Clinician’s perspective on 4D proton therapy

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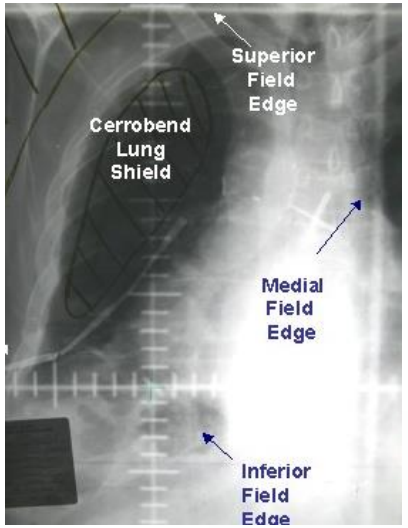
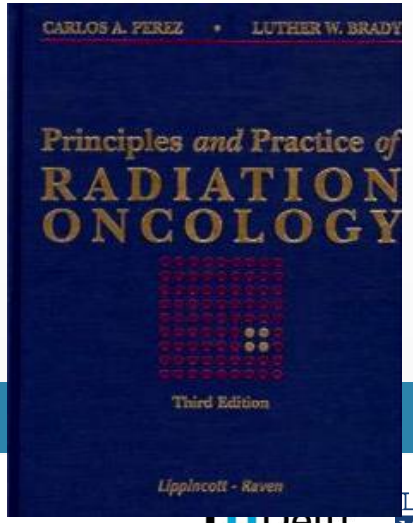
A clinical treatment in 2030…

- Pre-treatment
  - Optimal information on anatomy, biology, movement
  - Planning which deals with patient specific uncertainties
- Treatment
  - 45 minutes of treatment time
  - Look with optimal soft-tissue contrast
  - Adapt for movement of tumour
  - Dose accumulation / Anatomy of the day important:
    - If normal tissue is too close: stop treatment at safe level (e.g. 8Gy @ $1mm^3$) and come back another day
    - If not, treat until maximum time has elapsed. Maximum dose less important if safe (e.g. 40Gy)
    - No homogeneous dose
- Post-treatment
  - Optimal information on biology to check response
  - Re-treatment if required, same rules as above

Changing concepts in radiation oncology

- From elective to ablative intent
- Fractionation rules
- Why homogeneous dose
- Why set minimum or maximum dose
- ICRU 50/62/83
- Radioresistance
- Alpha/Beta
- High energy particles
- Retreatment rules (BED)
- Profession as a physicist / as a radiation oncologist?
- Contouring by radiation oncologists?
- GTV / (CTV?) / normal tissue
- Etc…





Main current clinical / physics topics

- Image guidance (contains 4D)
- Automation (contains 4D)
- Hypofractionation (contains 4D)
- FLASH (contains 4D)

Question / problem: what is the definition of 4D? Where in radiotherapy does 4D start and end?

Wikipedia: 4D is three-dimensional space, plus time. Conclusion: 4D is a physics approach and cannot stand alone in clinical practice. How to interpret 4D in the changing RTH landscape?

My conclusion: topic is to big to present “clinician’s perspective”. Touch 4D in current topics.

4D in image guidance

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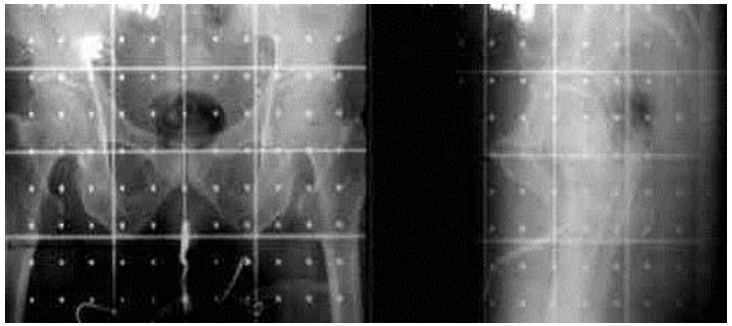
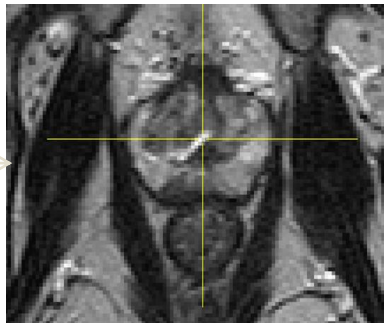
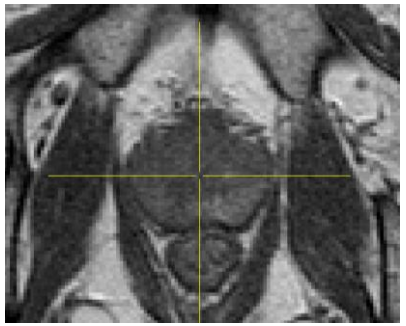
Radiotherapy towards image based

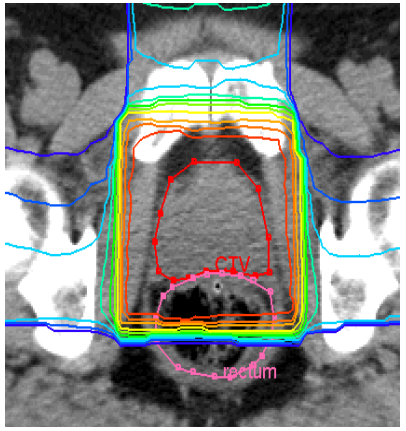
From Xray-based planning to planning with optimal resolution and constrast

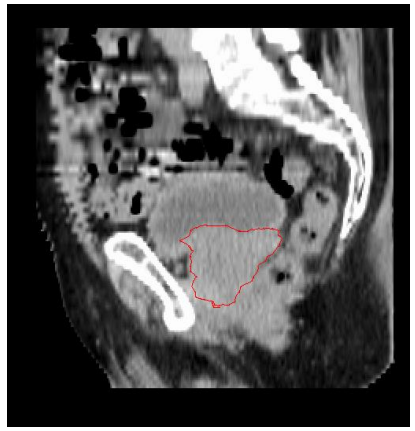


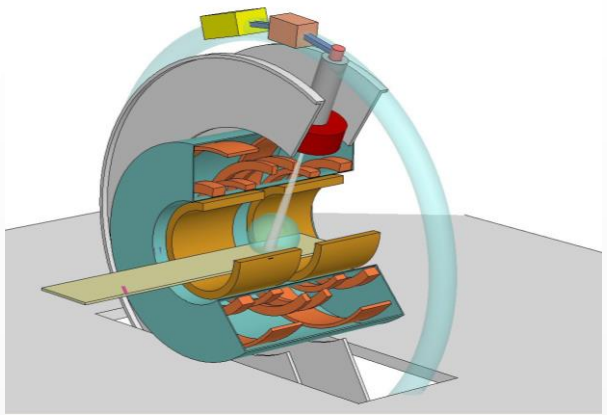




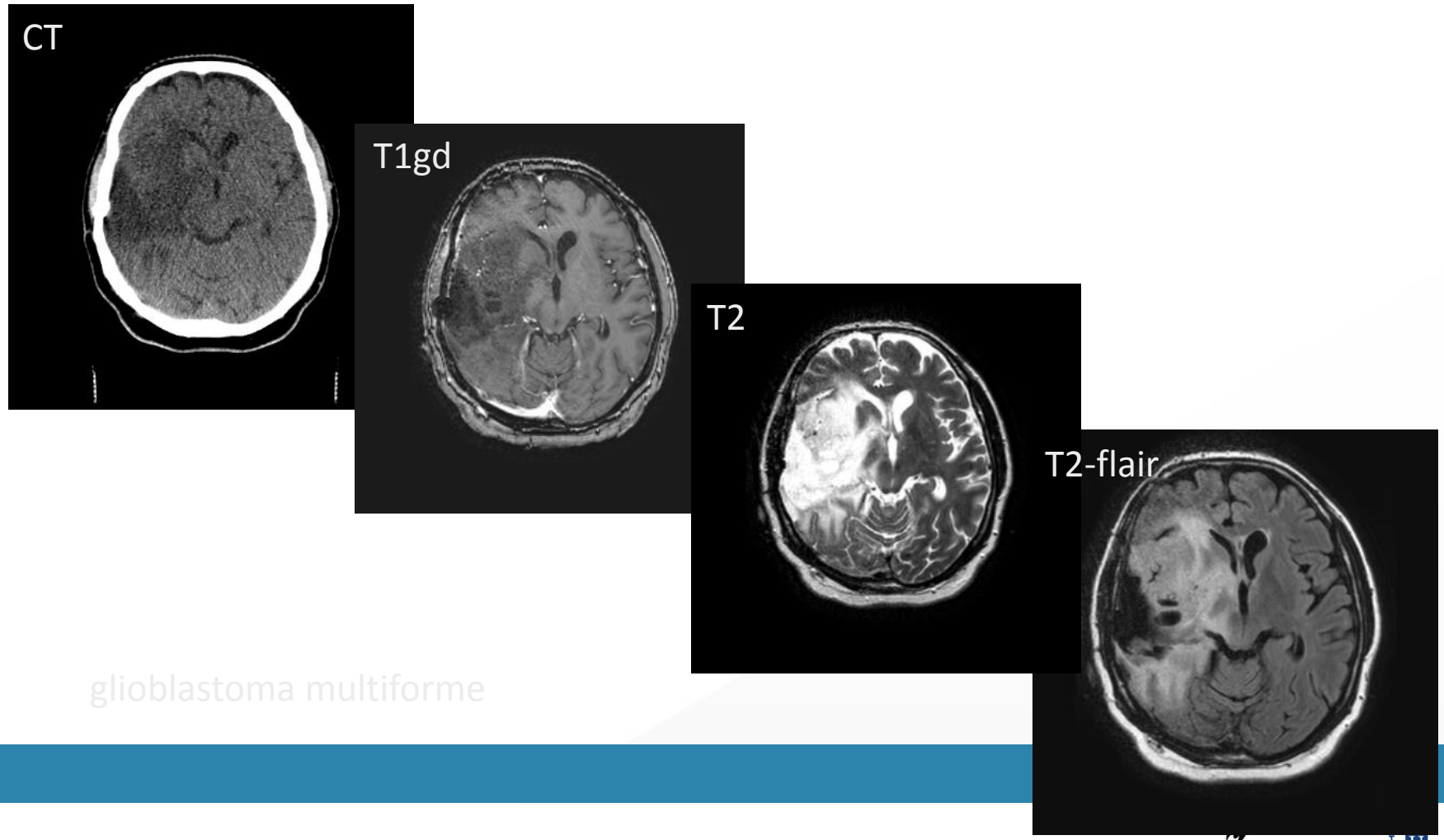
From no correction during treatment to (online) adaptation







