FLASH sciences lab @Stanford
biology+physics+engineering | PI: B Loo

Stanford MEDICINE | Department of Radiation Oncology

Clinical perspective of VHEE

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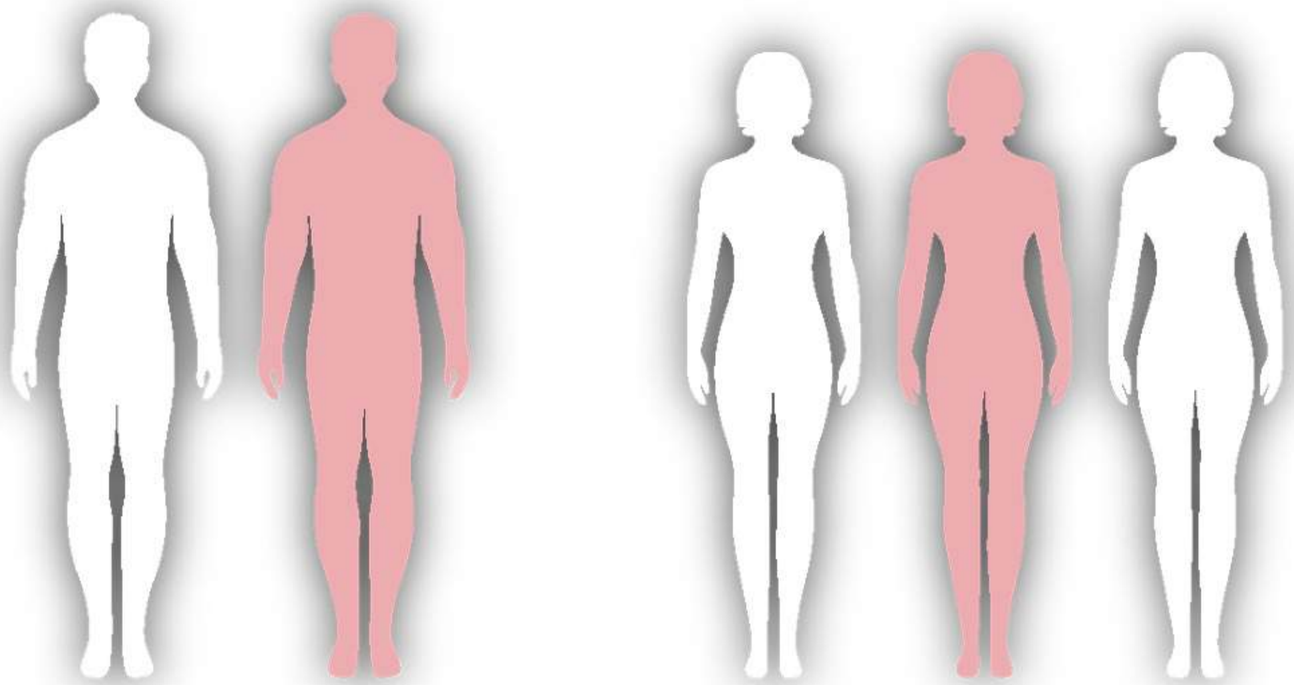
@BLoo_LT_SABR
#FLASH_RT #PHASER

International Workshop on Very High Energy Electron Radiotherapy (VHEE'25)
Sept 15-17, 2025
STFC, Daresbury Laboratory

The problem

Cancer is the #1 single cause of global deaths

In the US, 2 in 5 people will get it



1 in 5 people will die of it

***c.f.*, American Cancer Society, Siegel *CA* 2024**

What does it take to ***cure cancer***?

