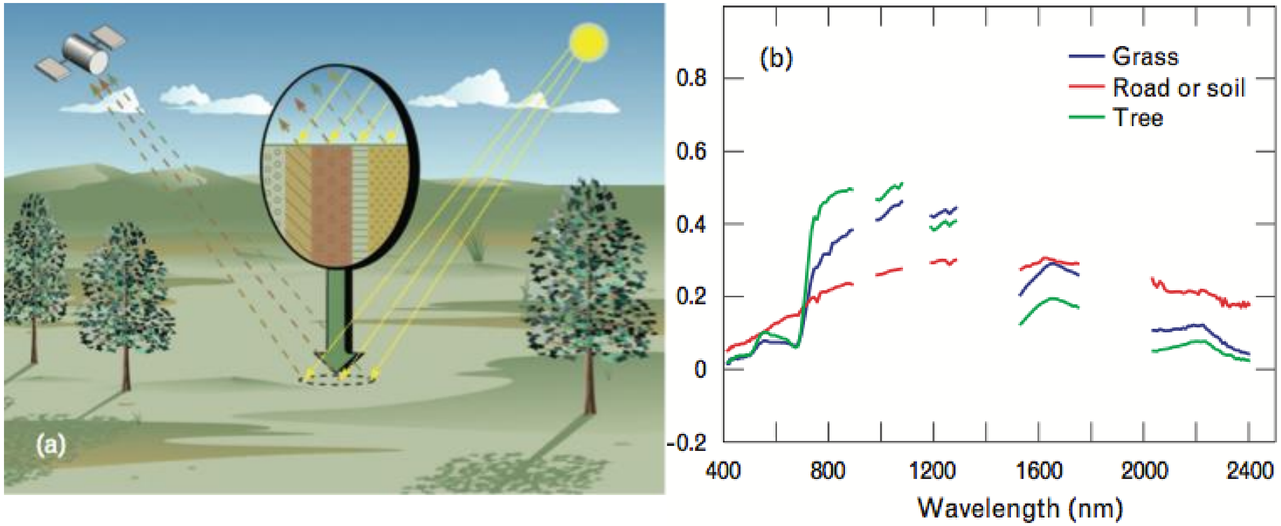


Multi-points PSD

- 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

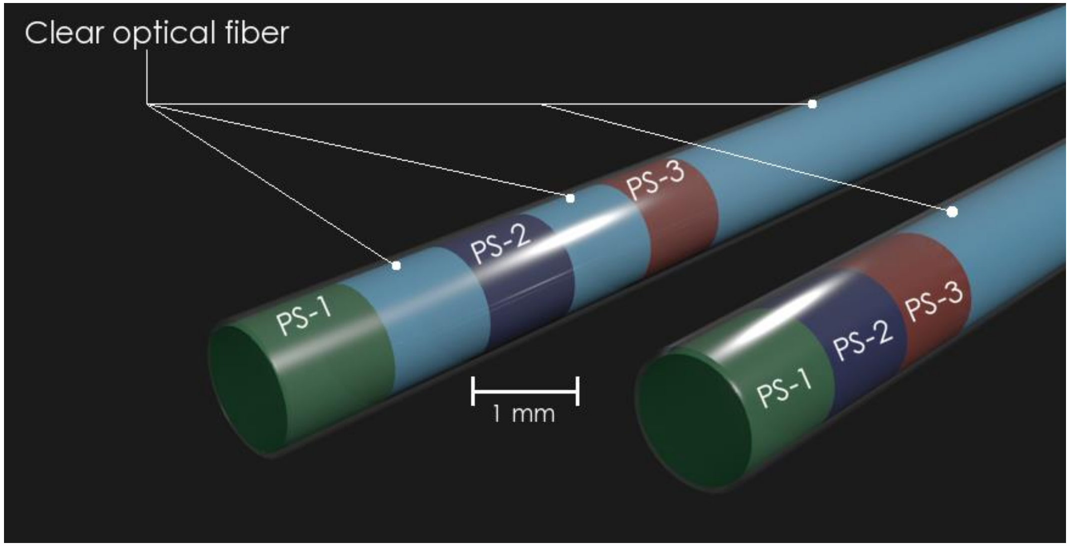
- The fun thing with applied science: scavenging ideas from other fields
- Hyperspectral imaging has tackled a far more complex problem:



