Ion Beams for Cancer Therapy

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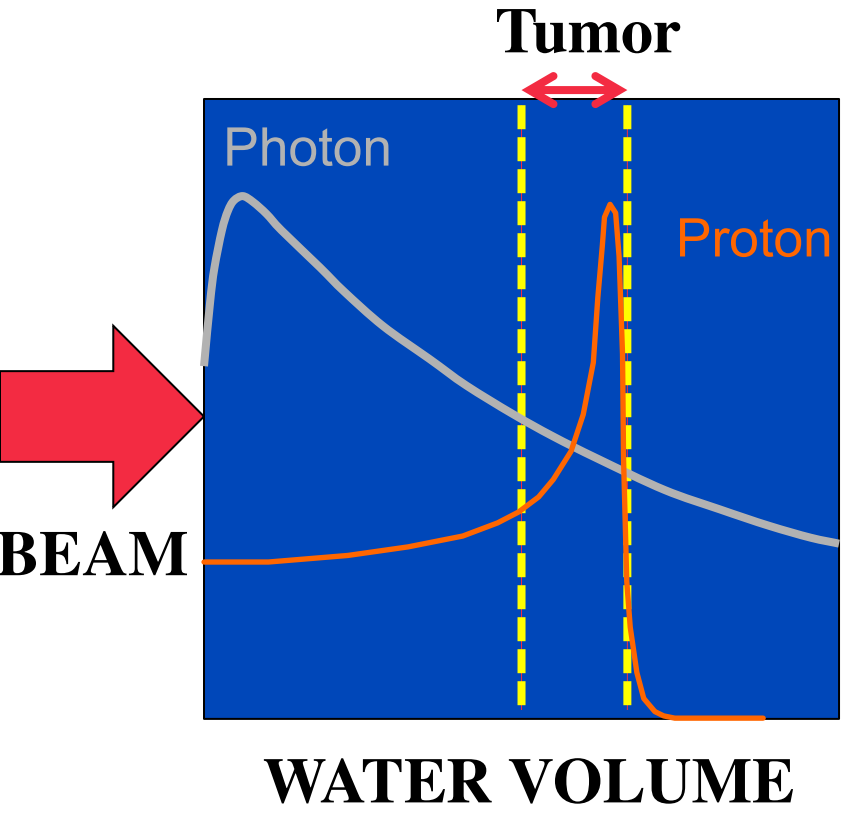
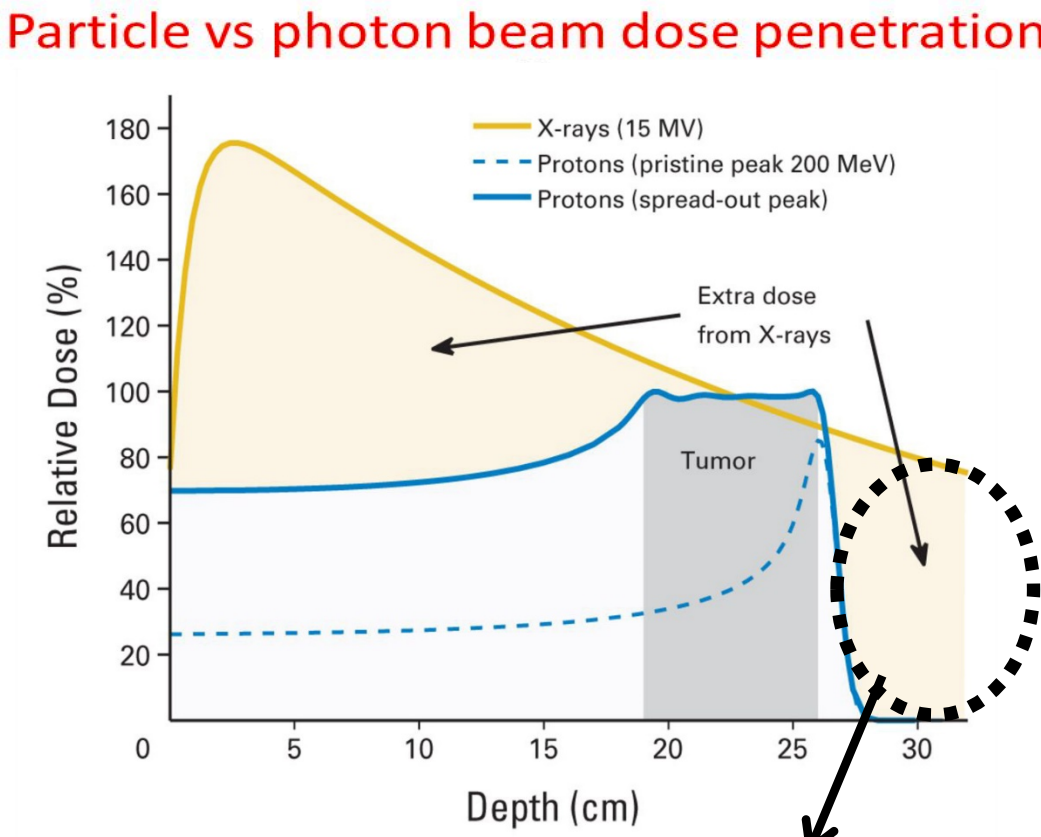
dkfz. GERMAN CANCER RESEARCH CENTER IN THE HELMHOLTZ ASSOCIATION

Research for a Life without Cancer

Why Ion Beam Therapy (IBT)?

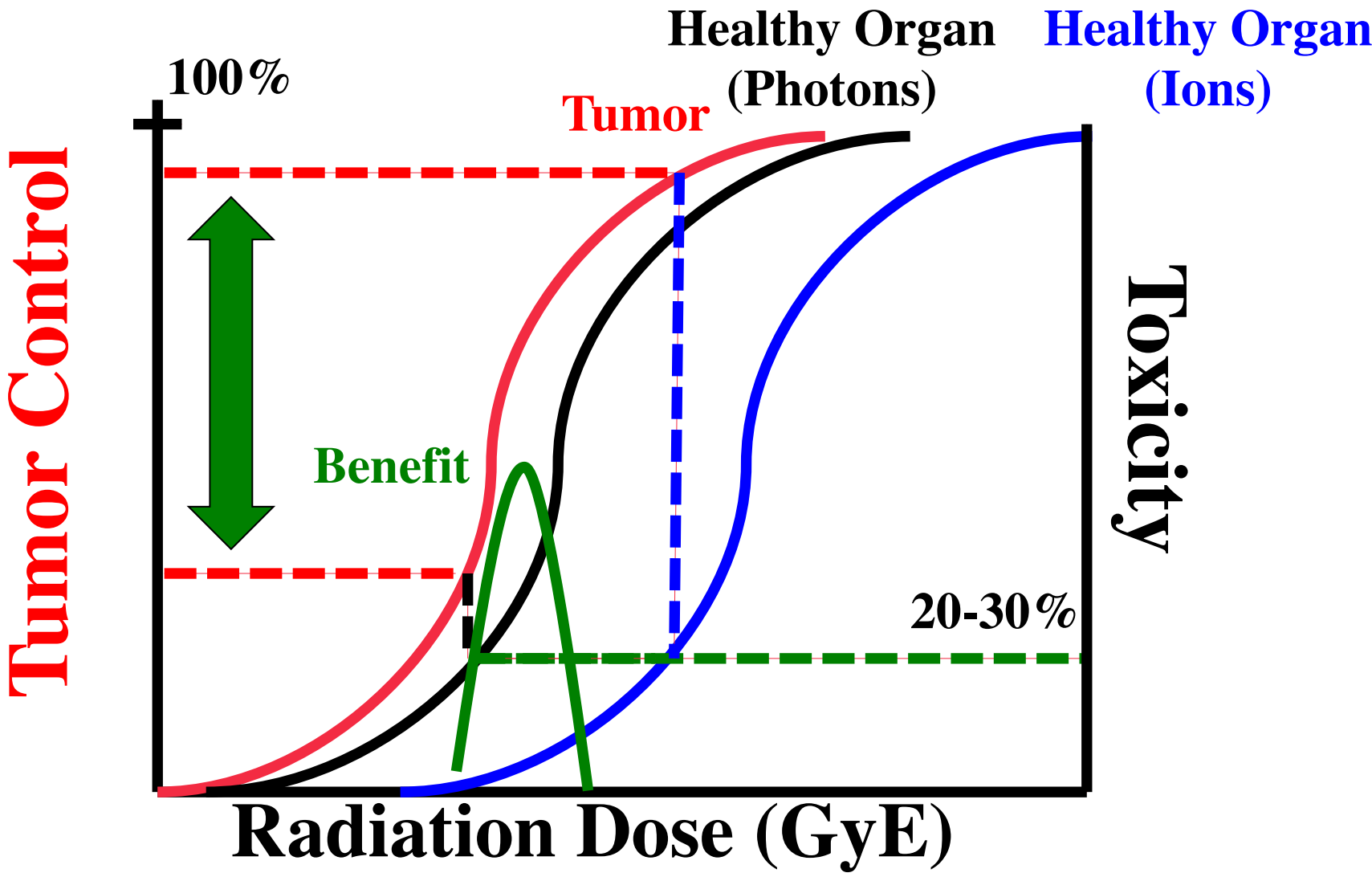
"Bragg Peak"