- Elimination of cancer

- Survival of patient *without* unacceptable collateral injury

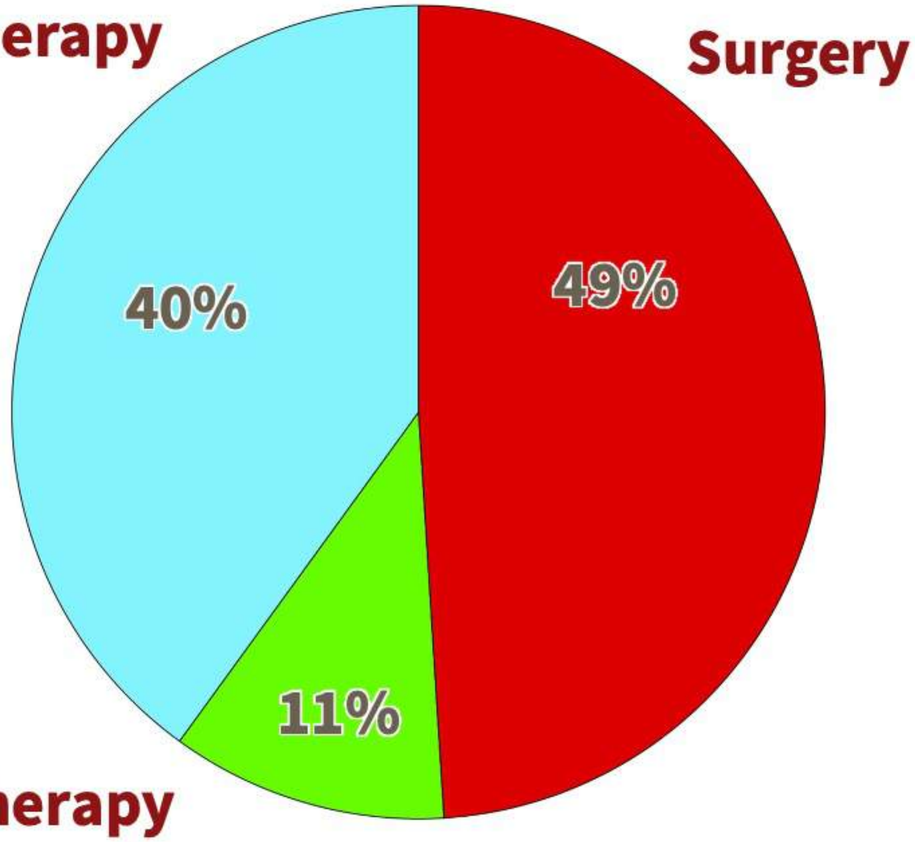
! *Cancer can **only** be cured if the treatment needed to eliminate the cancer **can be tolerated** by the patient*

Therapeutic precision:
Targeting cancer
Sparing normal tissue
(therapeutic index)

Precision targeted cancer therapy

In the US, **radiotherapy** is used to treat ~2/3 of patients with cancer, most with curative intent

Historically, radiotherapy has contributed to at least 40% of cures – growing with advances