MRI optimal soft tissue contrast; target definition

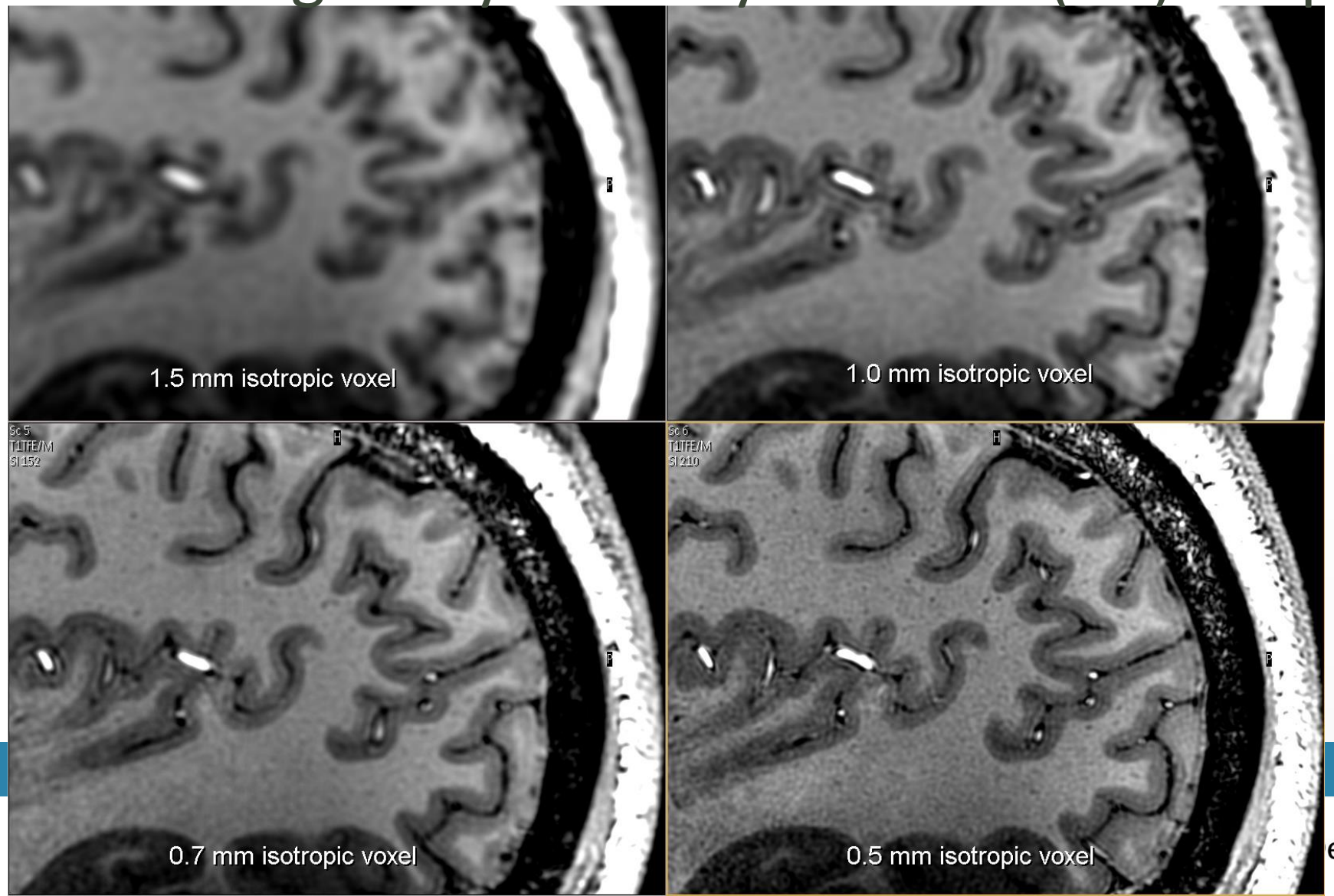


glioblastoma multiforme

Questions

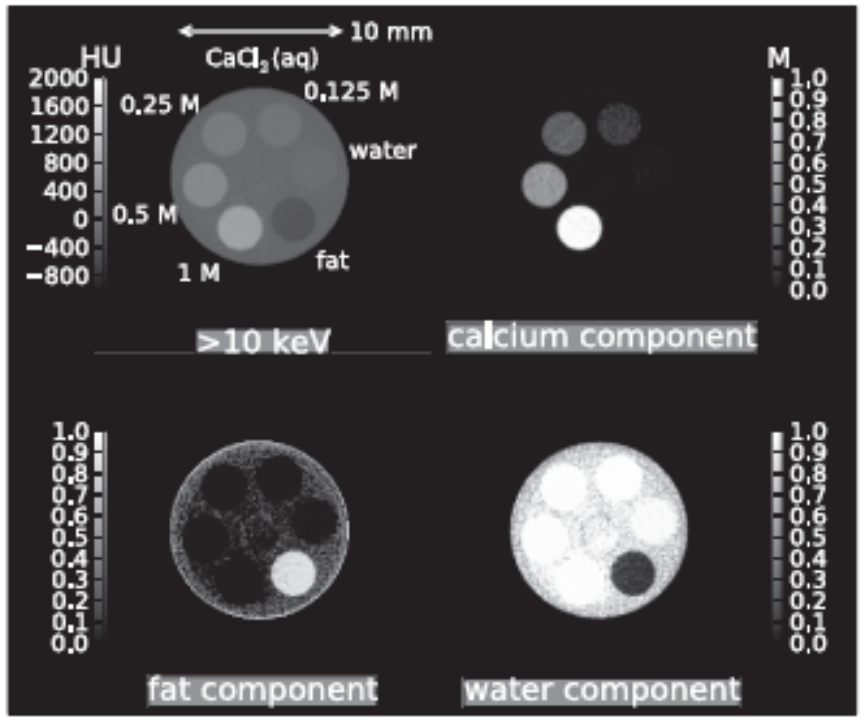
- What is the minimal resolution required to decide on adaptation? — 1 cm^3
- Is MRI the only option for optimal soft tissue contrast? — No
- Are all movements predictable? — Yes
- Do you need intrafraction treatment plan adaptation? — No
- How do you decide on an online adapted plan during treatment? — Automation
- Do we need an image during treatment? Do we need any image? Are vectors sufficient? — No / yes

Which image do you prefer?
Which image do you really need for (4D) adaptation?