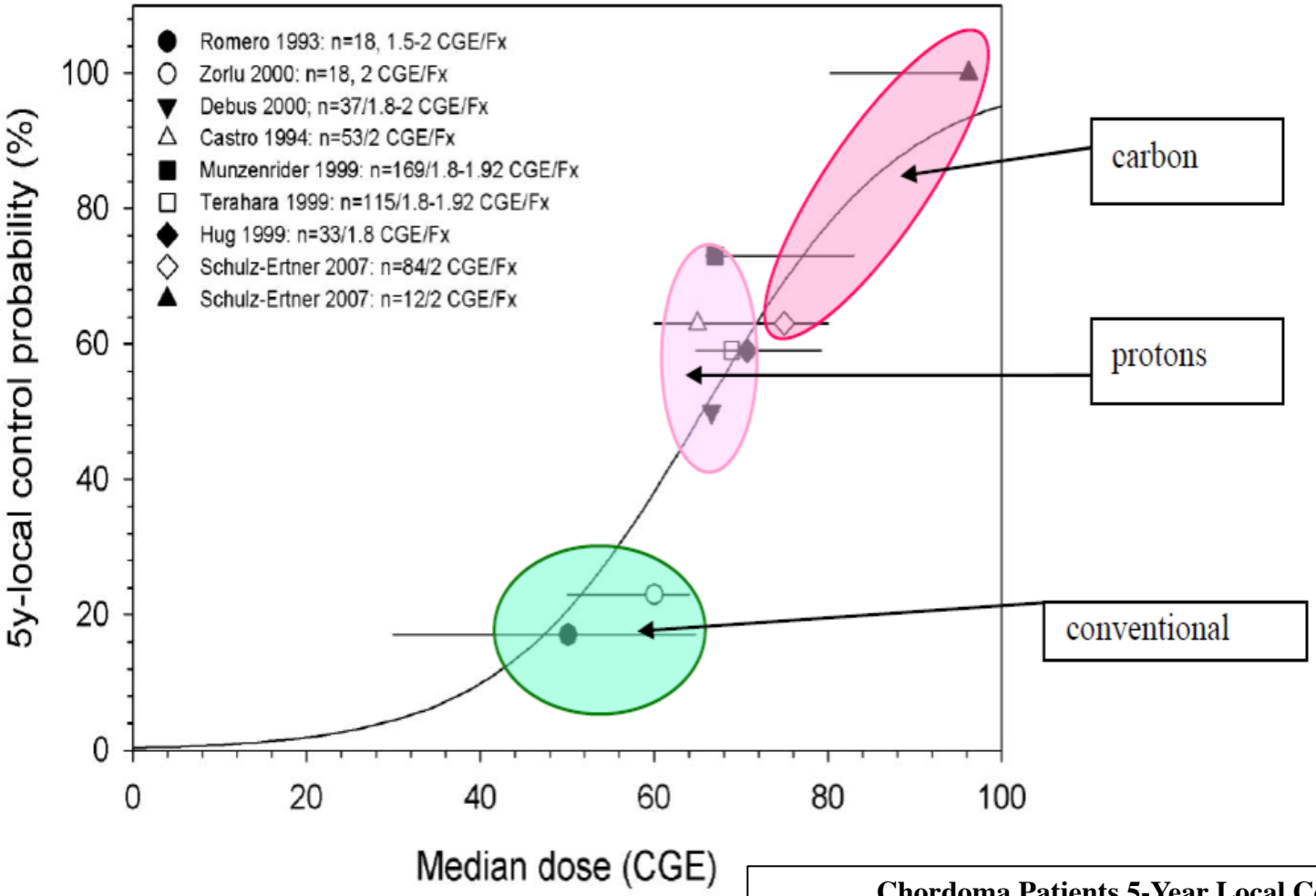
Organ Sparing Region

Quantifying Advantage of IBT



Advantage of Ion Beam Therapy

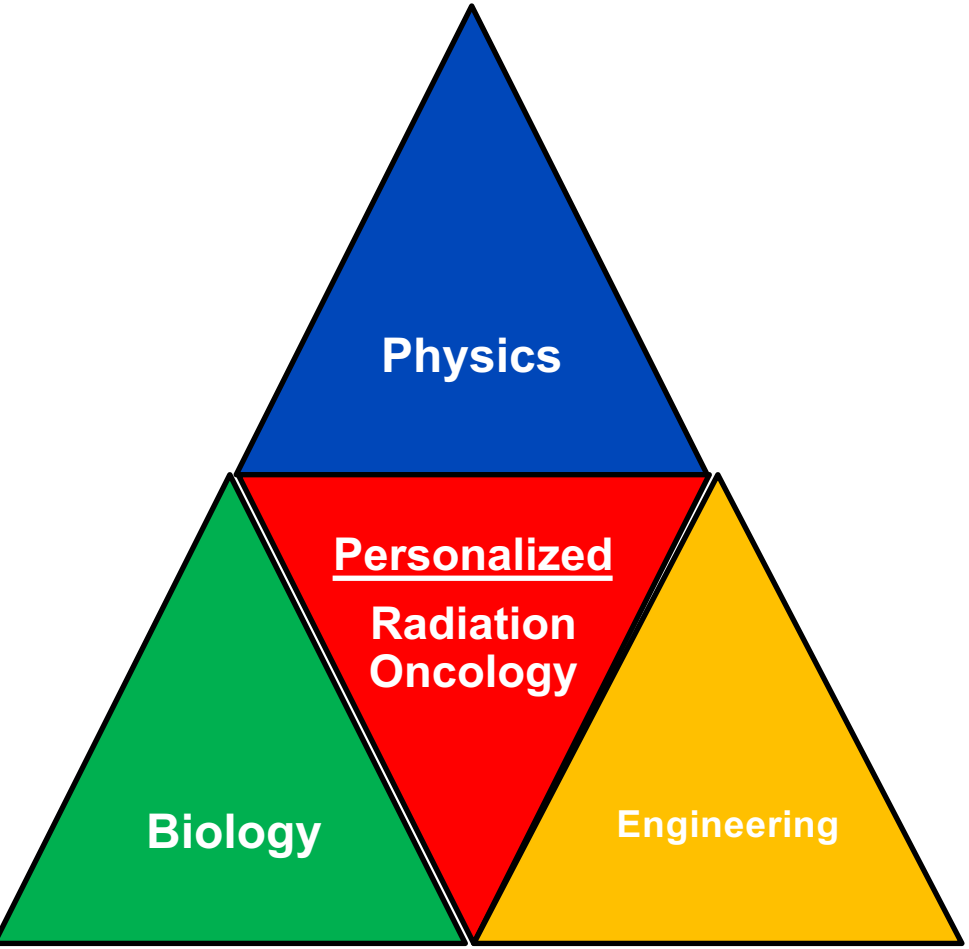
GSI – Darmstadt/Heidelberg Hospital, Germany



Chordoma Patients 5-Year Local Control
(source: Schulz-Ertner, Int J Radiat Oncol Biol Phys. 2007)

Research Directions in Ion Beam Therapy (IBT)

FUTURE: "Personalized" Radiation Therapy and IBT



"Non-Personalized"

- Patients with the same tumour disease and stage have typically received similar treatments
- Large clinical trials possible

"Personalized"