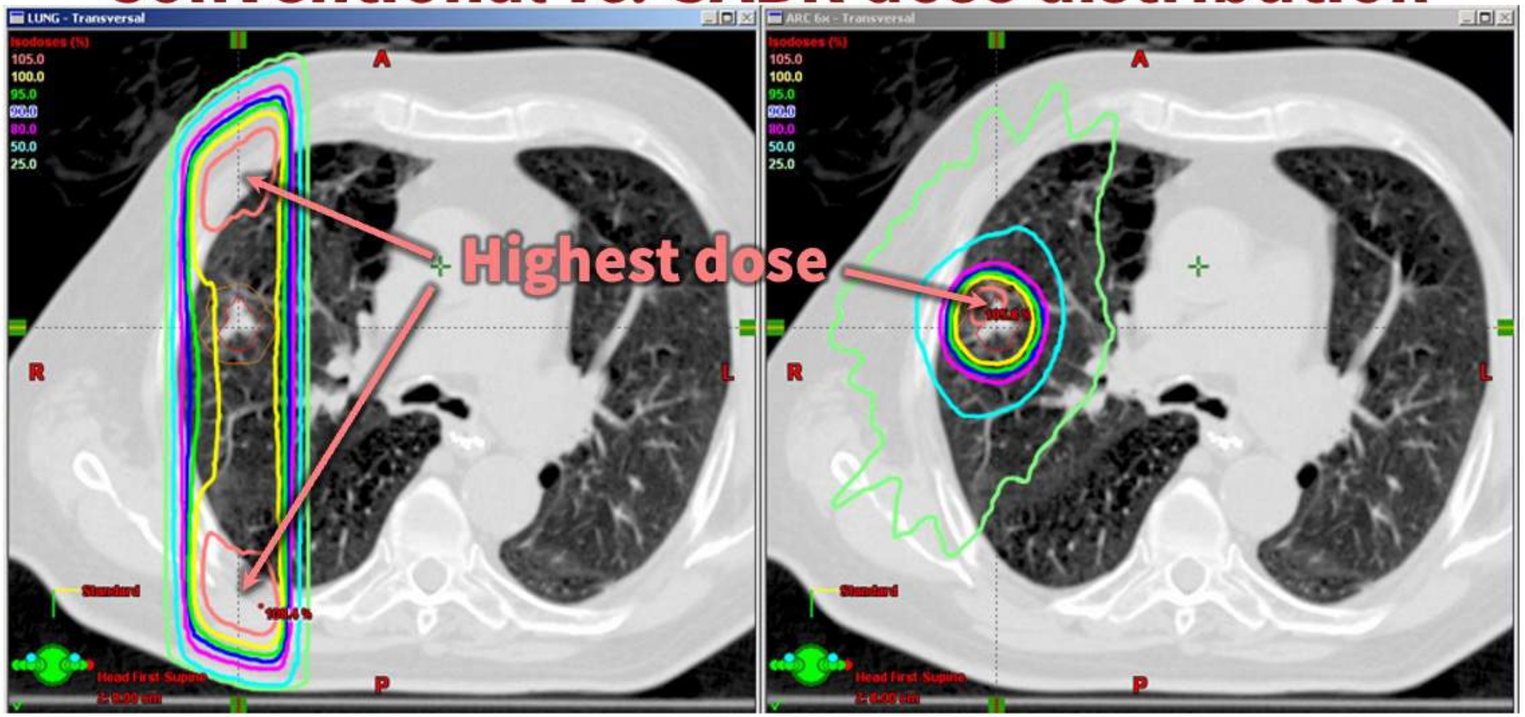


Mee *Br J Radiol* 2023

! *Breakthroughs in radiotherapy can revolutionize cancer therapy*

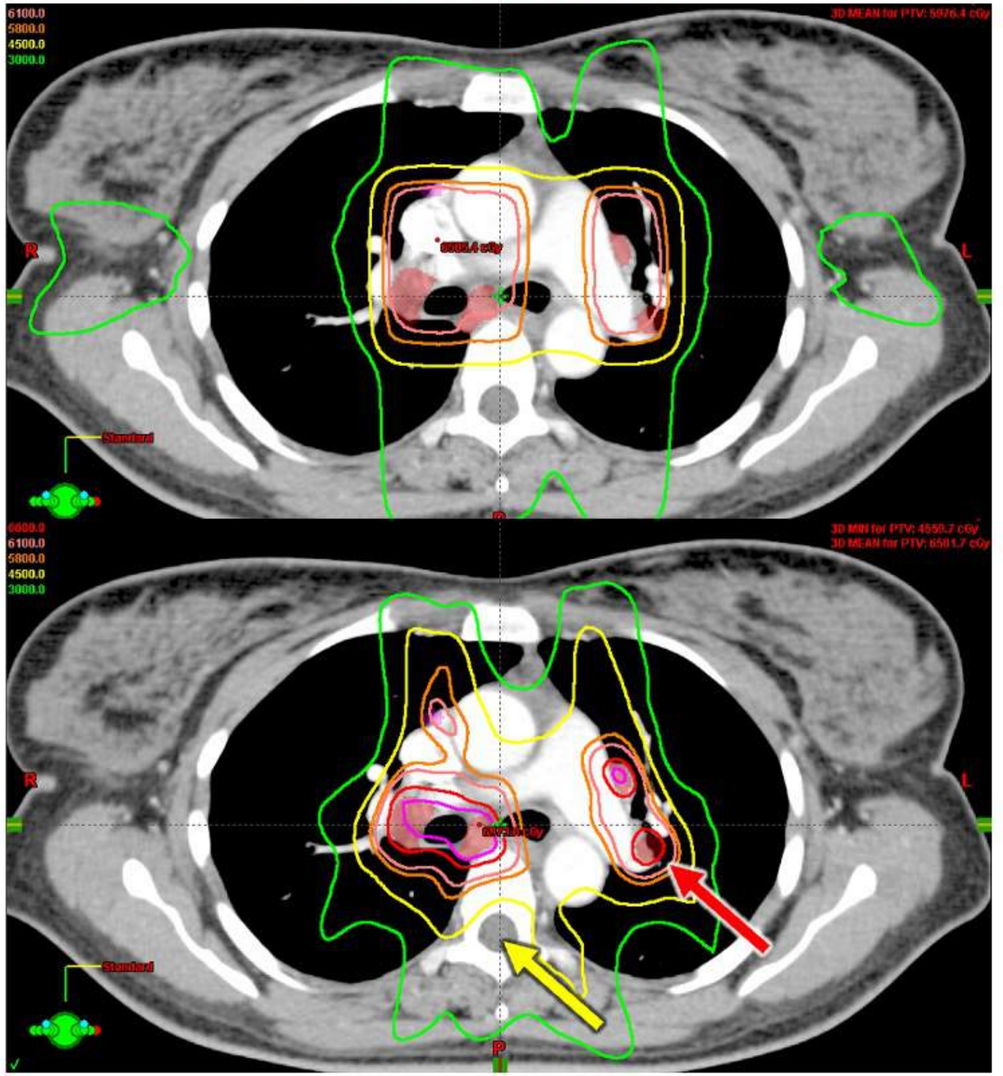
Precision radiotherapy

Conventional *vs.* SABR dose distribution



! *Major improvements in **therapeutic index** through **spatial precision***

Conformal RT

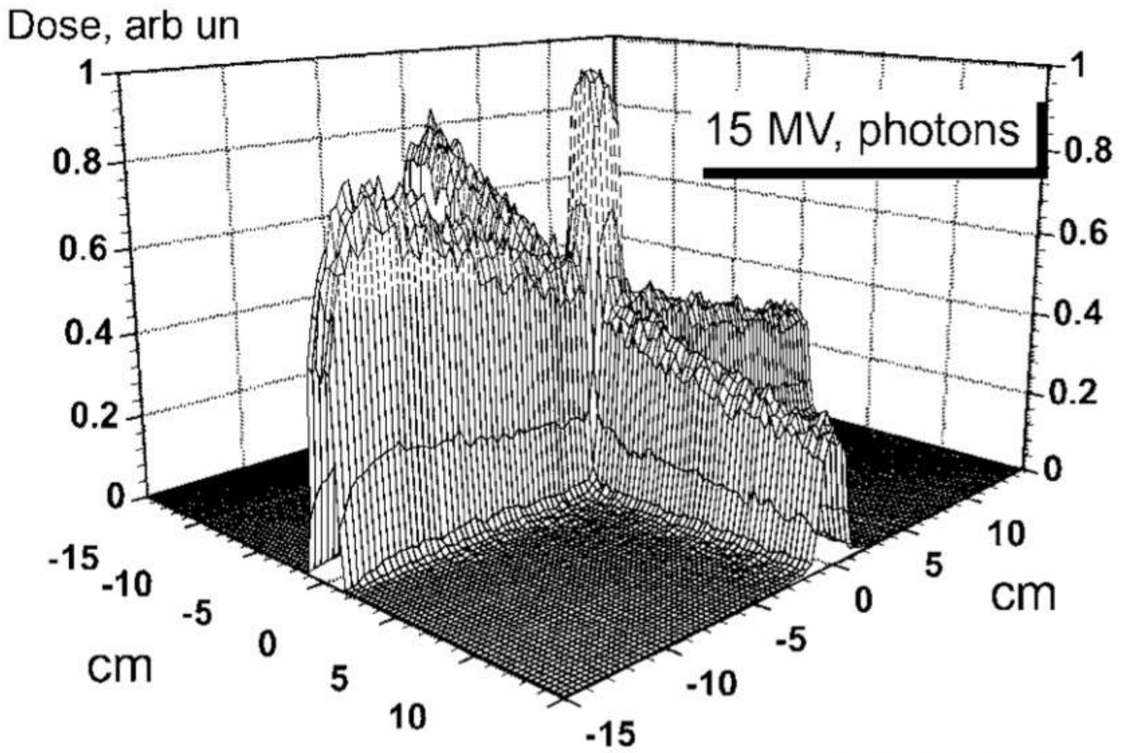