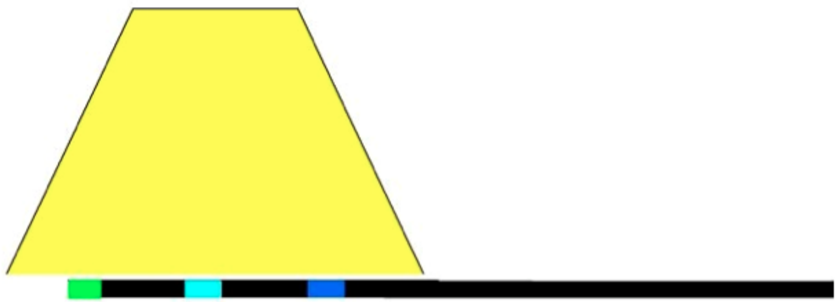
Kesheva 2003

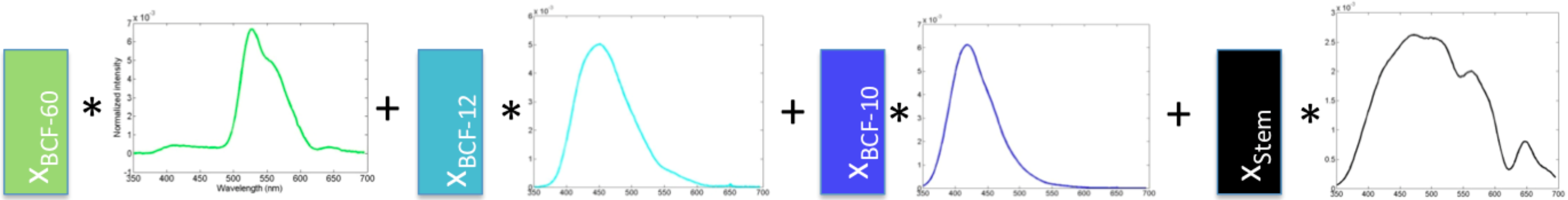
Hyperspectral PSD

- 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

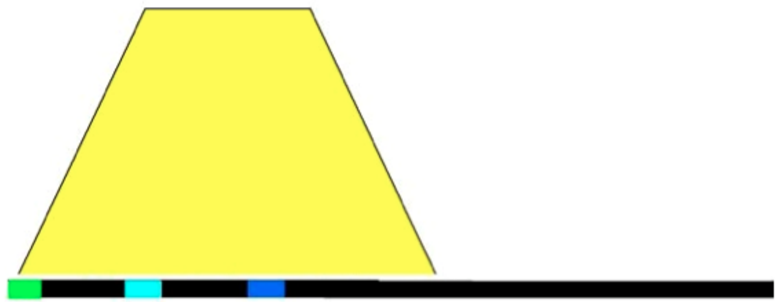


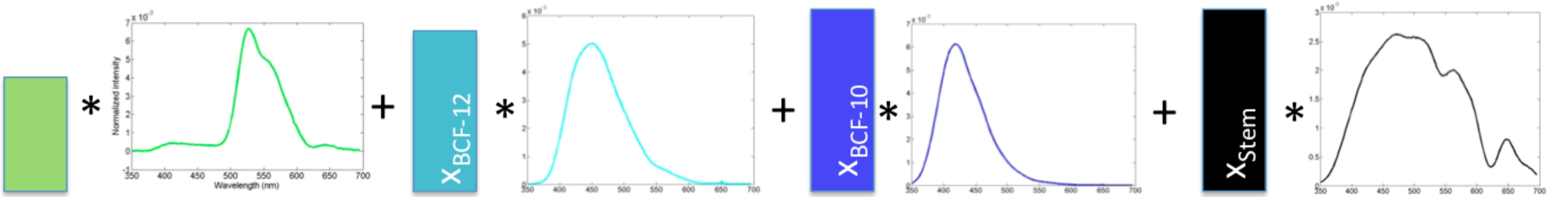
Archambault et al. Phys. Med. Biol. 2012





F. Therriault-Proulx





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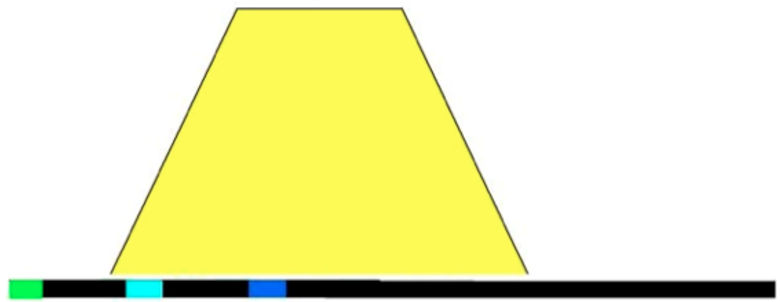

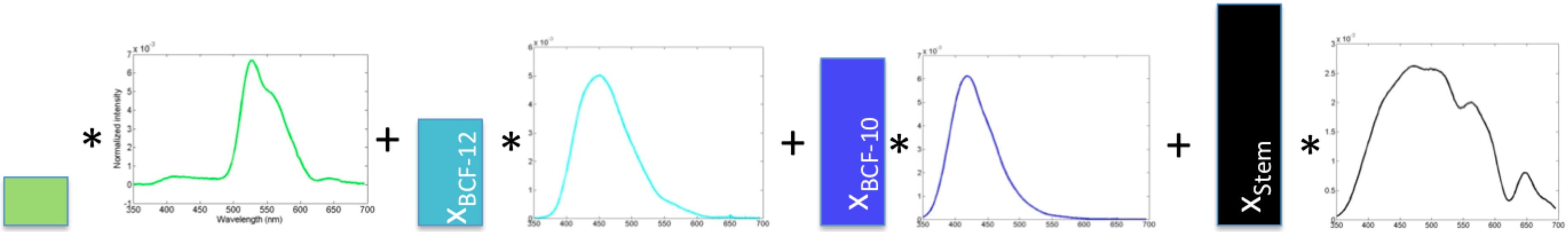

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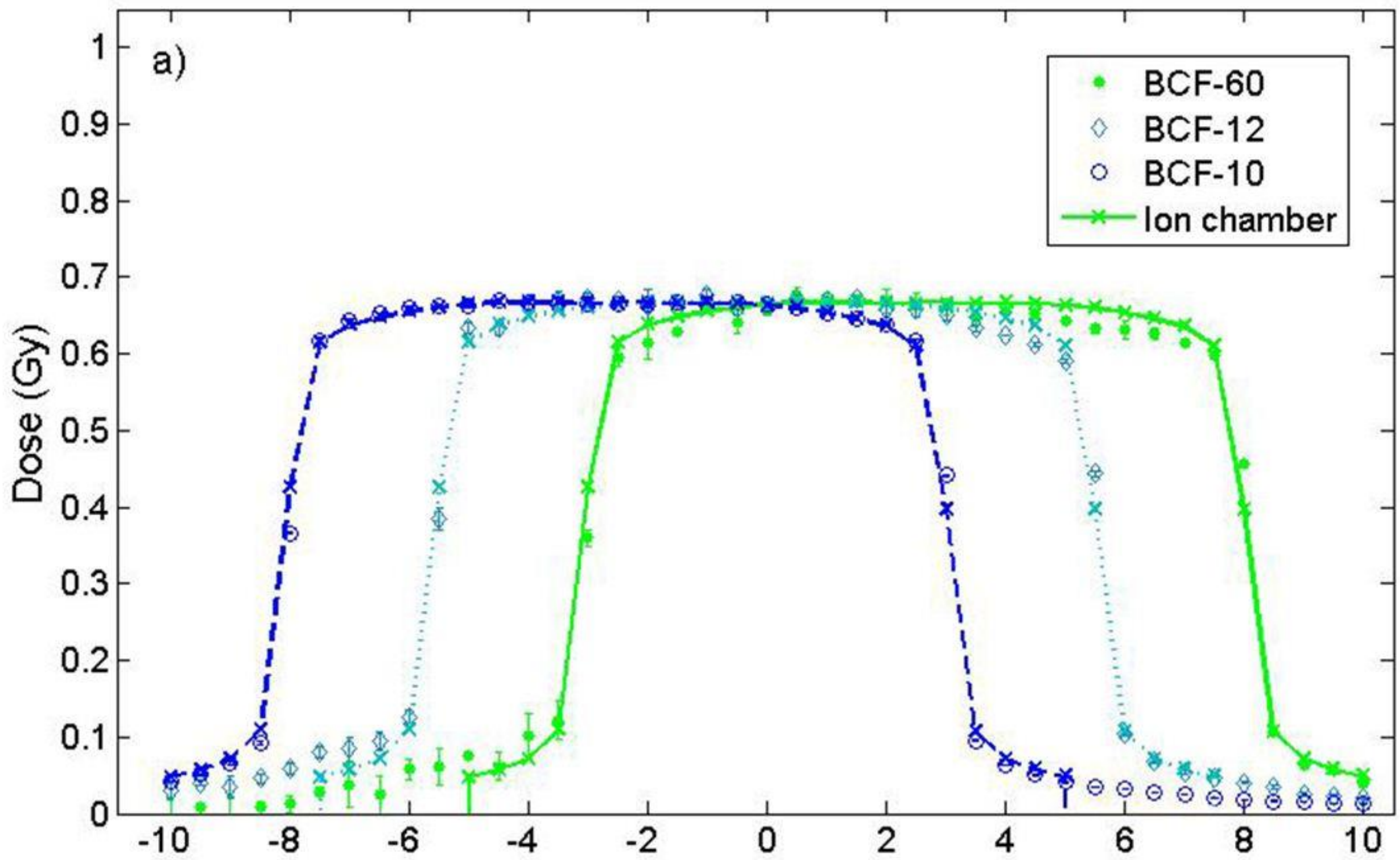