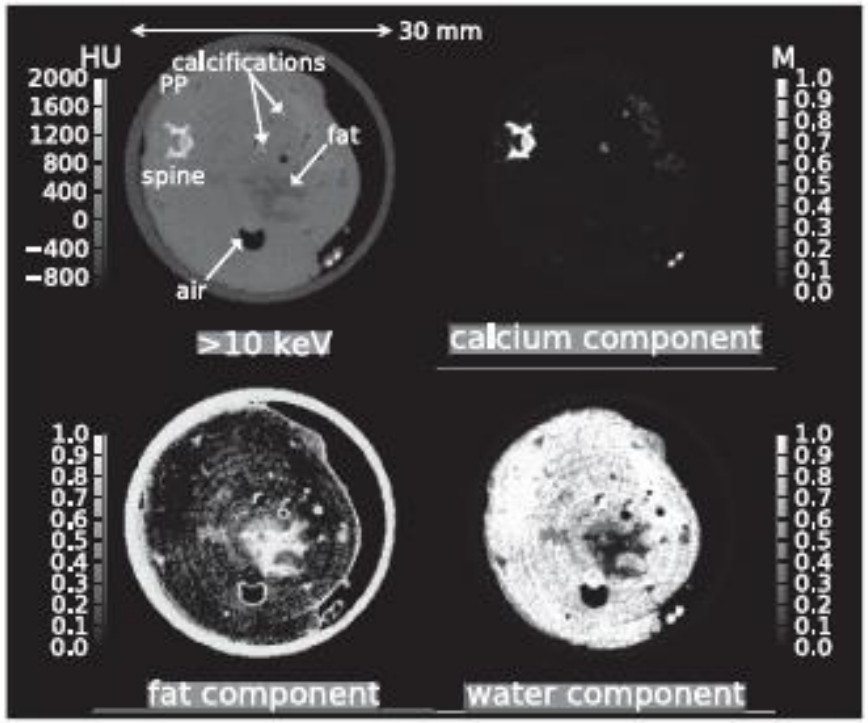


Spectral X-ray CT

Spectral CT image of the calcium chloride phantom and material component images for calcium, fat, and water obtained from the analysis of multispectral data.



Spectral CT image of a transgenic mouse and material component images for calcium, fat, and water obtained from the analysis of multispectral data.



JP Ronaldson et al, Toward quantifying the composition of soft tissues by spectral CT with Medipix3, Med Phys 39, 6847-57, 2012.

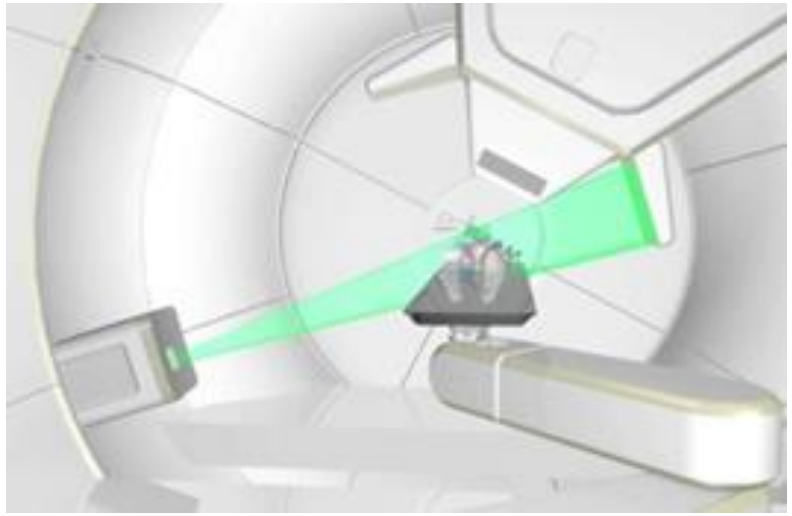
Courtesy to Dennis Schaart, TU Delft

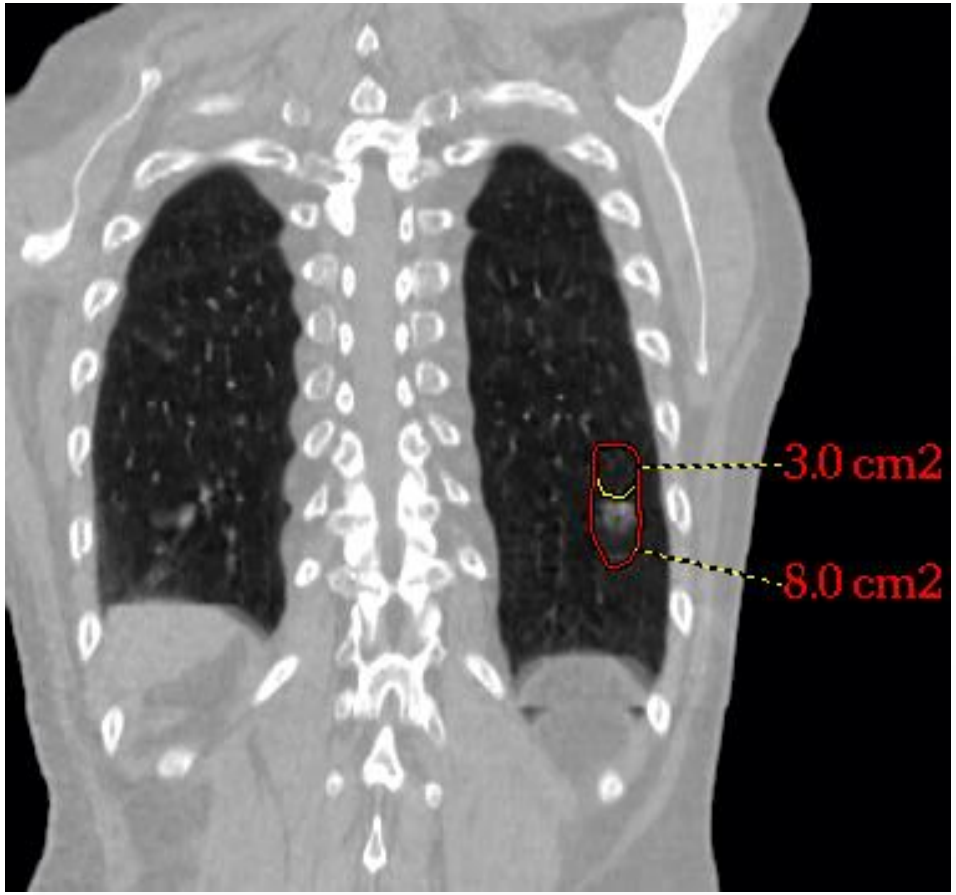
High-contrast isocentric X-ray imaging

Photon-counting X-ray technology.

Or use of multi-energy / spectral kV.

Benefits / downsides.

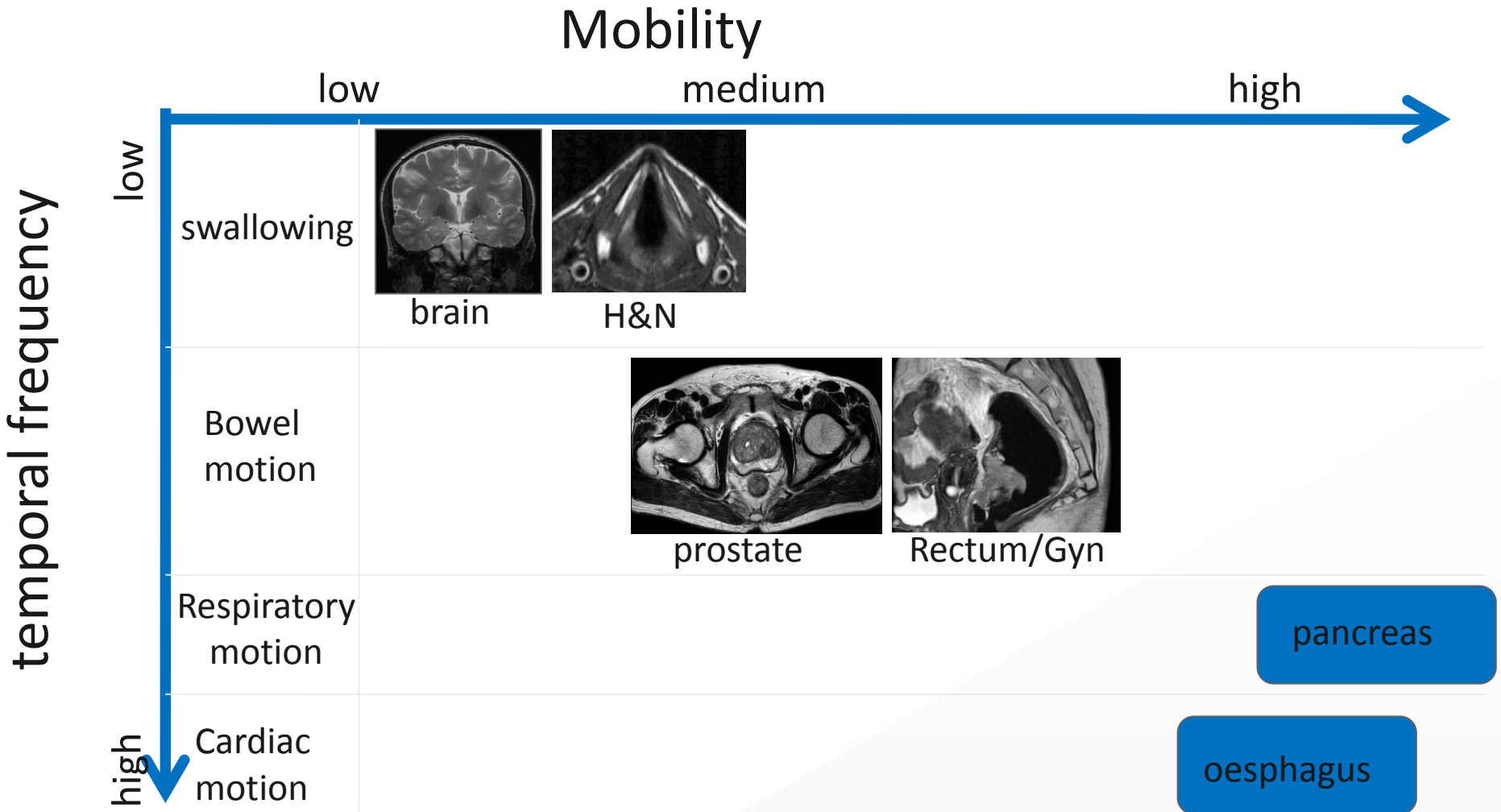




Courtesy to Dennis Schaart, TU Delft

Left mage: Varian Particle Therapy)