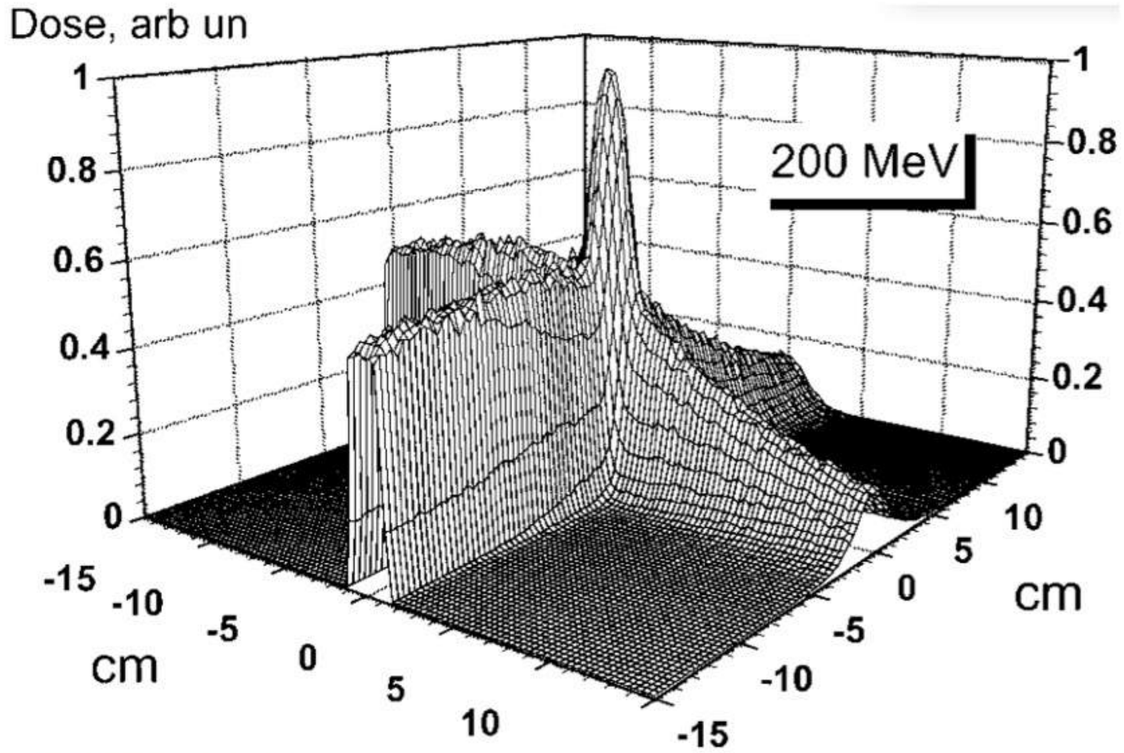
Highly conformal RT

Rationale for VHEE

Improved *depth dose* of very high-energy electrons (VHEE) *vs.* photons

Also less sensitive to electronic disequilibrium, sharper lateral penumbra





DesRosiers *Phys Med Biol* 2000

Debate over VHEE

POINT/COUNTERPOINT

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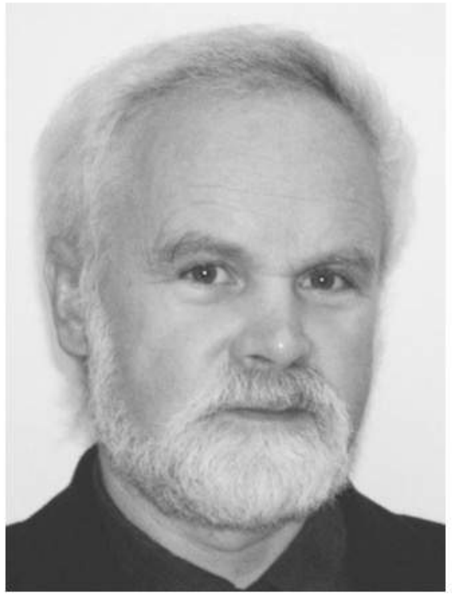