F. Therriault-Proulx

Bringing hyperspectral PSD to the clinic

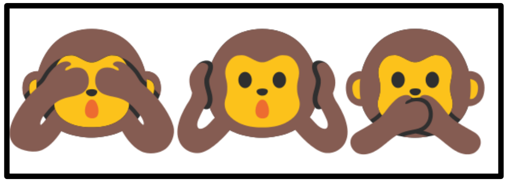
- What remain to be done to bring this new instrument in the clinic?
  - Optimize the design to improve precision
    - Uncertainty < 2% ideal for a clinical dosimeter
  - Demonstrate clinical benefits
  - Commercialize
    - Partnership with the industry or with a new ‘startup’

Image processing and data analysis workflow for patient monitoring

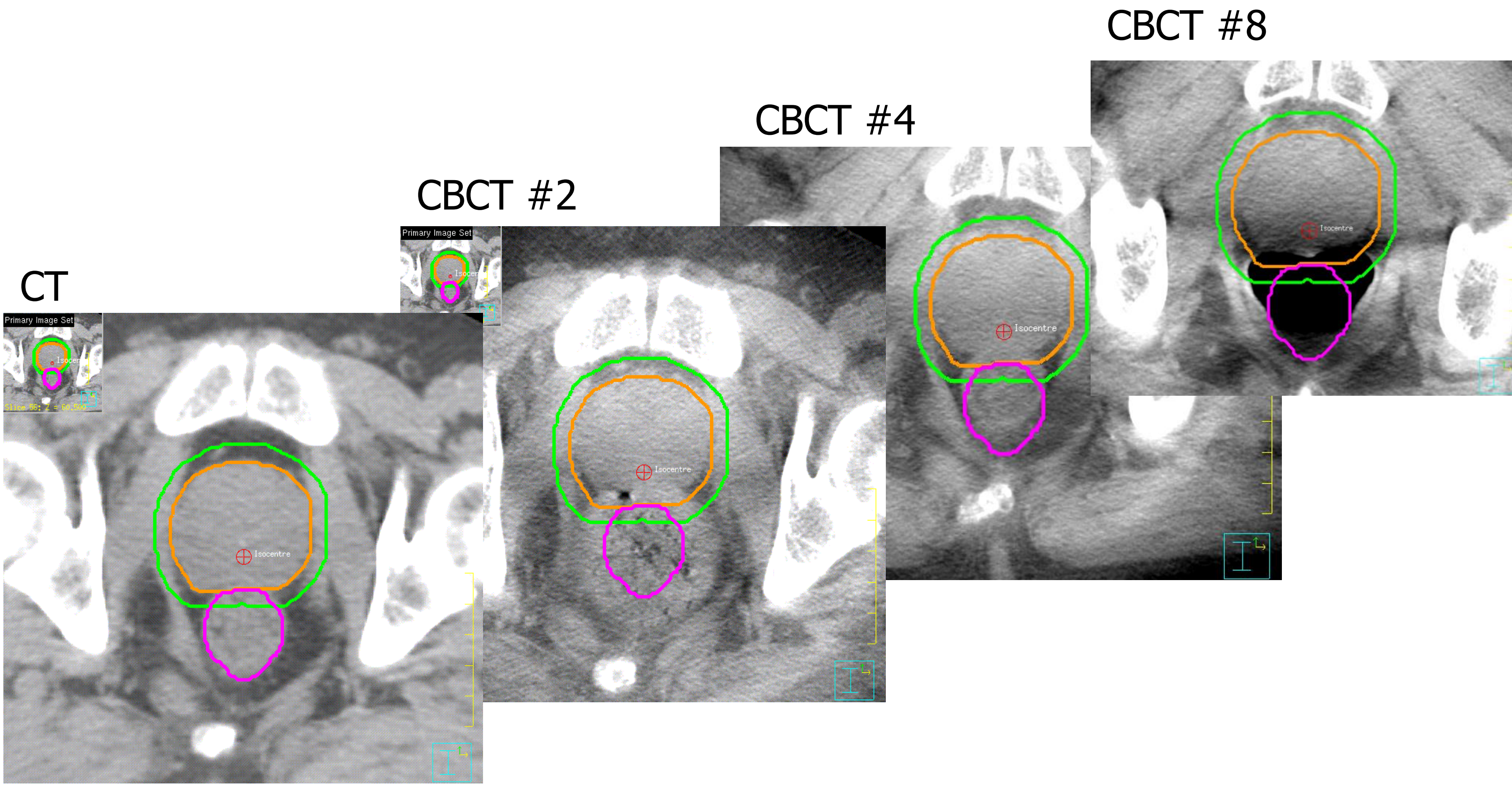
Patient classification during radiotherapy