Which movements count in 4D RTH



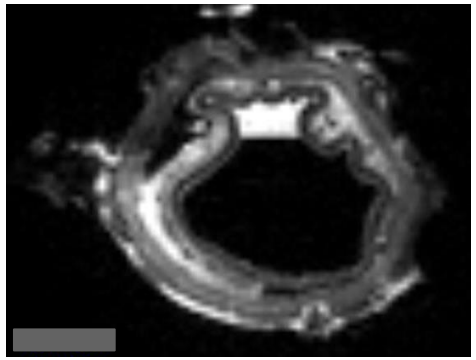
MRI-Linac for oesophageal cancer

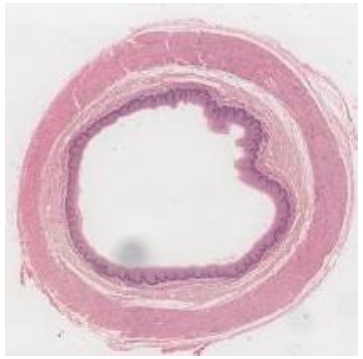
Pathology study

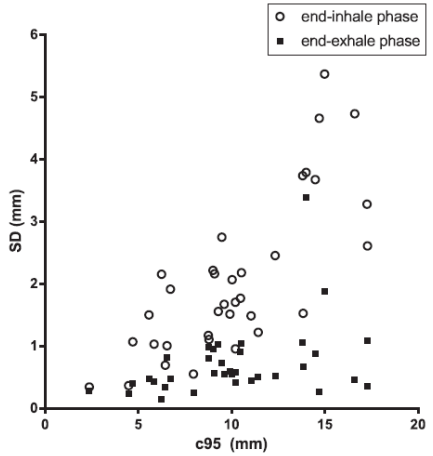
MRI sequence development

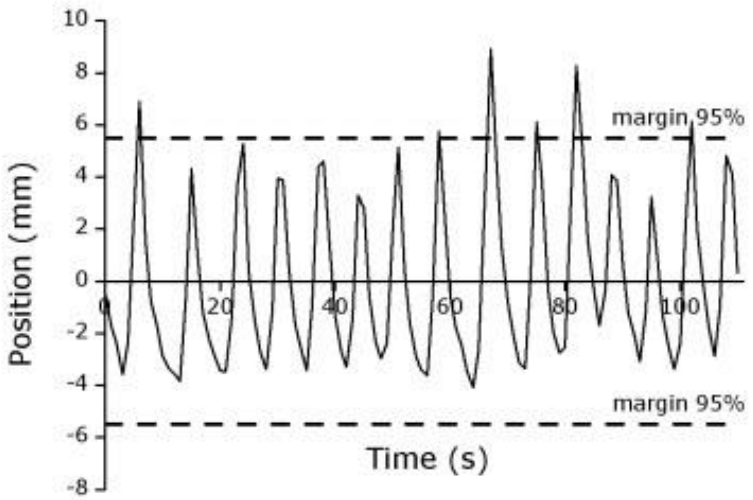
Movement , cine MRI

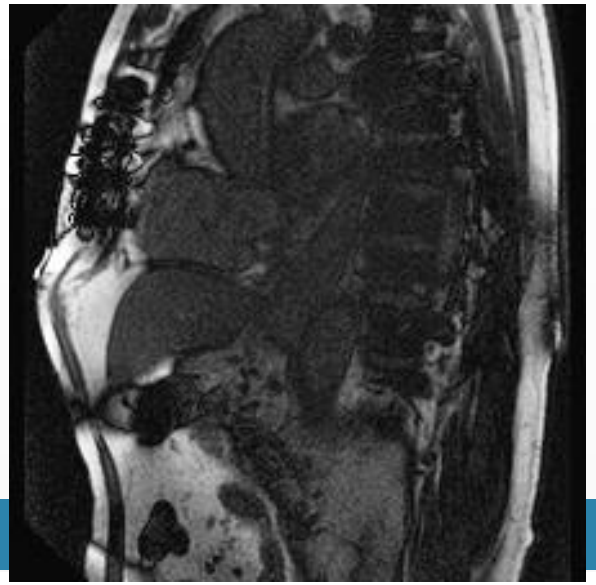
Planning study



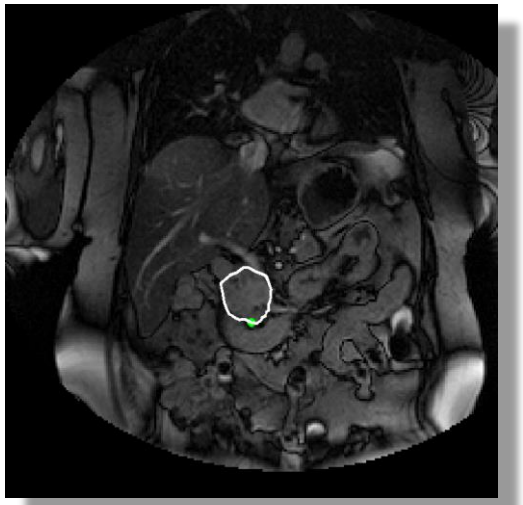


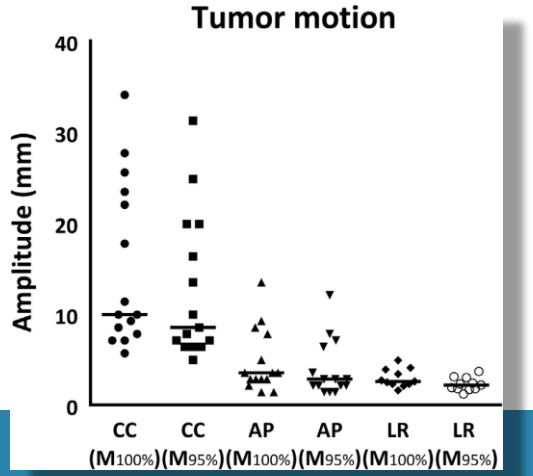


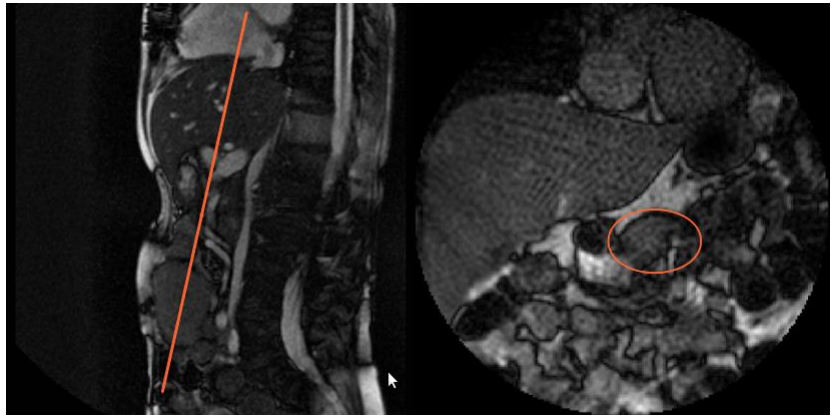




Movements largely predictable

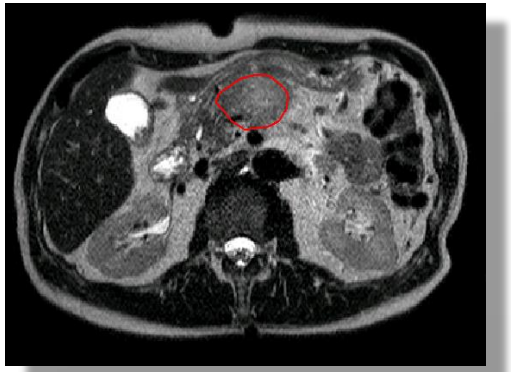


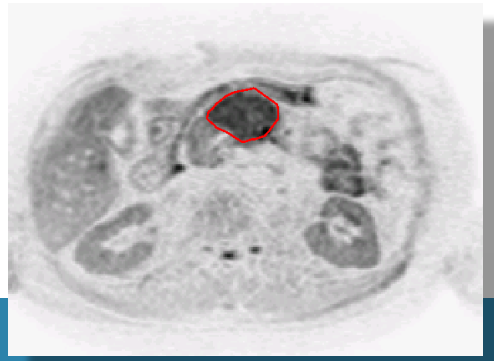