PHYSICS / ENGINEERING

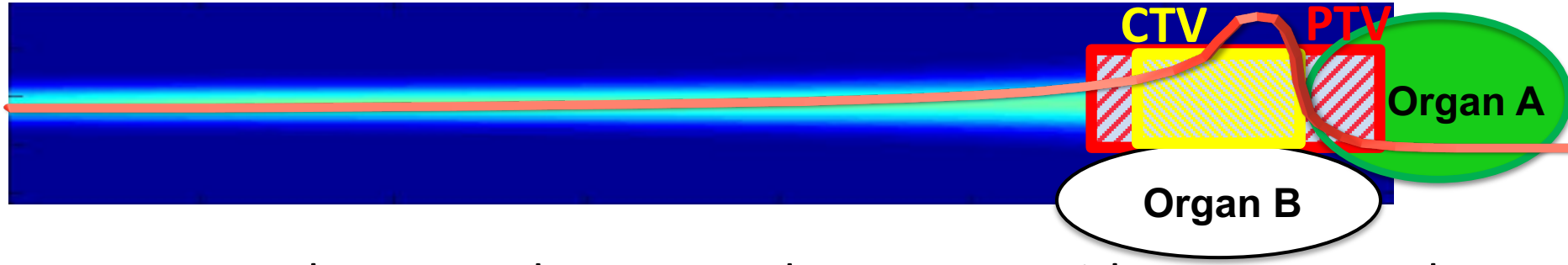
- **PRE-Treatment**
  - ❑ Dual Energy CT (DECT) for stopping power estimation and better estimation before treatment
  - ❑ Functional Imaging with PET-MRI for better staging
- **DURING-Treatment**
  - ❑ Prompt Gamma real-time Range Monitoring
  - ❑ FLASH Radiation Therapy (also **BIO**)
  - ❑ Mini-Beams Radiation Therapy (also **BIO**)
  - ❑ Adaptive Radiation Therapy with in-room 4D MRI
- **POST-Treatment**
  - ❑ Improved follow-up with PET-MRI or Whole Body PET to evaluate treatment response. (also **BIO**)

BIOLOGY

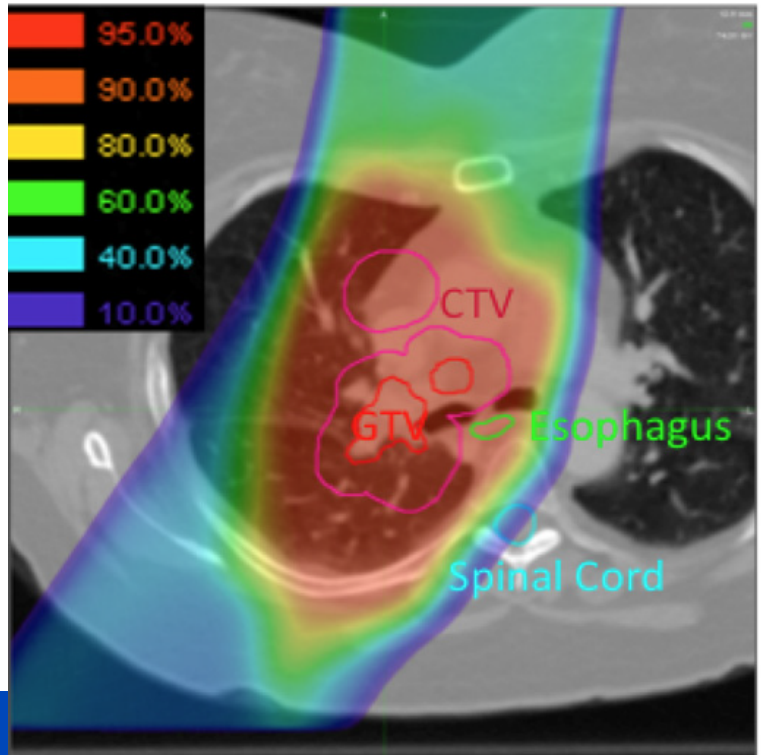
- **PRE-Treatment**
  - ❑ Genetic/Epi-Genetic Characterization and stratification of Tumor using biopsies or liquid-biopsies;
  - ❑ Whole-Body PET for improve tumor staging for Hypoxia and radio-resistant regions within tumor. “Novel Tracers”
- **DURING-Treatment**
  - ❑ During treatment functional characterization of Tumor to allow early treatment response assessment;
  - ❑ During treatment liquid-biopsy for genetic/epi-genetic characterization to assess treatment impact.
- **POST-Treatment**
  - ❑ Improved follow-up with PET-MRI and other functional imaging technology to evaluate treatment response.

"Bragg Peak" Range Uncertainty

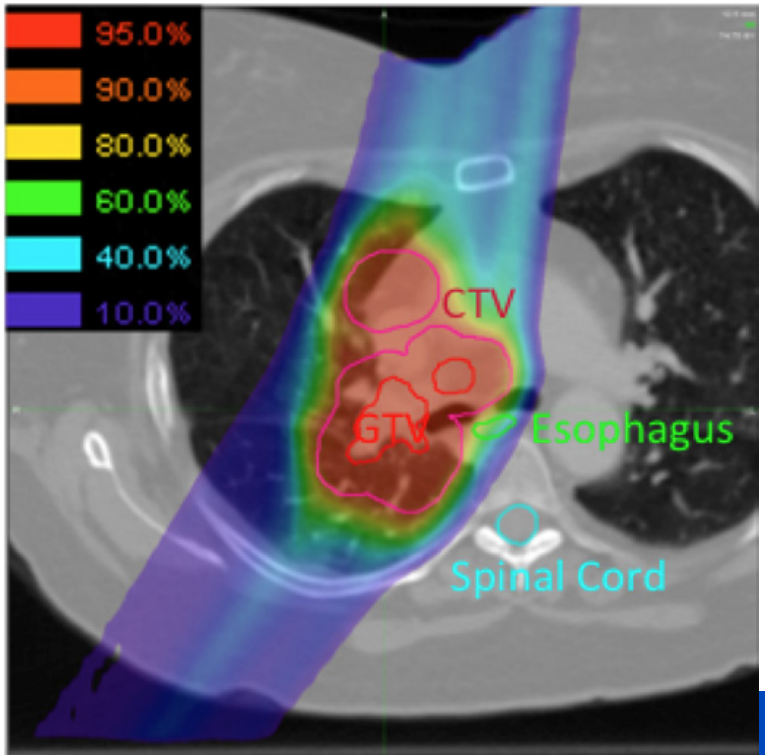
To treat the TUMOR (CTV) I need a dose distribution that's larger (PTV)



Proton therapy today…

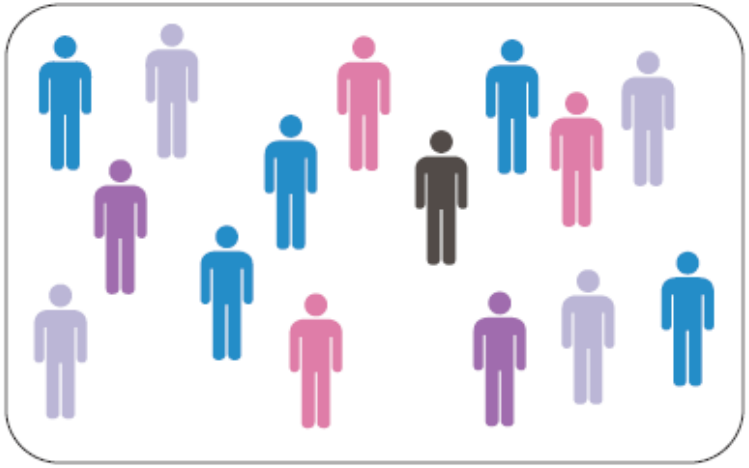


and tomorrow with range control



BIOLOGY

Exploiting Biological Knowledge to Stratify Patient Population



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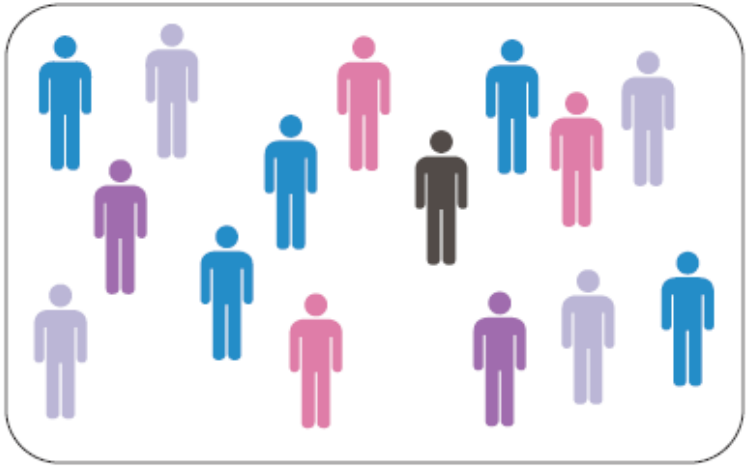

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- Biomarkers allow stratification into small subgroups
- Trials for treatment individualization