During radiation therapy (RT)

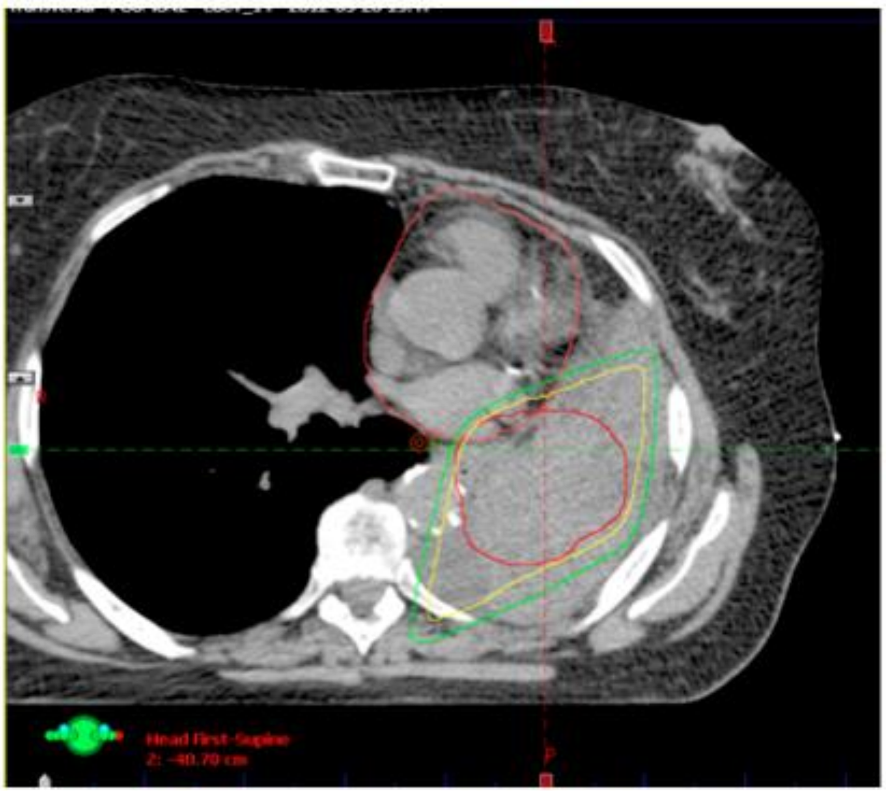
- RT is a long process (up to 6-8 weeks of treatments)
  - Treatment fractionation let us exploit biological differences between cancer and healthy cells
- Morphological changes are frequent during RT
  - However, patients often have a single treatment plan
    - Based on the anatomy at the beginning of RT
    - For the rest of treatment:



Morphological changes



Morphological changes



Adaptive RT

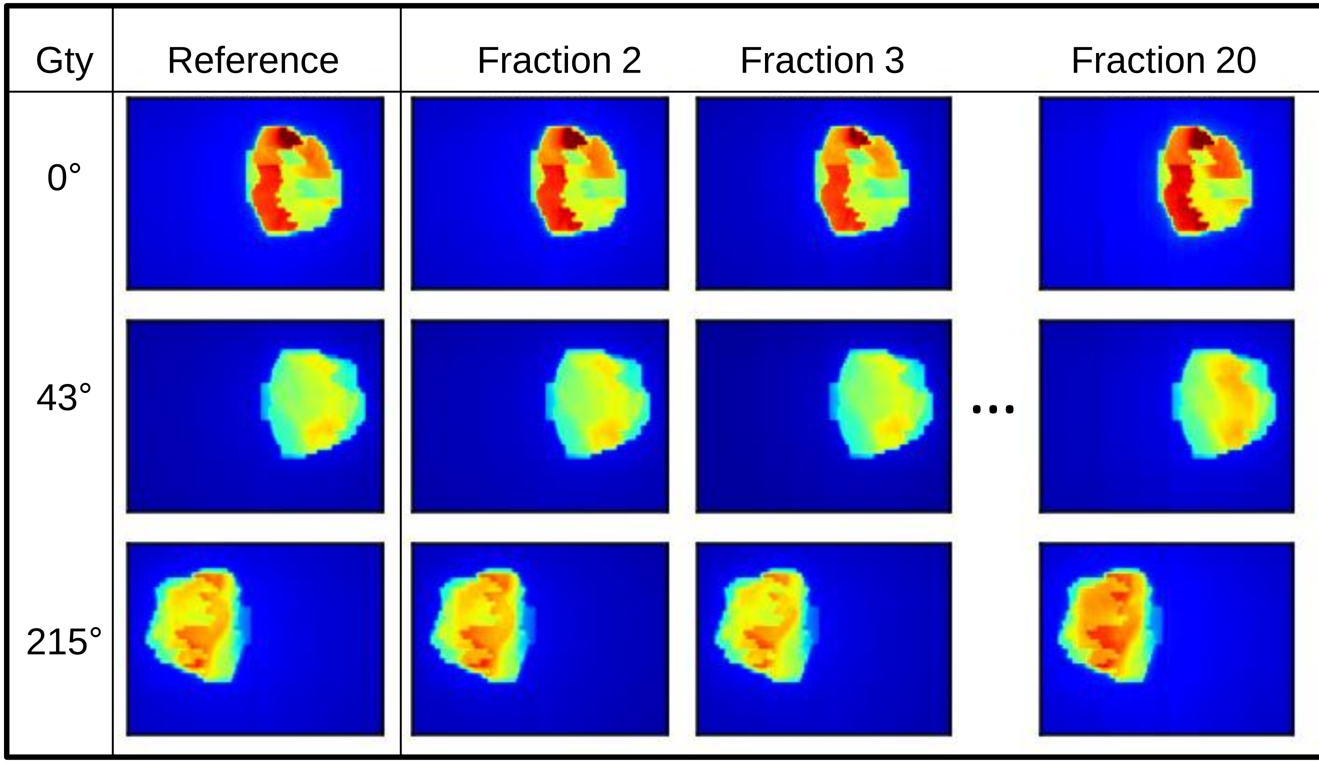
- Adaptive RT: treating the anatomy of the day
  - Desirable, but resource intensive
  - Clinically impossible to implement in most cases
- Shortcuts must be developed
  - Algorithms must do some of the work
    - Add an additional layer of complexity to RT
- However, not all patient changes
  - Can 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