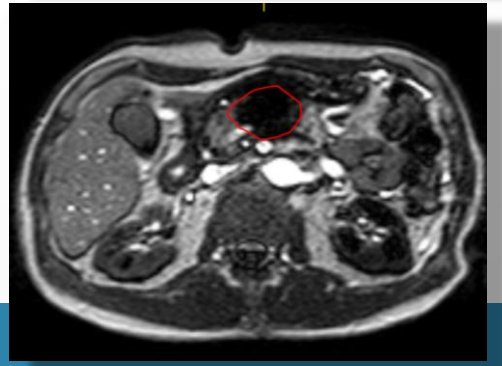
CT

T2



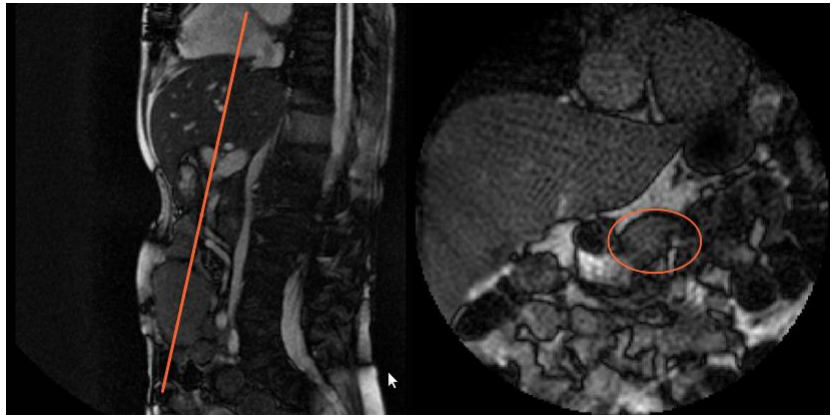


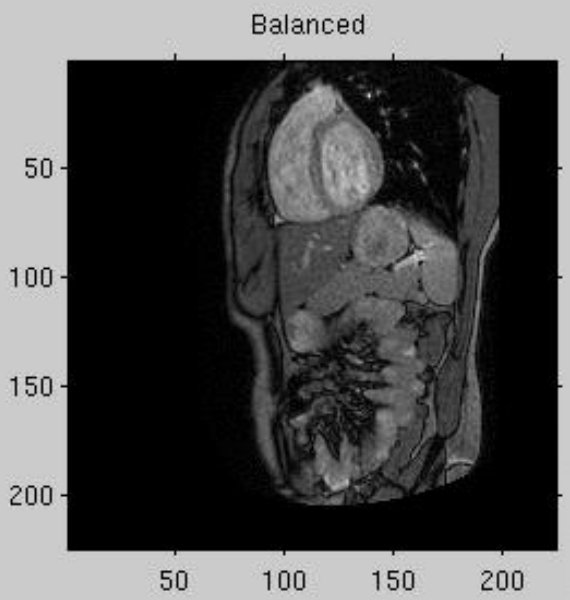
DWI



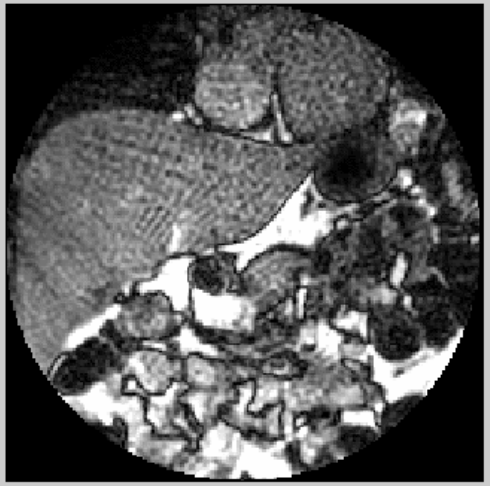
T1

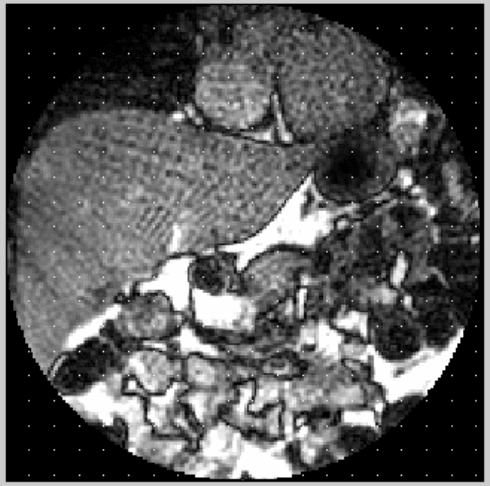
We only need 4D vectors for (online) adaptation





Different images to show: the movement / vectors / dose delivery on a static anatomy / only deformations





4D in automation

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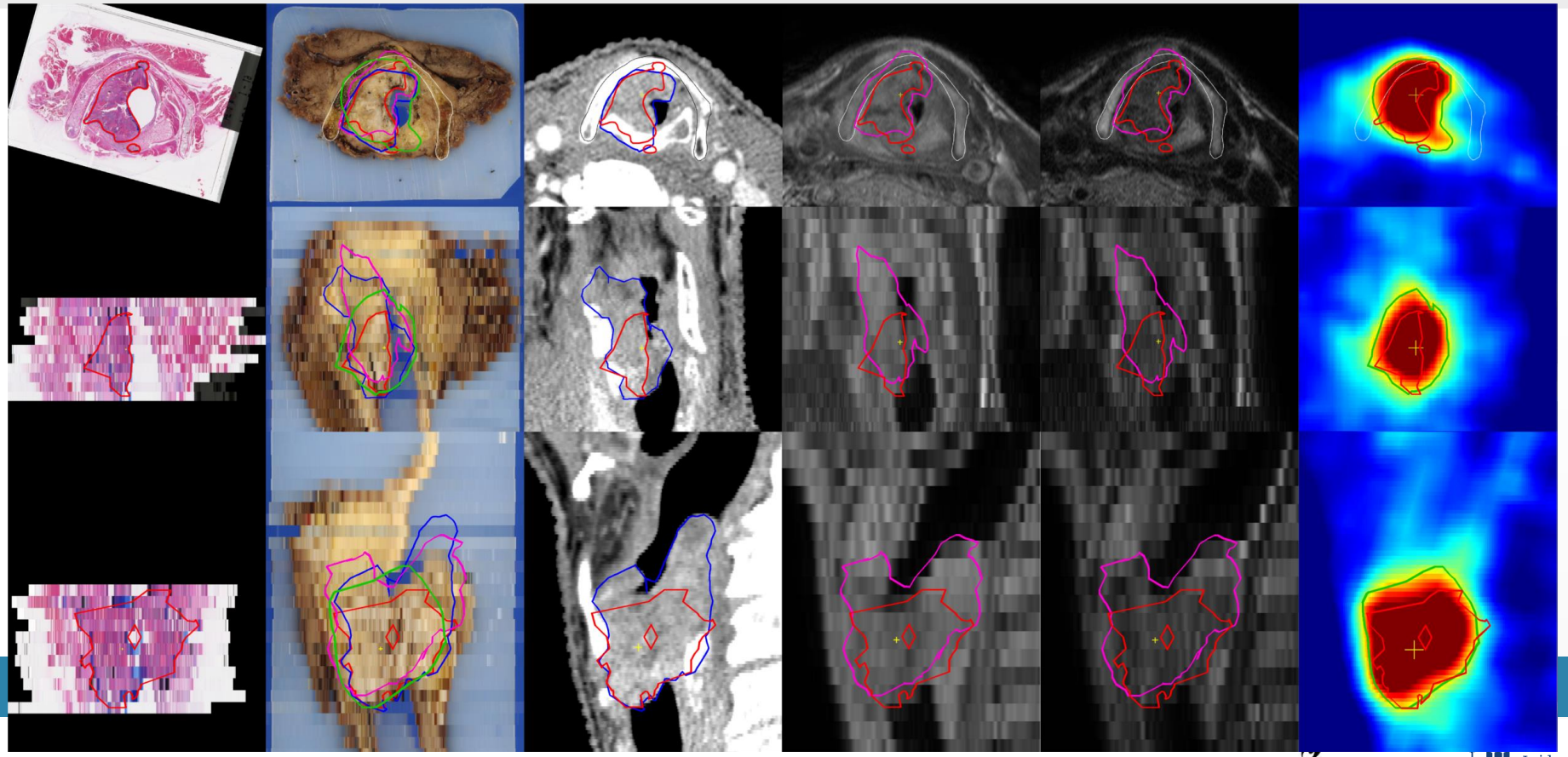
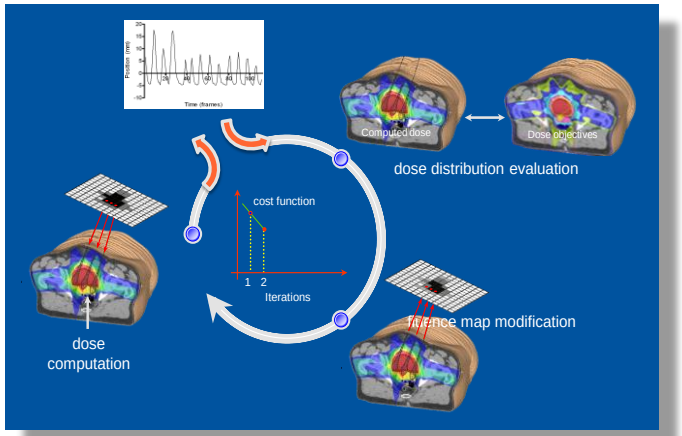
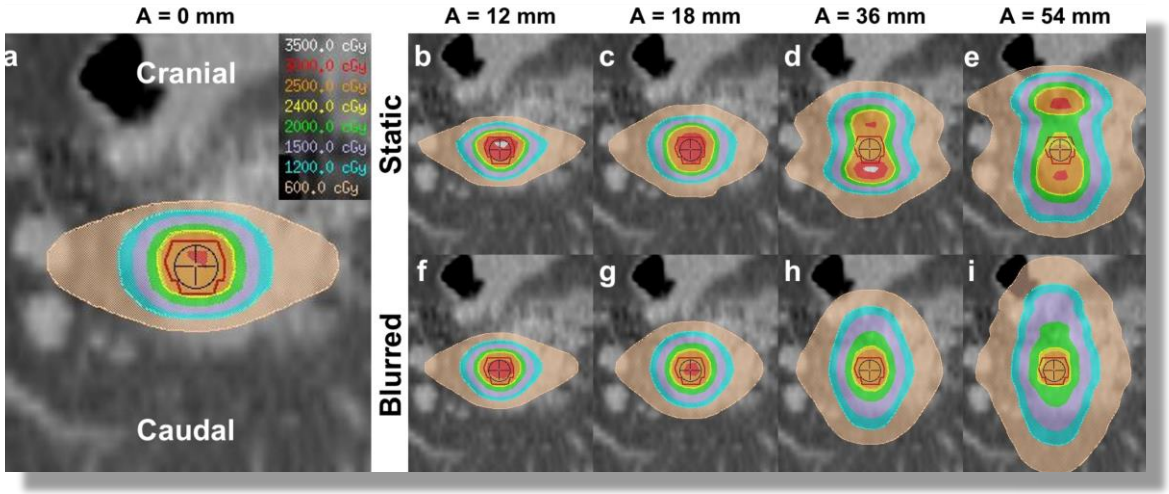
(4D) Delineation best be automated