Very high energy electromagnetically-scanned electron beams are an attractive alternative to photon IMRT

Pro



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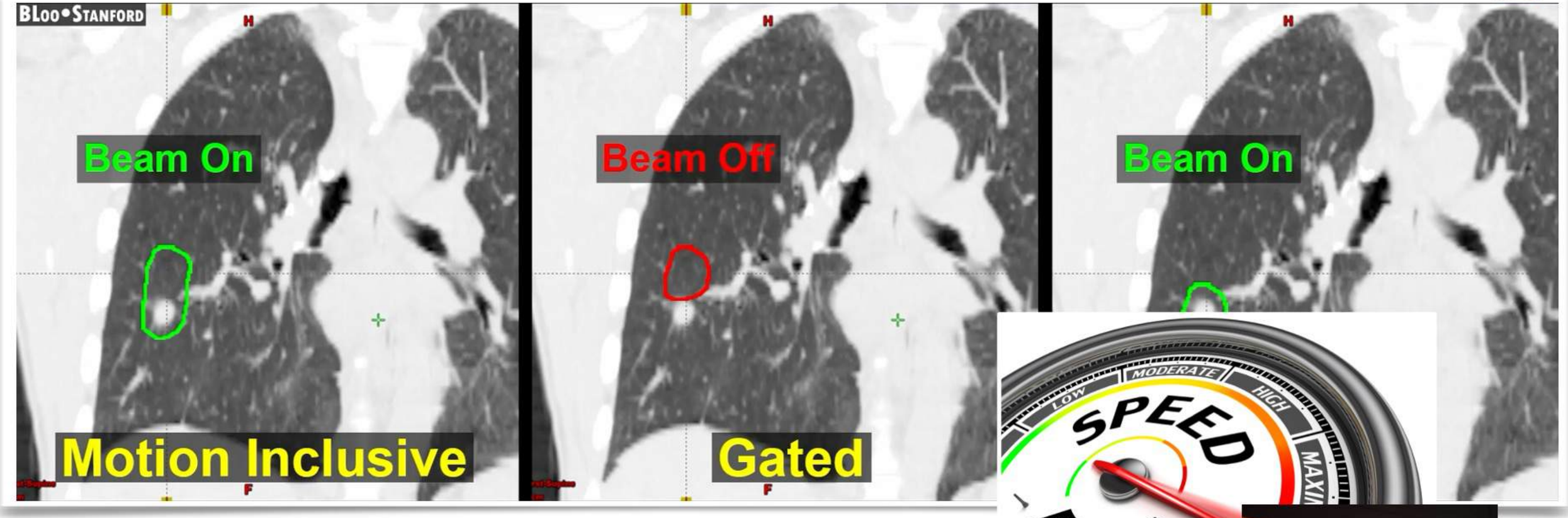
Con

Papiez: “fast-scanning VHEEB allows realistic, efficient solutions to problems of 4D image guided radiotherapy”