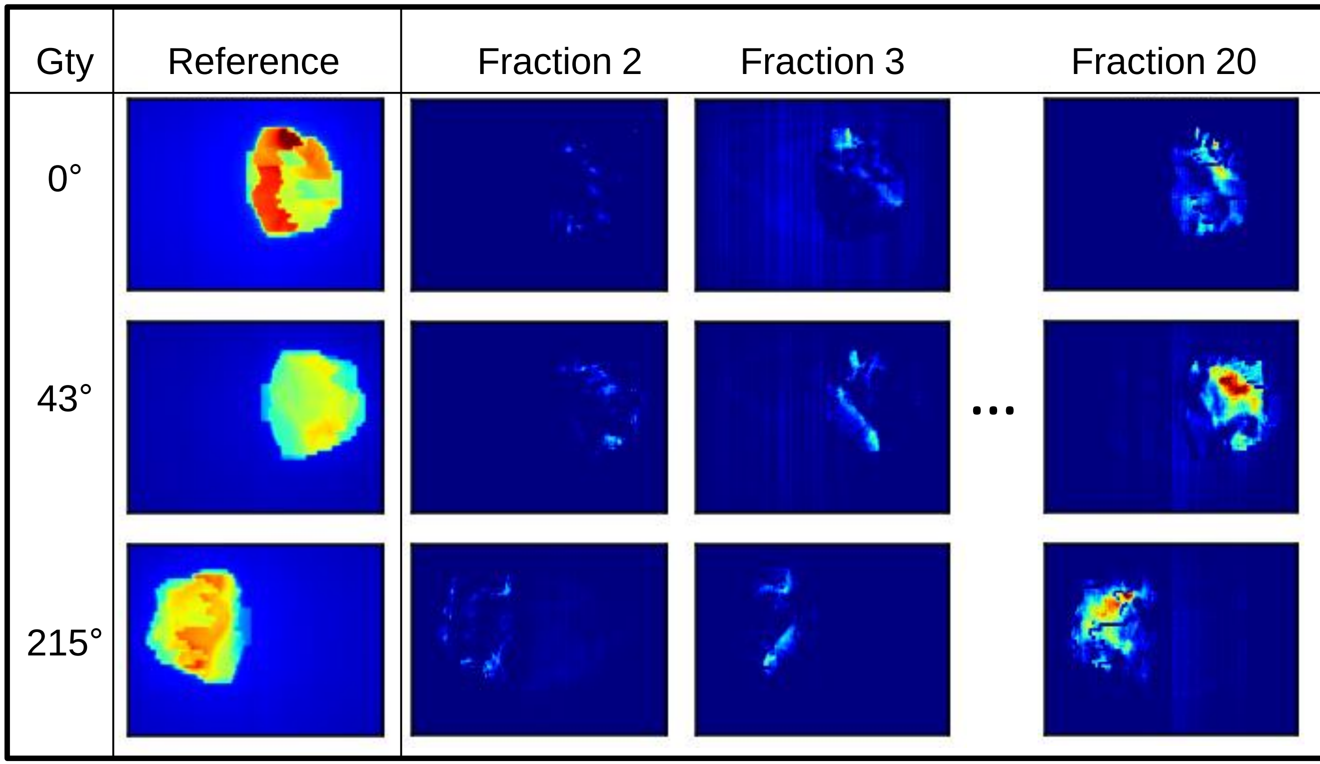
- Daily EPID
- Automated image collection
- Comparison to a reference
  - Validate reference with CBCT