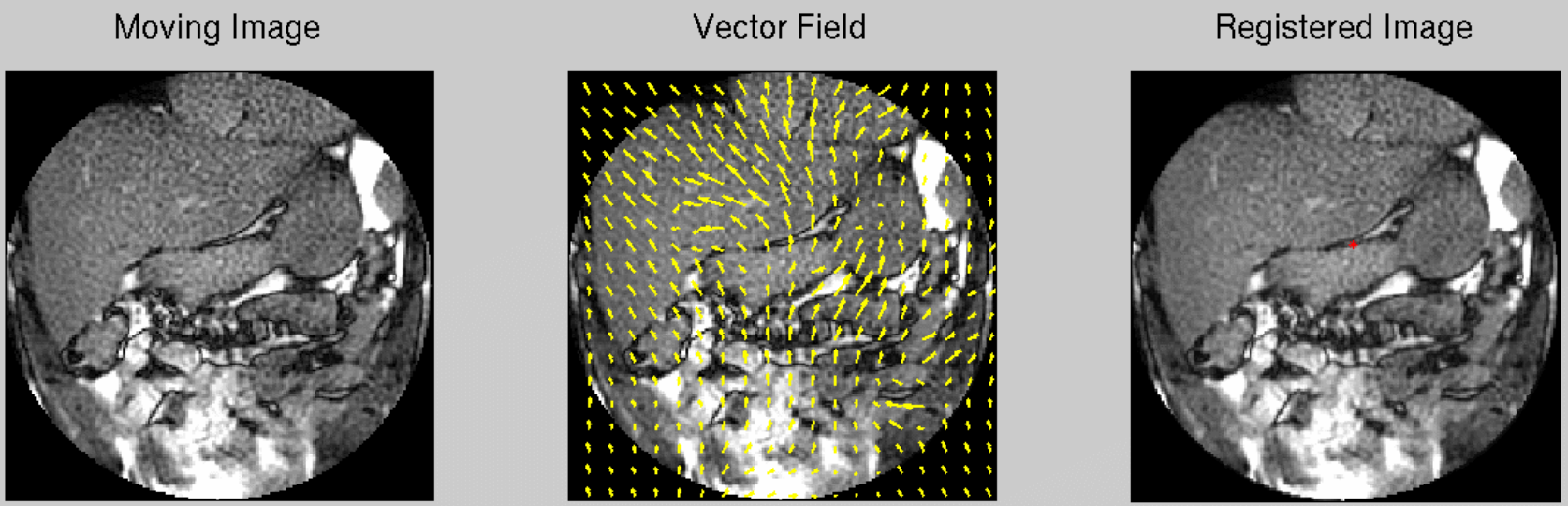
Caldas Magalhaes IJROBP 2011

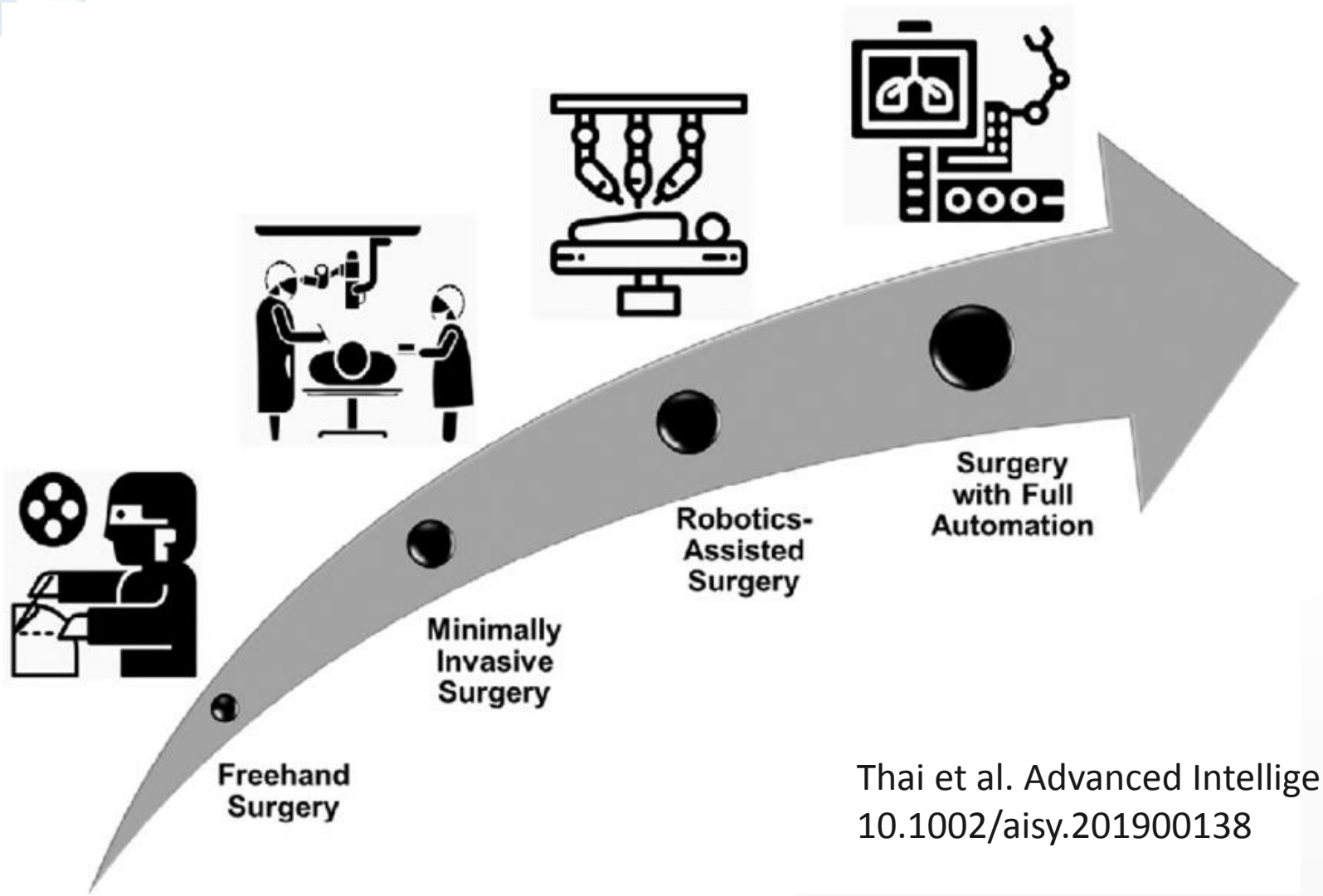
Towards motion incorporated plan optimization