Exploiting Biological Knowledge to Stratify Patient Population

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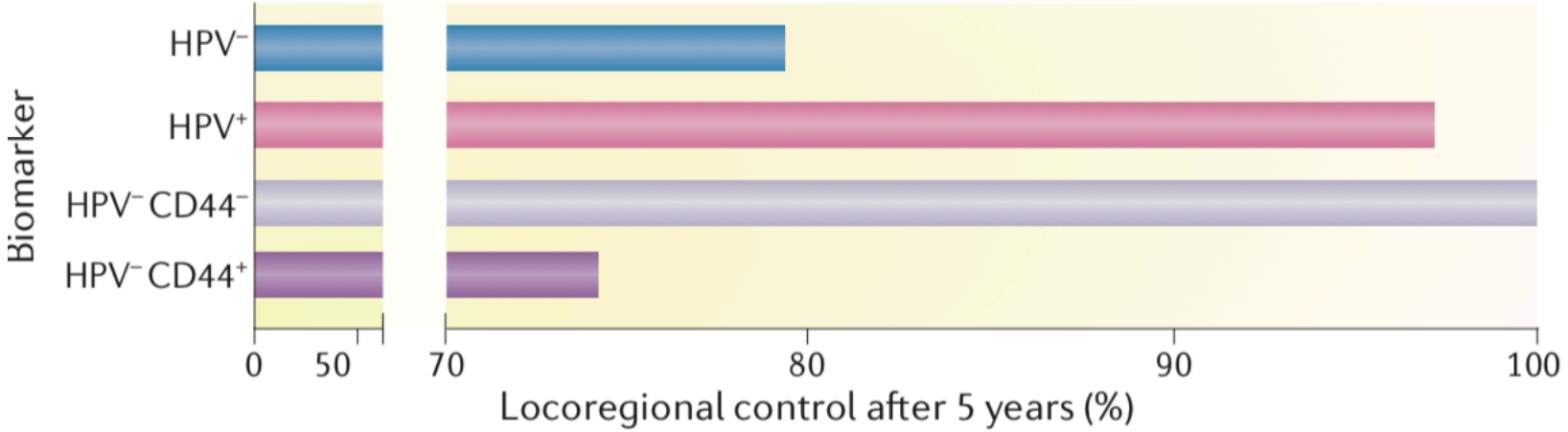
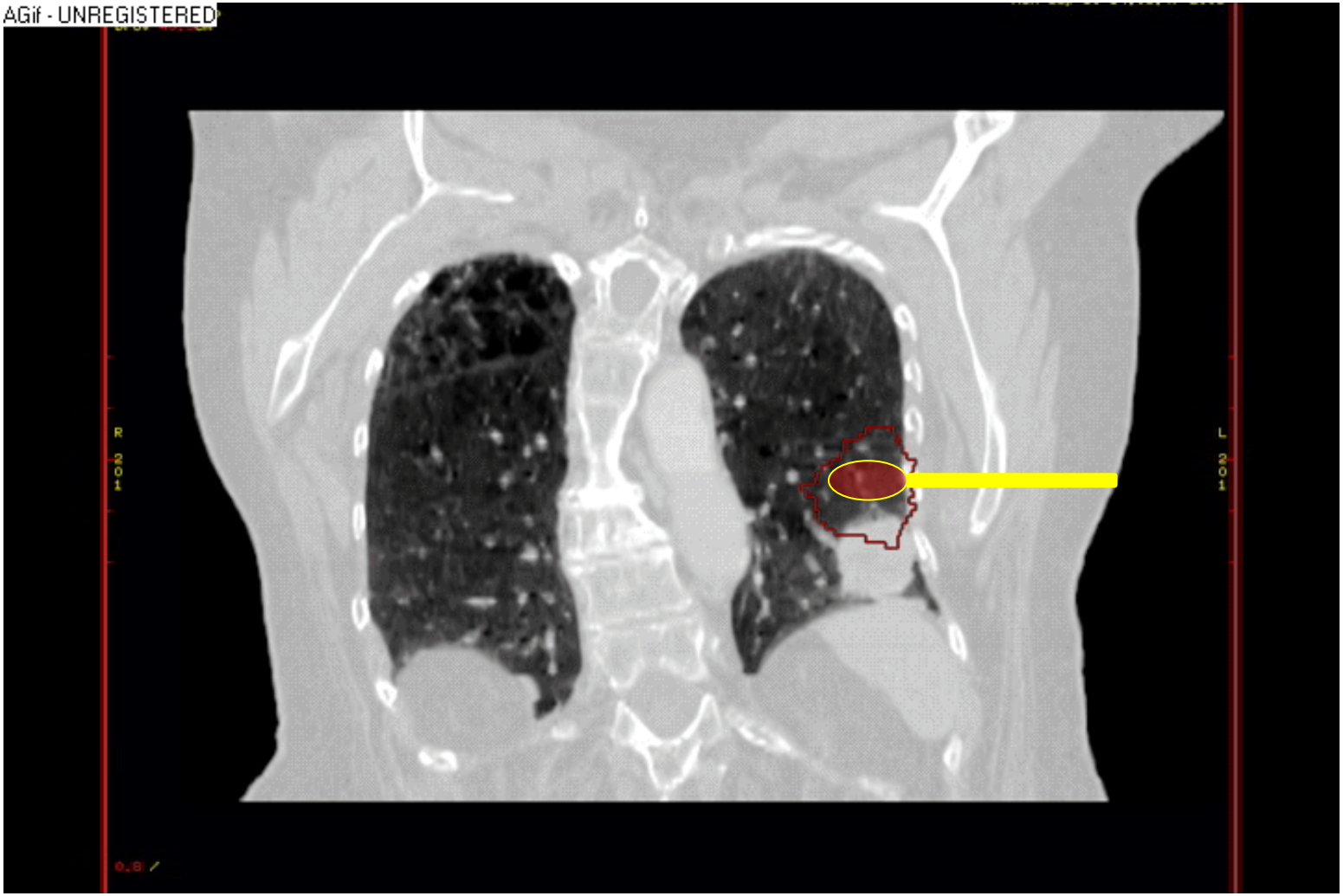
HPV - Human PapillomaVirus, CD44 - STEM Cell Marker