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

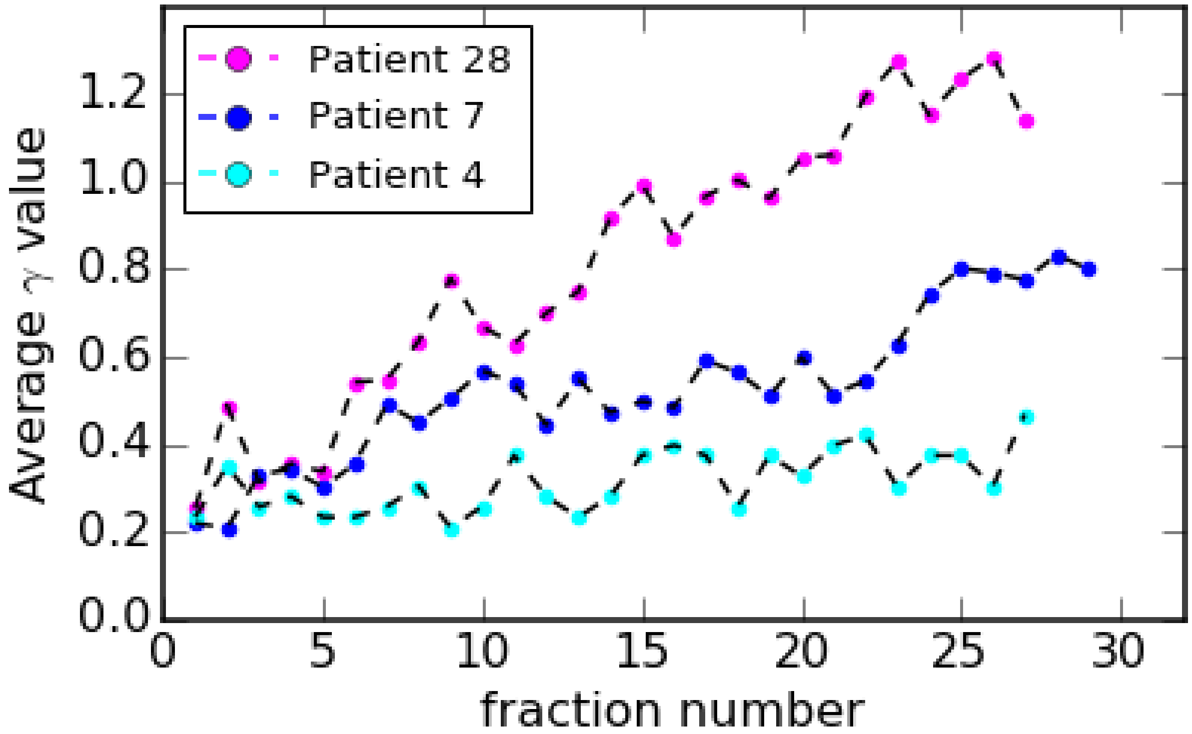


Only 3 out of 5 gantry angle shown for clarity

PhD student: O. Piron

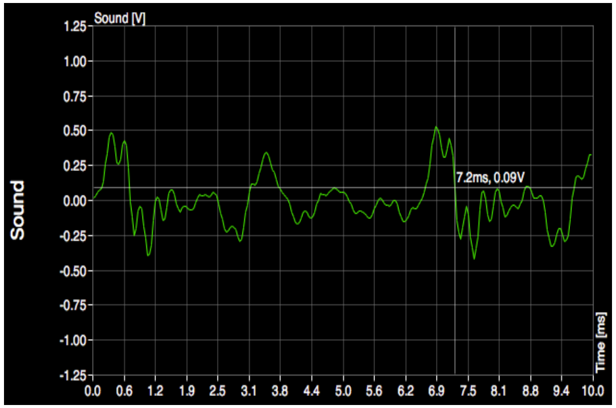
Patient time series

- Each patient is a time series



Time series

- Time series are omnipresent in many fields



- Environment
- Climate science
- Gene expression
- …

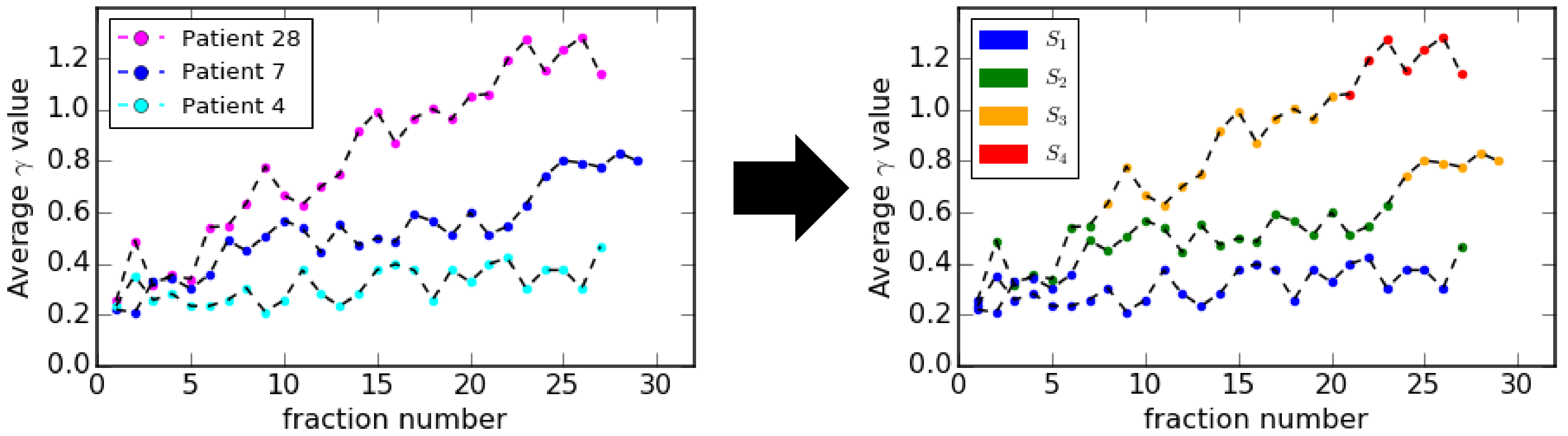
- Stock market analysis
- Speech recognition