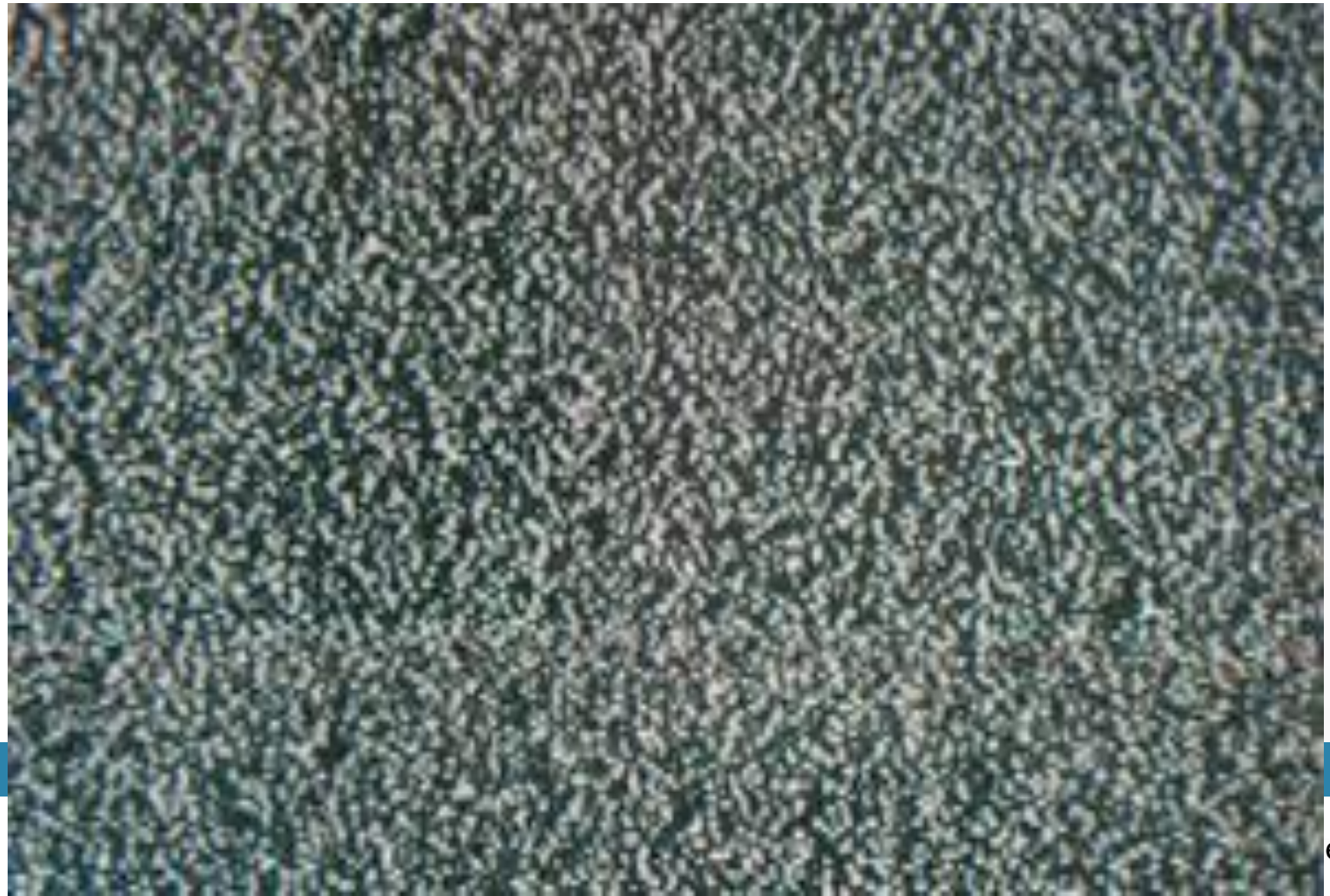
Patel 2015





Thai et al. Advanced Intelligent Systems for Surgical Robotic 10.1002/aisy.201900138

Do you need an image in (4D) adaptation?



Questions

- How do you decide on an online adapted plan during treatment? Who / what decides?
- How much should we reduce operator dependency? Totally?
- What is the optimal level for Automation? E.g. surgery approach: just a button for “on”, rest is unknown / is what the machine does? (e.g. cyro / HIFU). Do we need an image for re-assurance?

My wish: I prefer total automation.

4D in hypofractionation

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4D in hypofractionation

- Hypofractionation will be introduced for all tumour sites in radiation oncology.
- The need for 4D adaptation / checks will be bigger in case of a larger reduction in fractions.
- Hypofractionation cannot be safely performed without image guidance.

4D in FLASH

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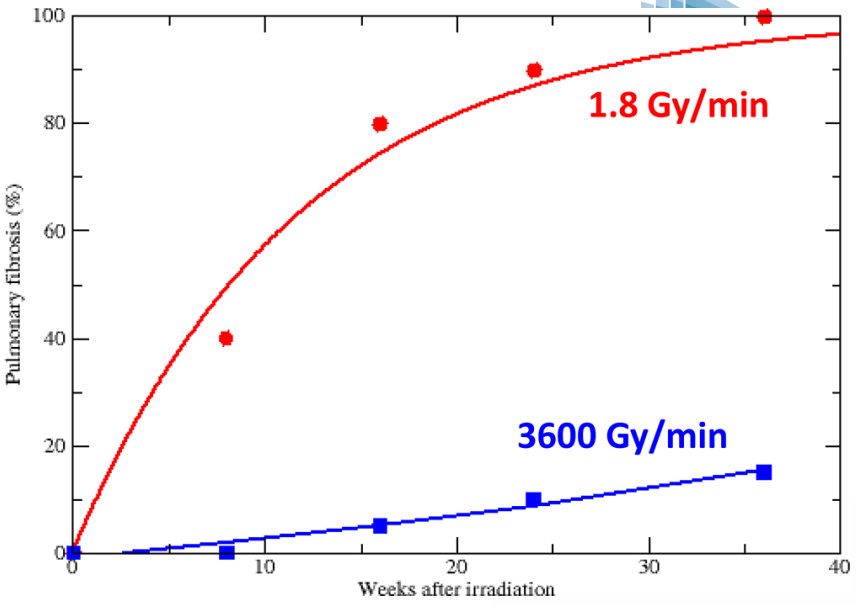
Flash-RT?

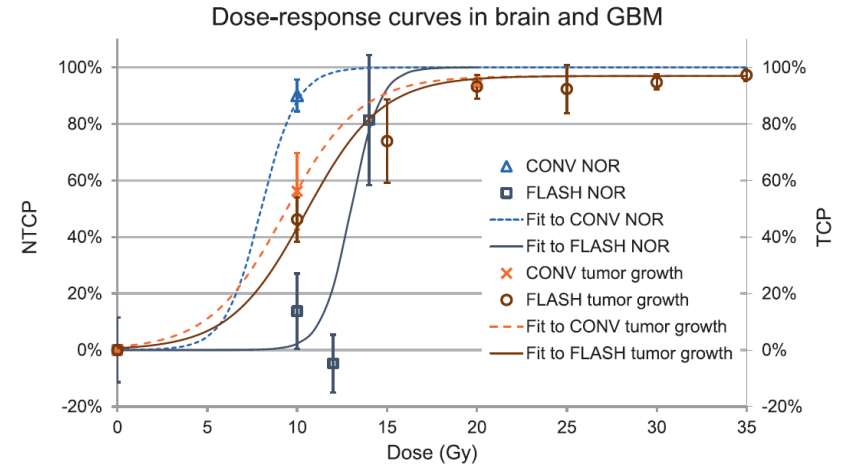
Biology: FLASH-effect

- Increases the differential effect between tumors and normal tissues
- Protects normal tissues with similar tumor kill as conventional dose rates

Physics: ~~FLASH~~ (dose tempo) effect

- Extreme hypofractionation
- Consequence: short beam delivery time
- Will intra-fraction imaging still be necessary?