ENGINEERING

Addressing Movement of Tumors during Treatment

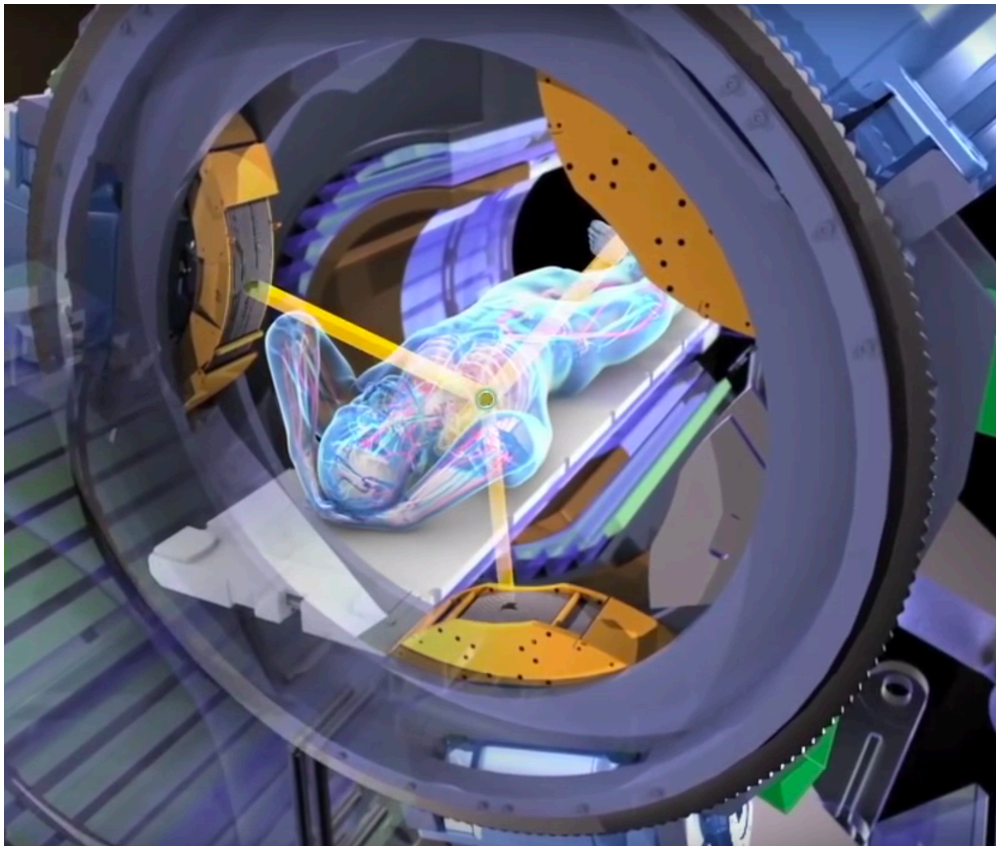
4D CT of Moving Lung Tumor



ENGINEERING

Addressing Movement of Tumors during Treatment

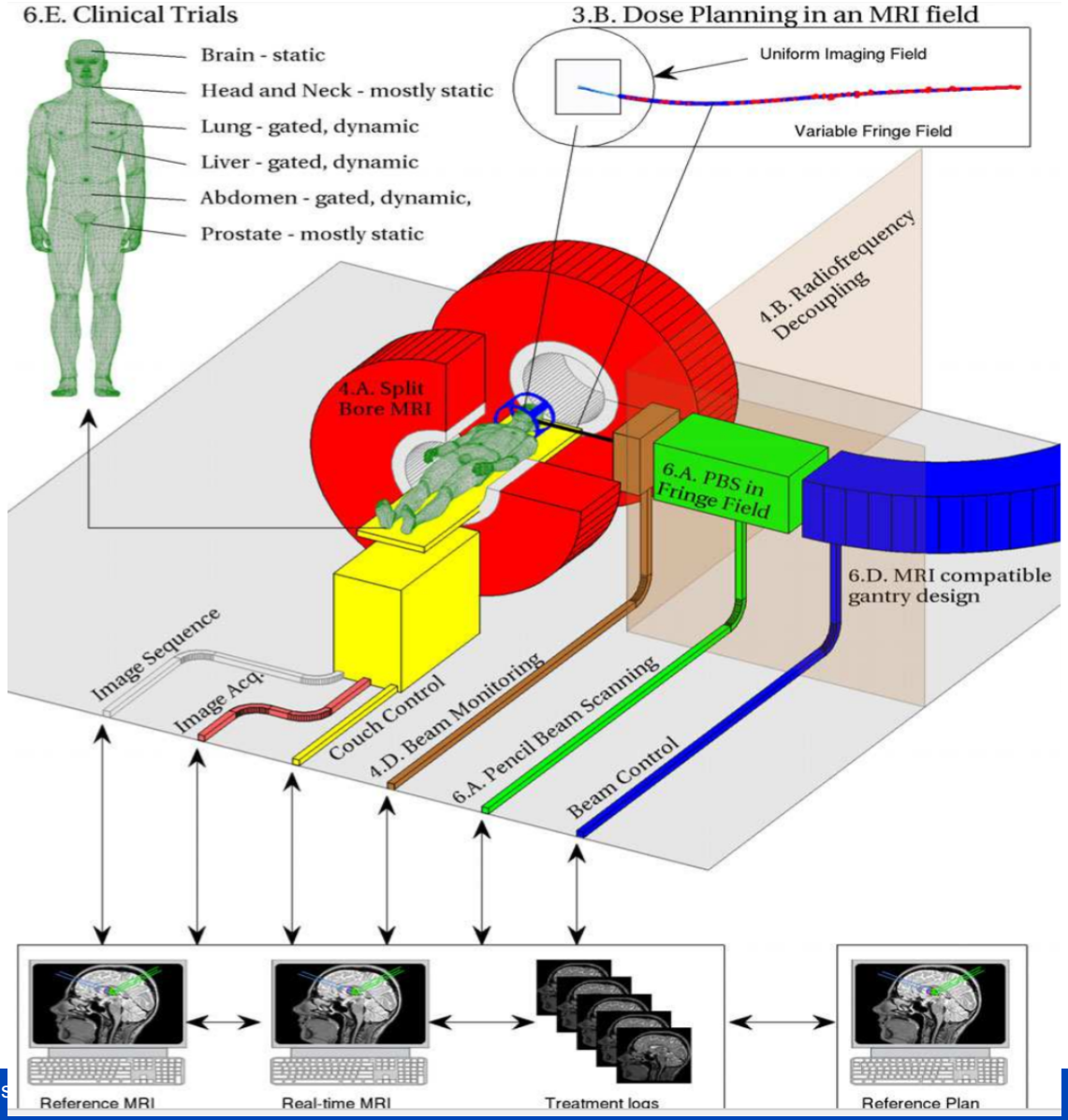
ViewRay MRIdian



MRI of Moving Liver/Lung

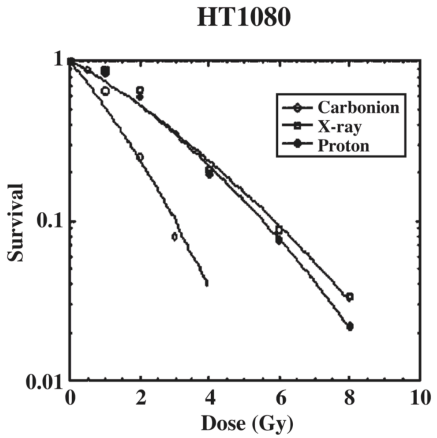
ENGINEERING

Addressing Movement with Proton MRI

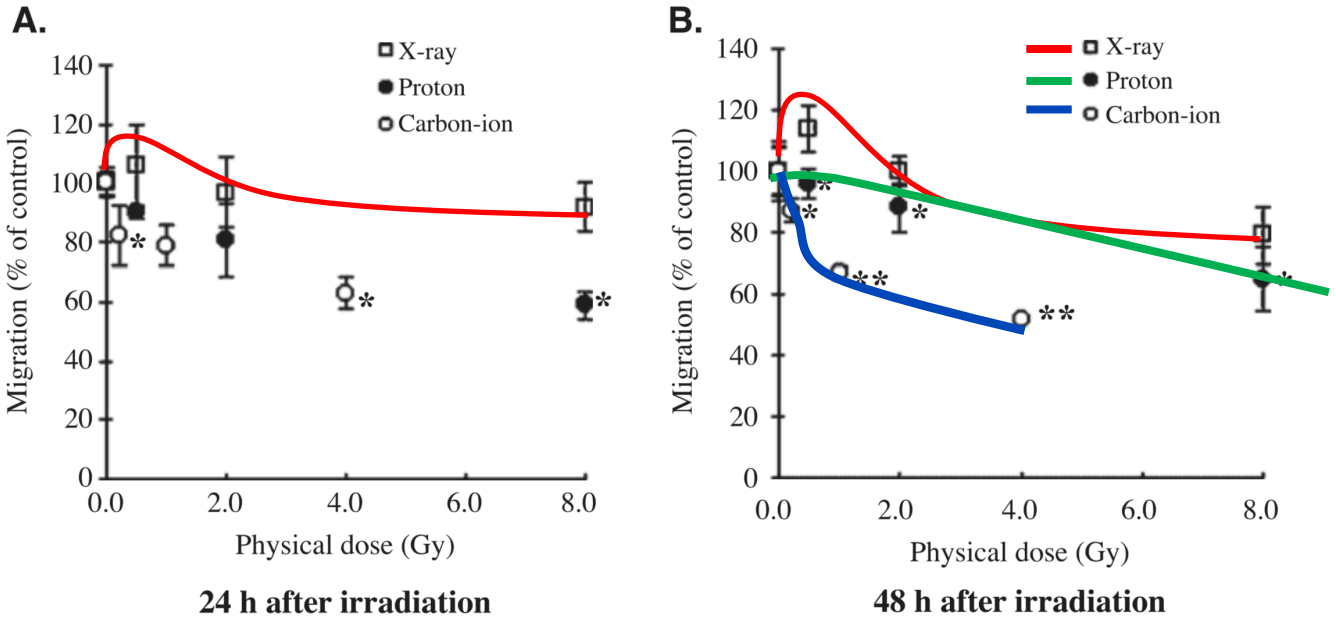


BIOPHYSICS

1) Reducing Metastastic/Migration Capacity



HT1080
Human
Fibrosarcoma

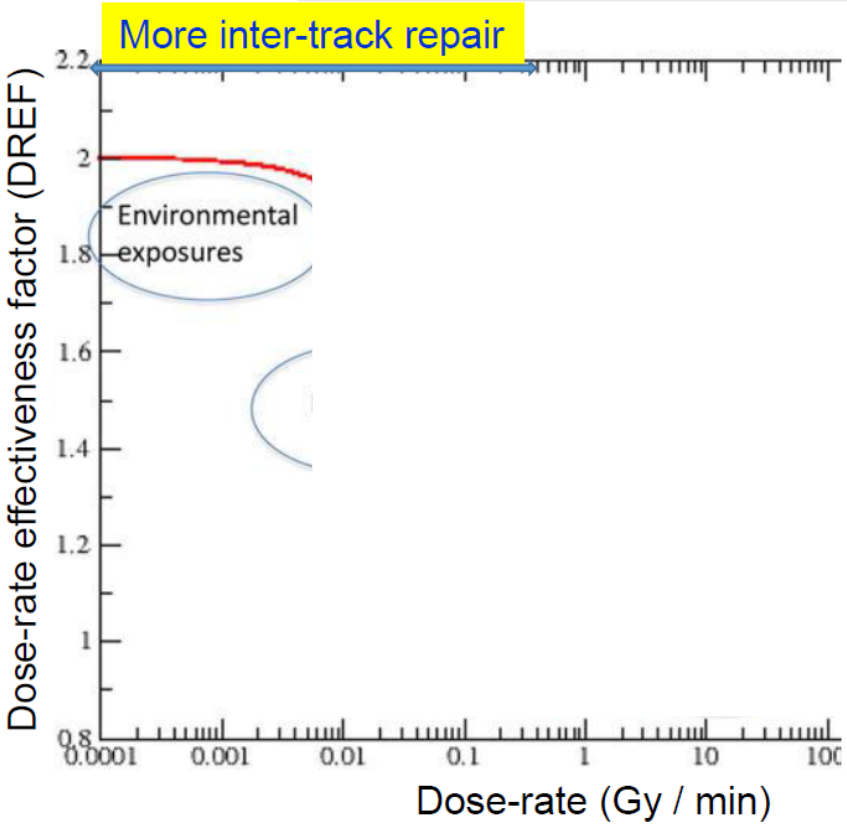


Ogata, et al. Particle irradiation suppresses metastatic potential of Cancer Cells. Cancer Res.. 2005, 65(1)

BIOPHYSICS

2) FLASH Radiation Therapy

Dose Rates Effects



Durante *et al.*, BJR 2018, **91**: 20170628

FLASH: Reduces Normal Tissue Toxicity

- **4.5 MeV electron** or γ-ray irradiated thorax of C57/B6 mice
- The two radiation qualities had similar effectiveness in lung fibrogenesis when delivered at the same **conventional dose rate of 1.8 Gy min^{-1}**.

Favaudon et al., Sci Trans Med 2014; Commentary in Durante et al., BJR 2018