- 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

Retrospective analysis of treatment plans to guide future treatments

A stochastic frontier analysis to improve treatment planning

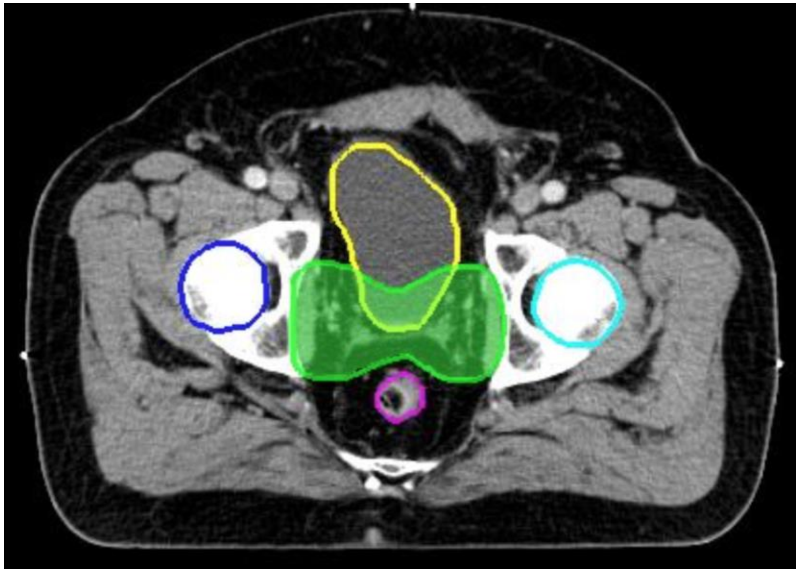
Treatment planning

- 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

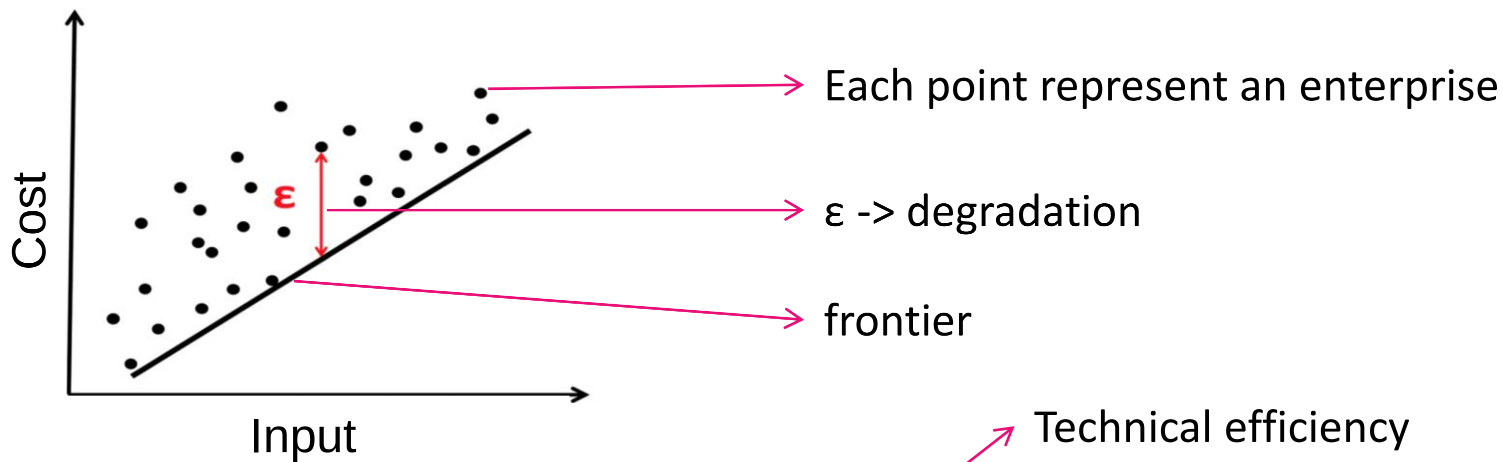


- If true:
  - Dose/geometry relationship of past patients can predict dose distribution of future patient

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

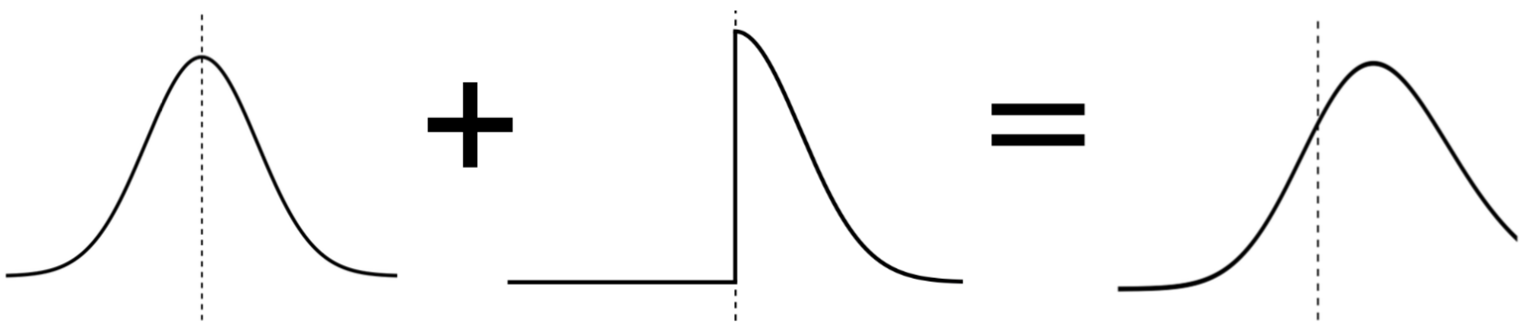
Stochastic frontier analysis (SFA)