Fauvadon et al. Sci Transl Med 2014; 6: 245ra93 (2014) and M.-C. Vozenin, M. Baumann, R. P. Coppes et al., FLASH

TU Delft · Leiden University Medical Center · Erasmus MC

A clinical FLASH treatment in 2030…

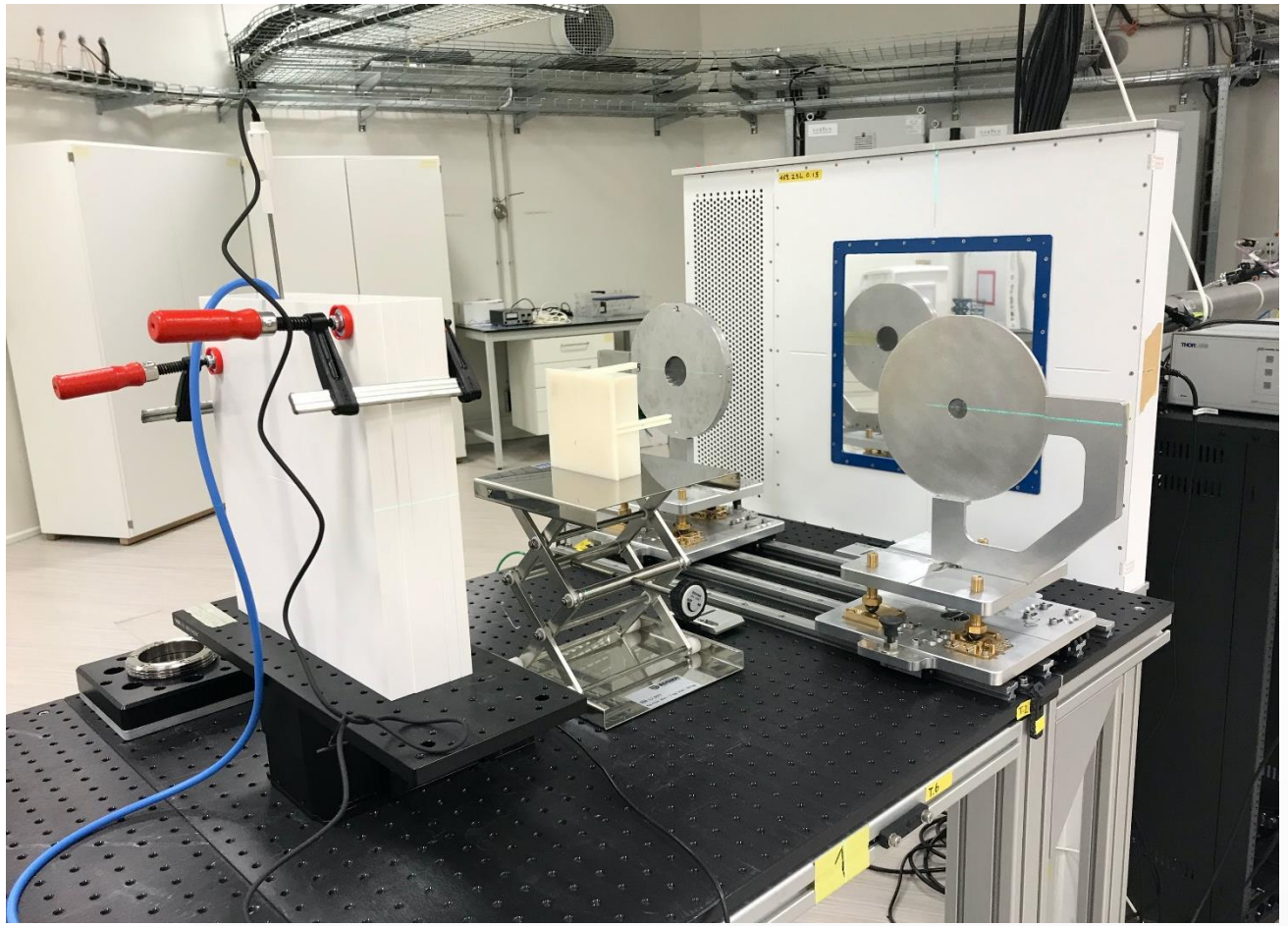
- Pre-treatment
  - Optimal information on anatomy, biology, movement
  - Planning which deals with patient specific uncertainties
- Treatment
  - 45 minutes of treatment time
  - Look with optimal soft-tissue contrast
  - Adapt for movement of tumour
  - Dose accumulation / Anatomy of the day less important.
- Post-treatment
  - Optimal information on biology to check response
  - Re-treatment if required, same rules as above

Absolute dose measurements

Device: Advanced Markus chamber

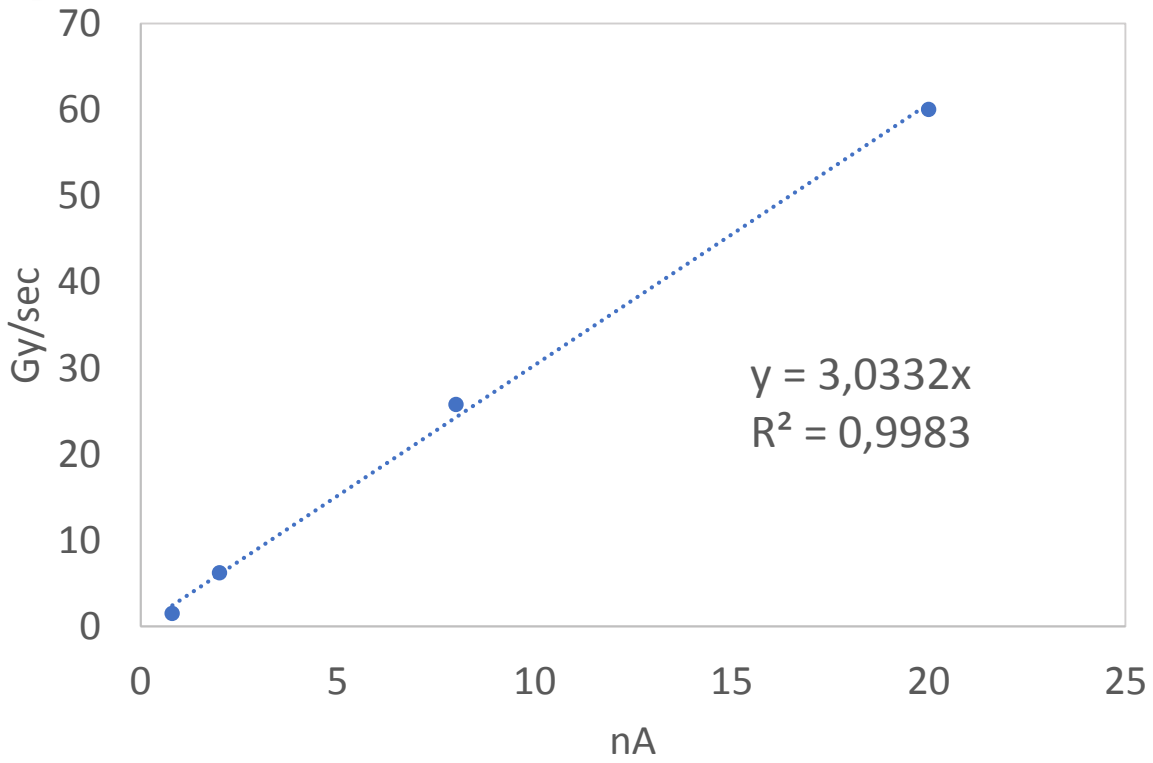
Beam Energy: 250 MeV

Nominal nA	Time (sec)	nC	D (Gy)	Gy/sec	Depth RW3 (cm)
0,8	10,2	10,15	16	2	5
2	10,2	41,3	64	6	5
8	10	166,9	258	26	5
20	10,2	403,5	613	60	5



Courtesy to Marta Rovitoso

Absolute dose measurements



Intensity @ target (nA)	Gy/sec	Gy/s/cm2
2	6	11
4	12	21
8	24	43
20	61	107
40	121	213
120	364	639
200	607	1066
320	971	1705

FLASH regime

Courtesy to Marta Rovitoso

A clinical high dose tempo treatment in 2030…

- Pre-treatment
  - Optimal information on anatomy, biology, movement
  - Planning which deals with patient specific uncertainties
  - Plan the most optimal moment to deliver the radiation
- Treatment
  - Deliver the radiation at the optimal moment
  - QA of delivery
- Post-treatment
  - Optimal information on biology to check response
  - Re-treatment if required, same rules as above

Conclusions

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Conclusions

- 4D in radiation oncology is a very broad topic with poorly defined boundaries.
- Before we further develop 4D in radiation oncology should discuss where we ultimally want to go.
- This presentation is meant to start this discussion.


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