Building Evidence for FLASH

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journal homepage: www.clinicaloncologyonline.net

Overview

Biological Benefits of Ultra-high Dose Rate FLASH Radiotherapy: Sleeping Beauty Awoken

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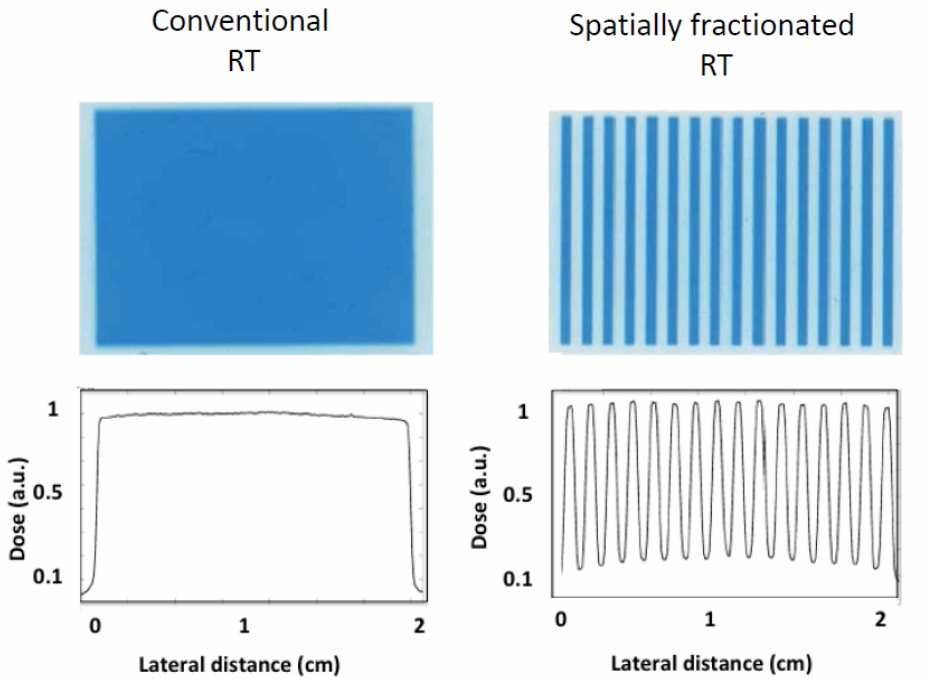
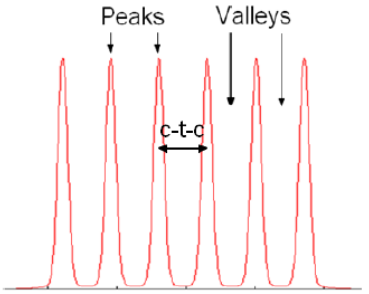
Table 1
In vivo studies of FLASH response for various normal tissues

Dose (Gy) at conventional dose rates	FLASH dose rate (Gy/s)	Dose modifying factor	System	Anaesthetic	Assay	Reference
Normal tissues						
11.9	17–83	1.3	Mouse intestine	Nembutal	LD50/5	[3]
14.7	70–210	1.3–1.24	Mouse intestine	?	LD50/5	[14]
24	56–83	1	Mouse foot skin	Sodium amytal	Early and late reactions	[4]
50	17–170	1.6	Mouse tail skin	None	Necrosis ND50	[5]
22–34	300	≥1.36	Minipig and cat skin	General anaesthesia	Early and late reactions	[13]
15–17	40	1.3	Mouse lung	Ketamine/xylasine/ acepromazine	Fibrosis	[9]
10	100–10^6	1.4	Mouse brain	Isoflurane	Memory	[10] Montay-Gruel *et al.* (in revision)