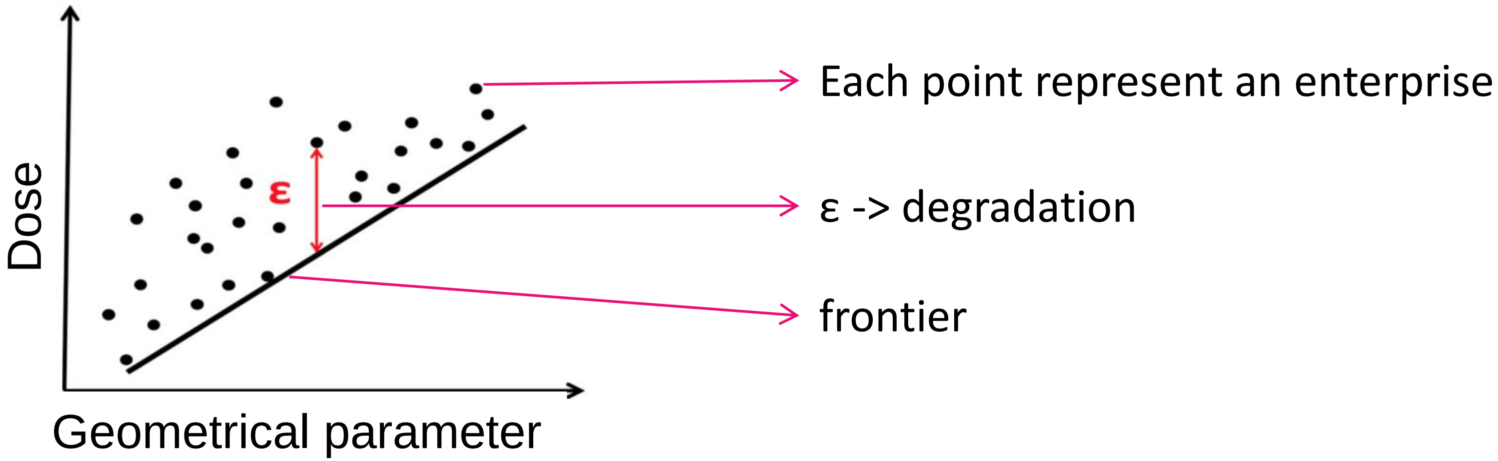
Technical efficiency

Random variations

$$\varepsilon_i = v_i + u_i$$



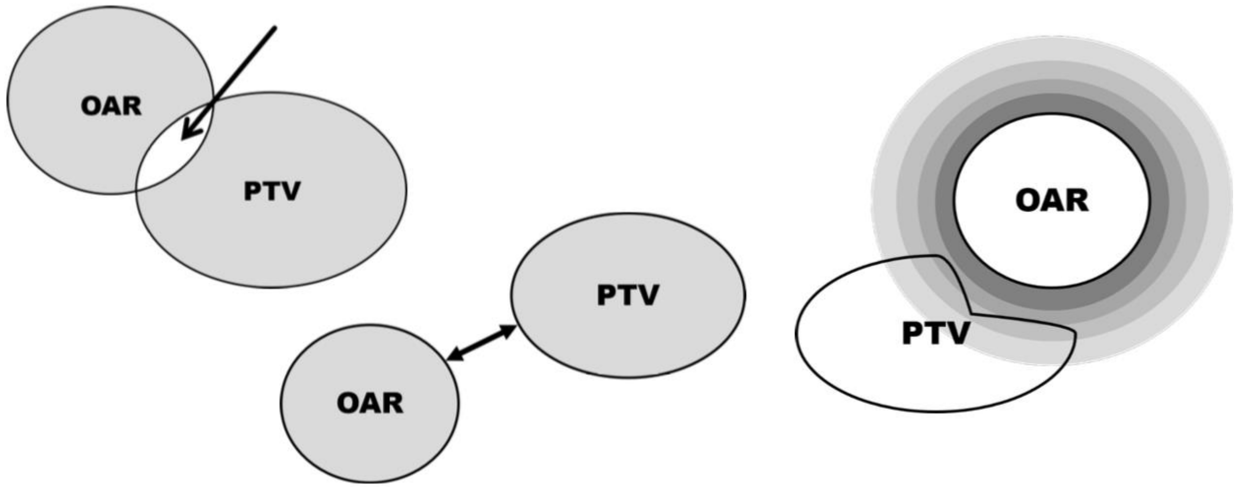
Stochastic frontier analysis (SFA)



- 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 …

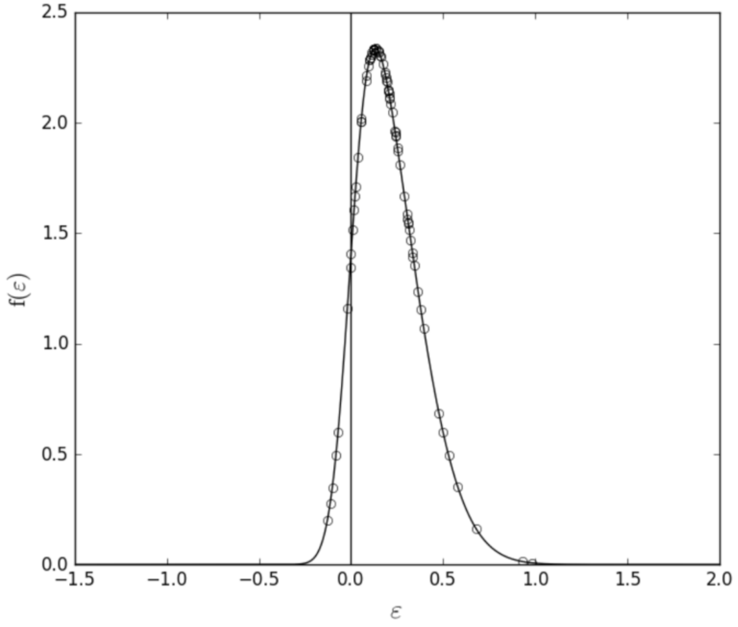


- These serves as ‘inputs’

Computing the frontier

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

Rectum dose in prostate treatment

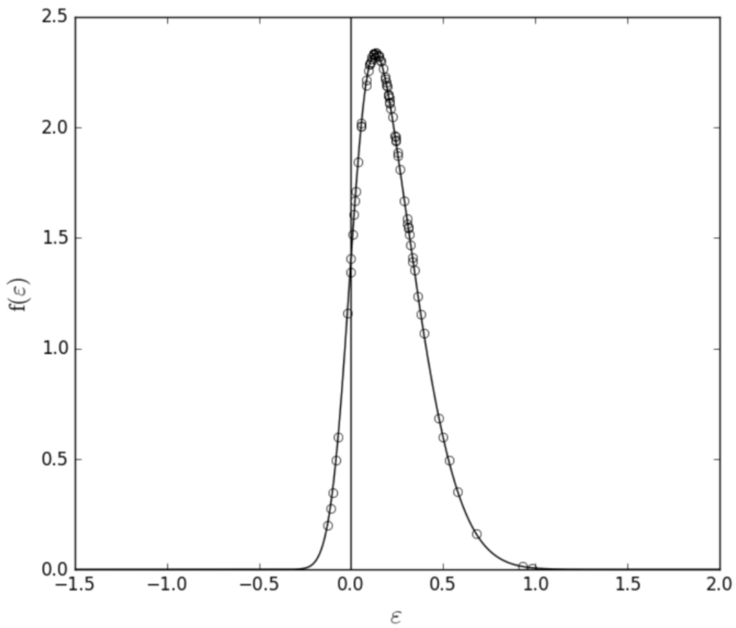


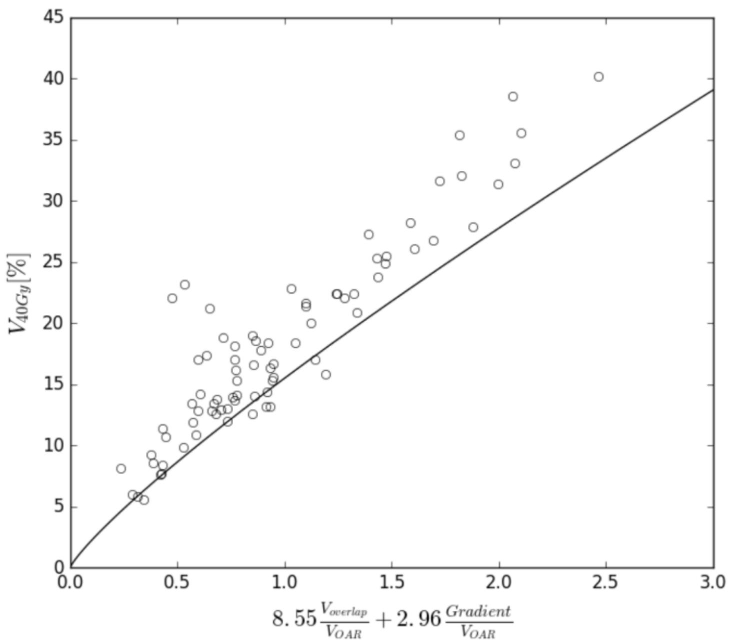
PhD student: A. Kroshko

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