Papiez, Bortfeld *Med Phys* 2004

Precision – hitting moving targets

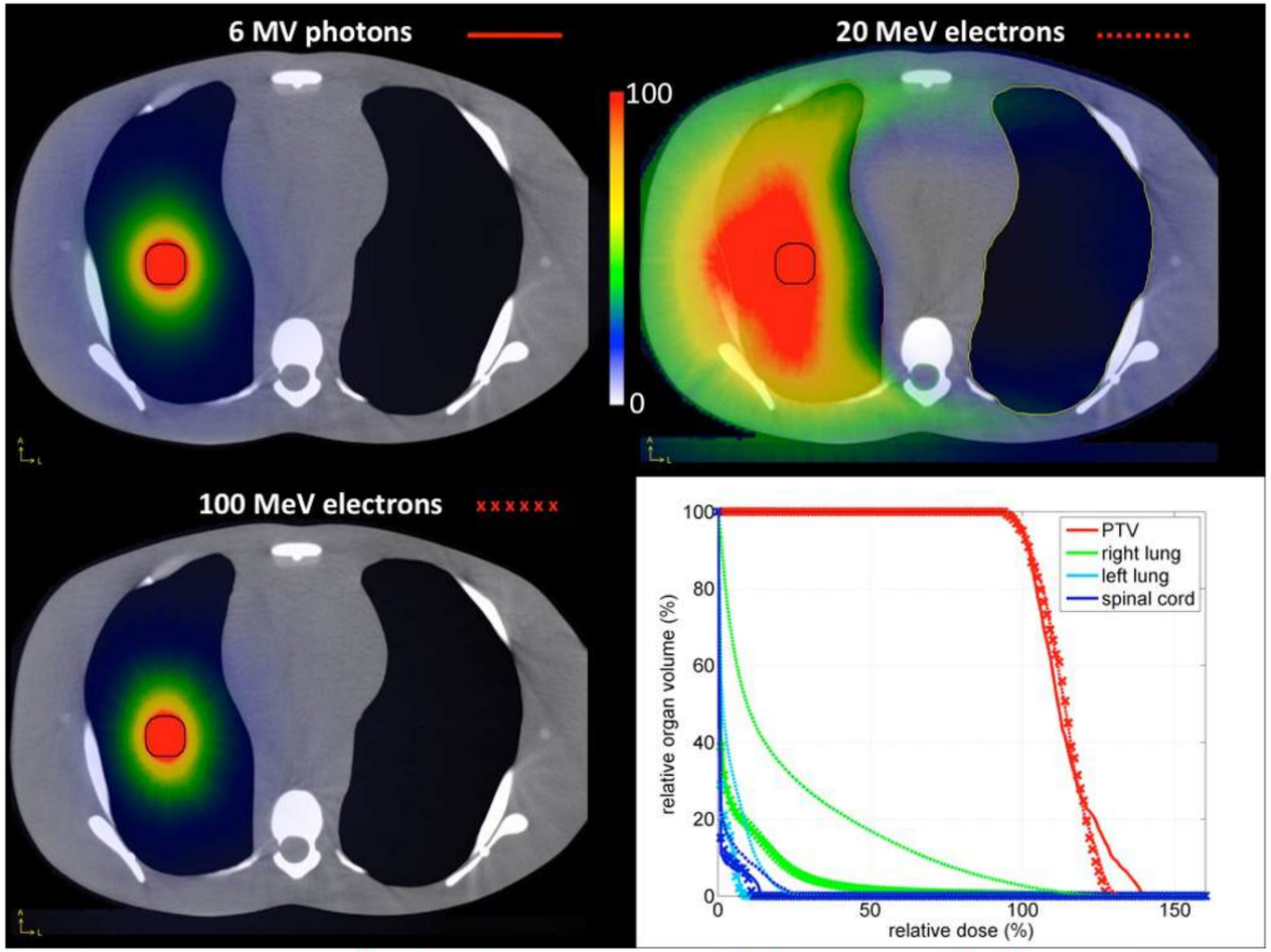
"Motion management"



Need. For. Speed.