BIOPHYSICS

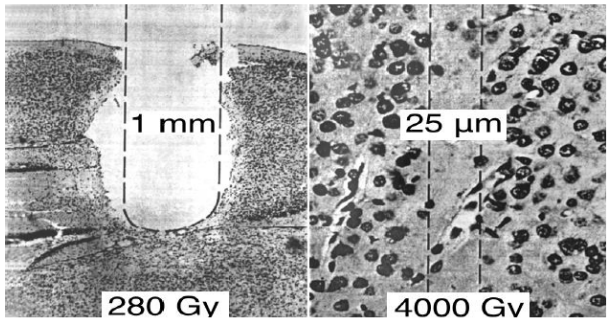
3) Mini-Beam Radiation Therapy



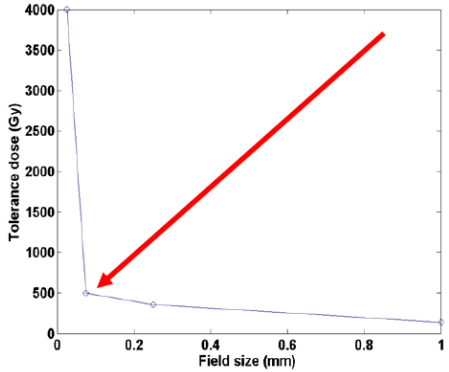


$$PVDR = \frac{D_{\text{peak}}}{D_{\text{valley}}}$$

Dose-volume effect: the smaller the field size is, the higher the tolerance

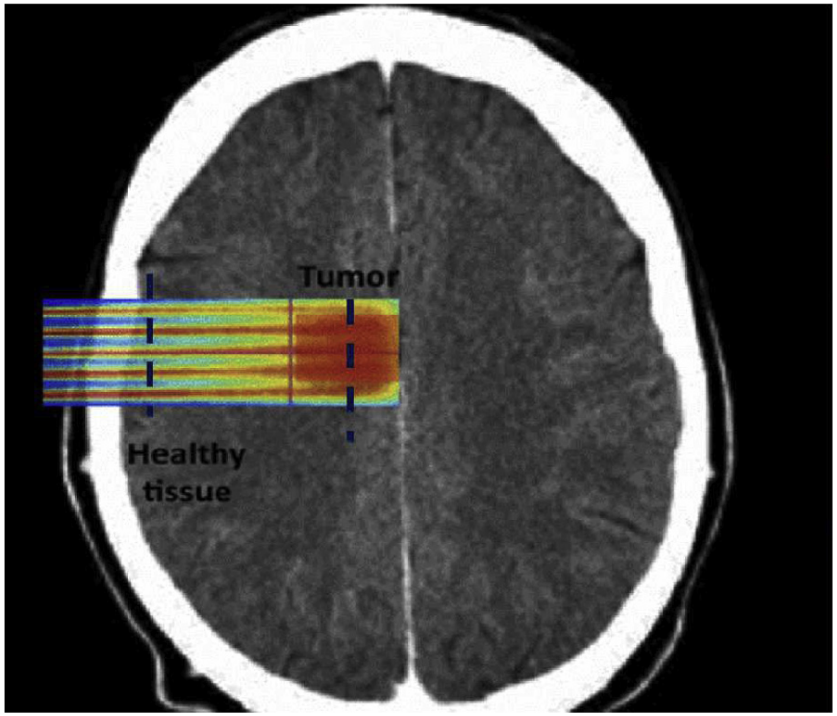


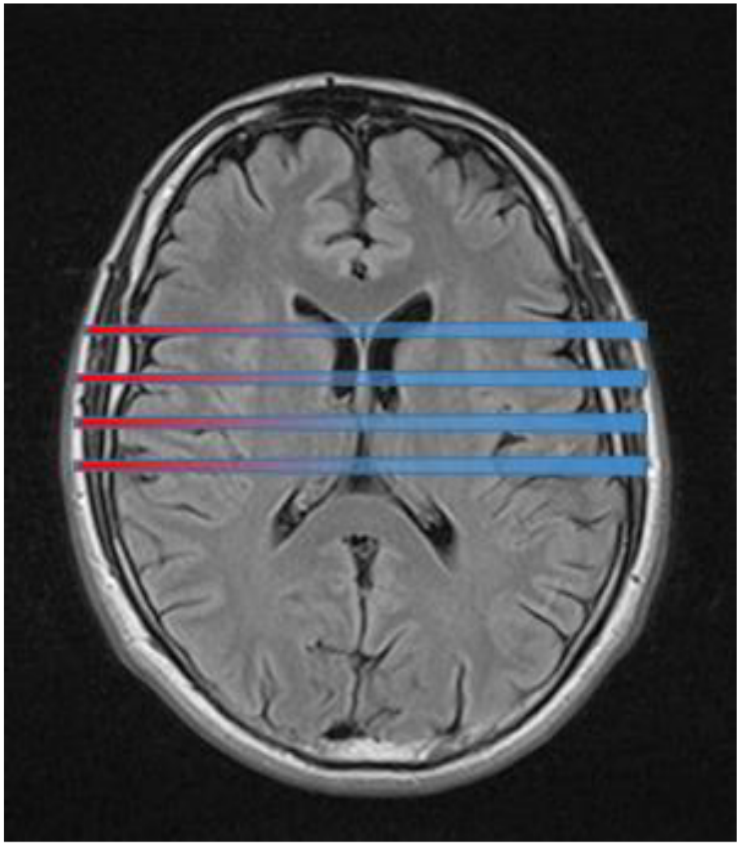
Zeman et al., Science (1959)



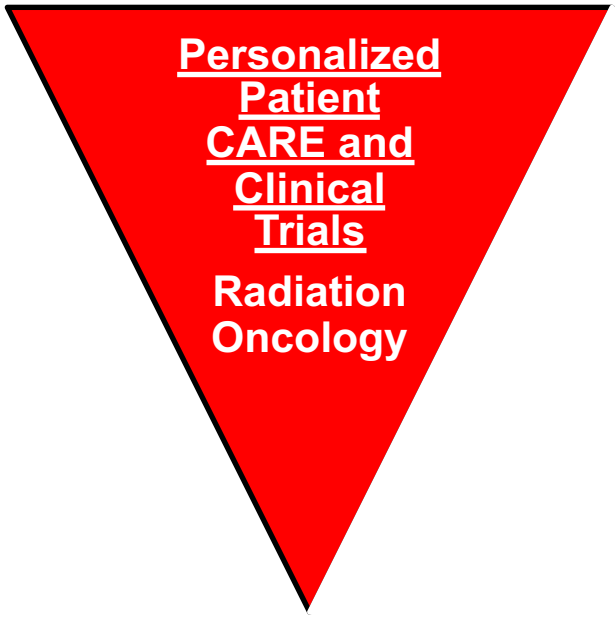
BIOPHYSICS

4) Mini-Beam Radiation Therapy





Conclusions: 20 Year Vision Ion Beam Research



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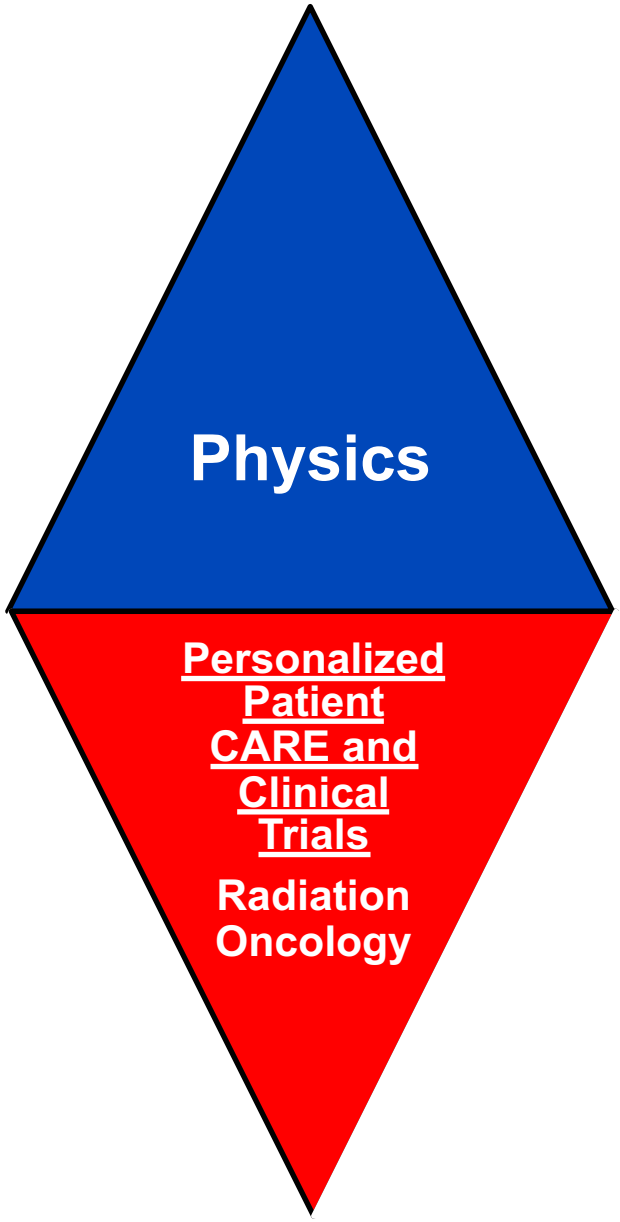
Conclusions: 20 Year Vision Ion Beam Research