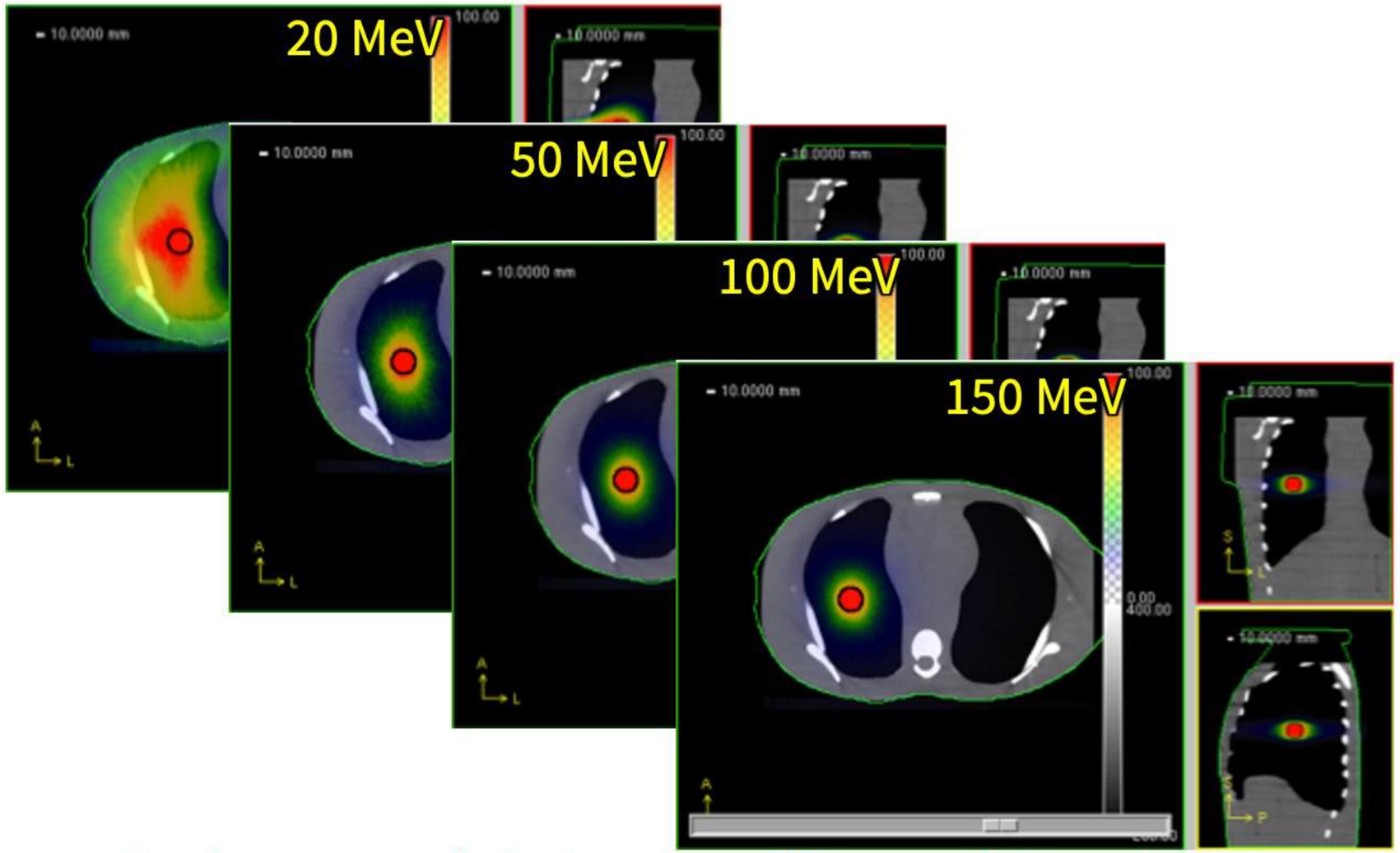
Instantaneous treatment to "freeze" motion

Preliminary VHEE simulations



Coplanar arc of electron pencil beams in lung target
(Monte Carlo simulation)