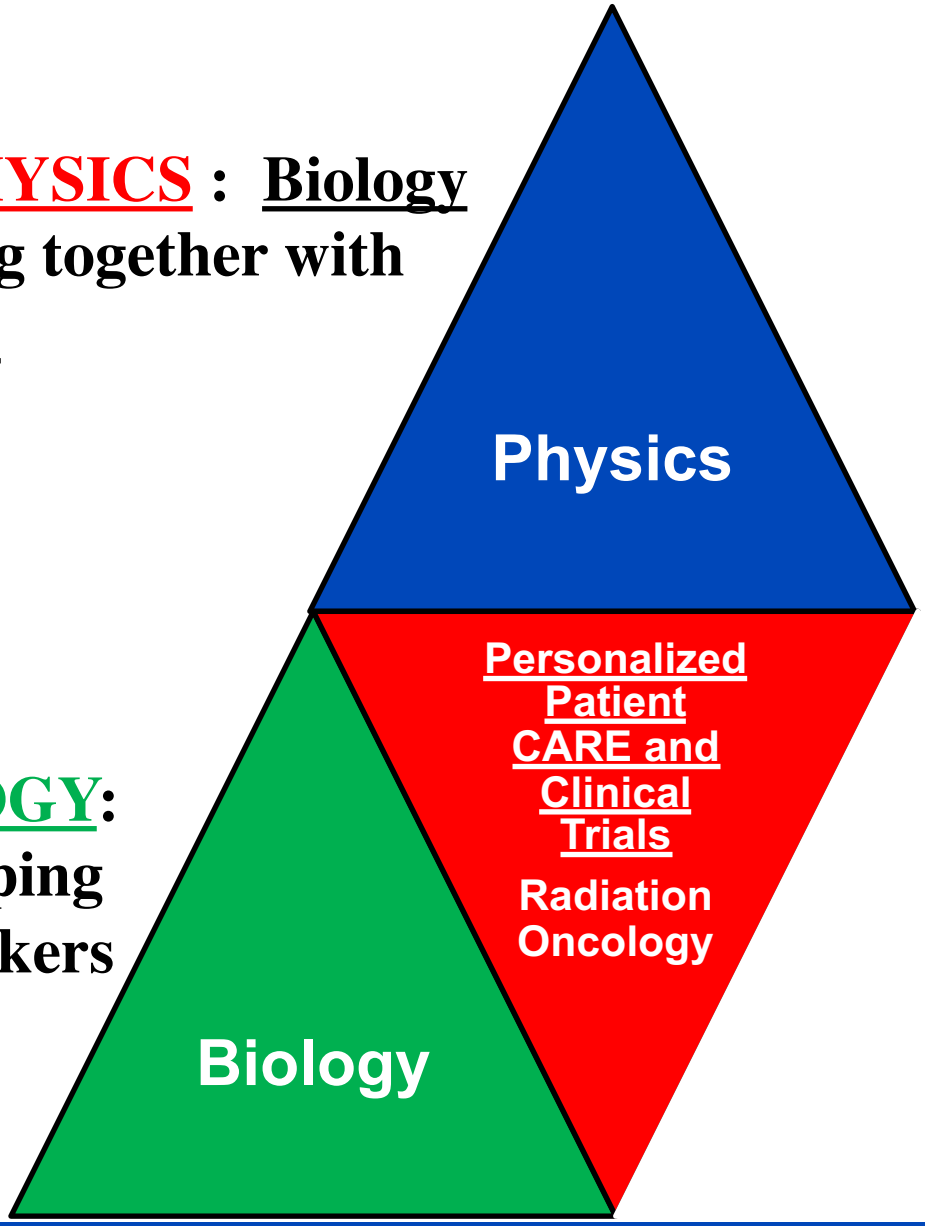


PHYSICS: Dealing with imaging and range issues real-time during treatment

Conclusions: 20 Year Vision Ion Beam Research

BIOPHYSICS : Biology working together with Physics

BIOLOGY: Developing biomarkers



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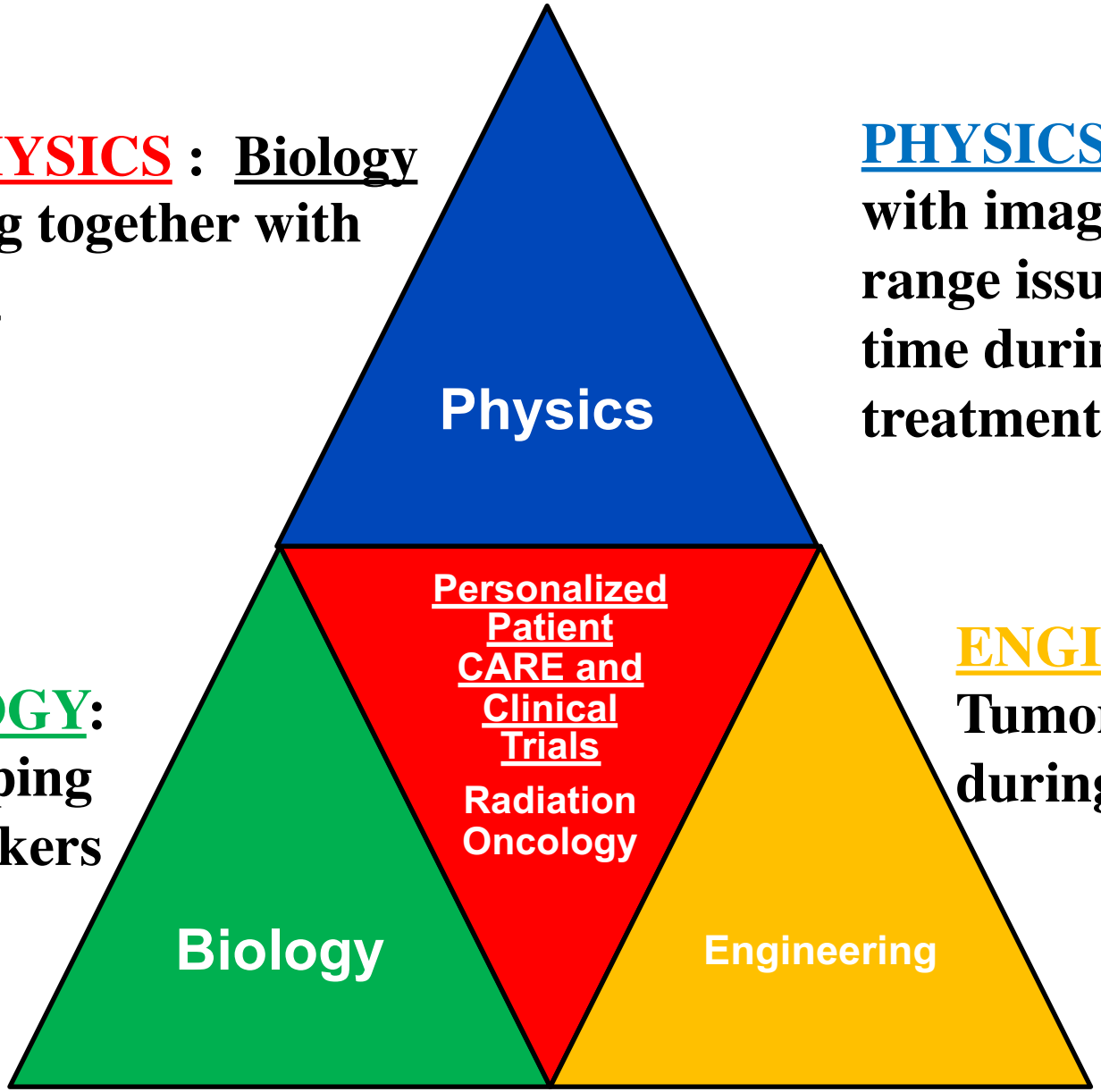
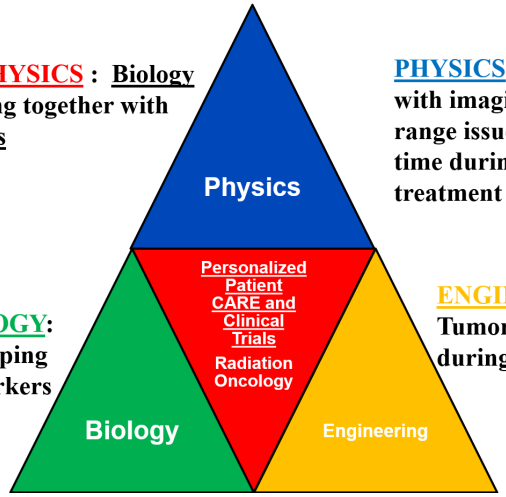


BIOLOGY: Developing biomarkers

ENGINEERING: Tumor Movement during Treatment

BIOPHYSICS : **Biology** working together with **Physics**

PHYSICS: Dealing with imaging and range issues real-time during treatment

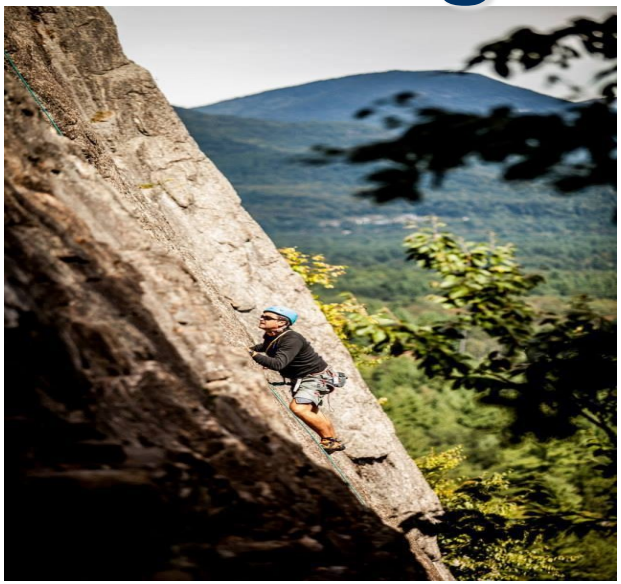


BIOLOGY: Developing biomarkers

ENGINEERING: Tumor Movement during Treatment

DKFZ Group

Relaxing!



Thank You for Your Attention ☺

QUESTIONS….

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