Preliminary VHEE simulations



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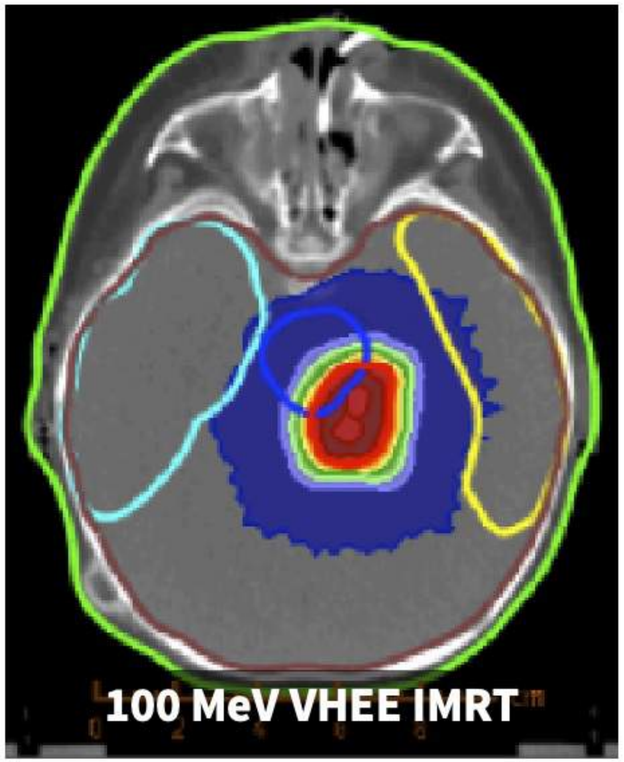
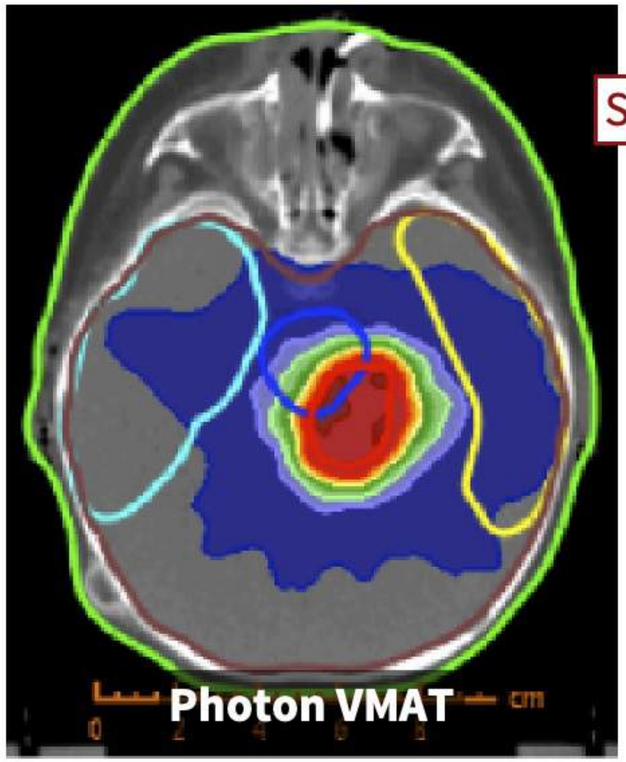
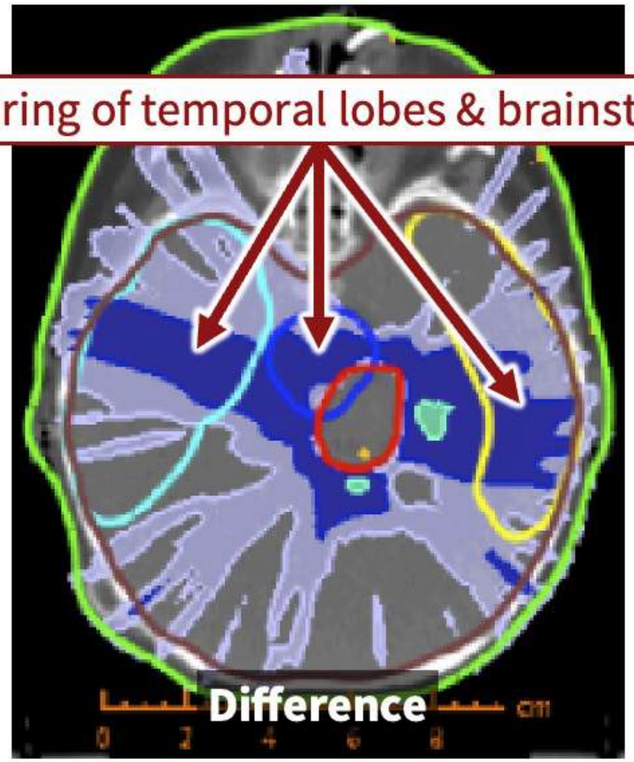
VHEE dose advantage

Superior dose distribution for VHEE: pediatric brain tumor







Inverse planned VHEE IMRT achieves complex dose shaping and compact dose, intermediate between photon and proton therapy

Bazalova-Carter *Med Phys* 2015

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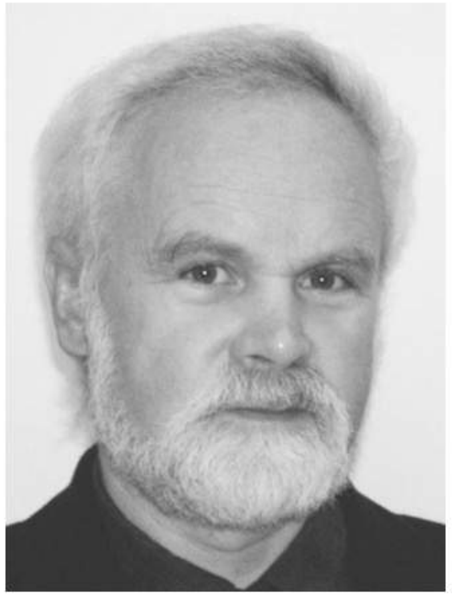

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(Tel: 617/724-1180, E-mail: tbortfeld@partners.org)

Con

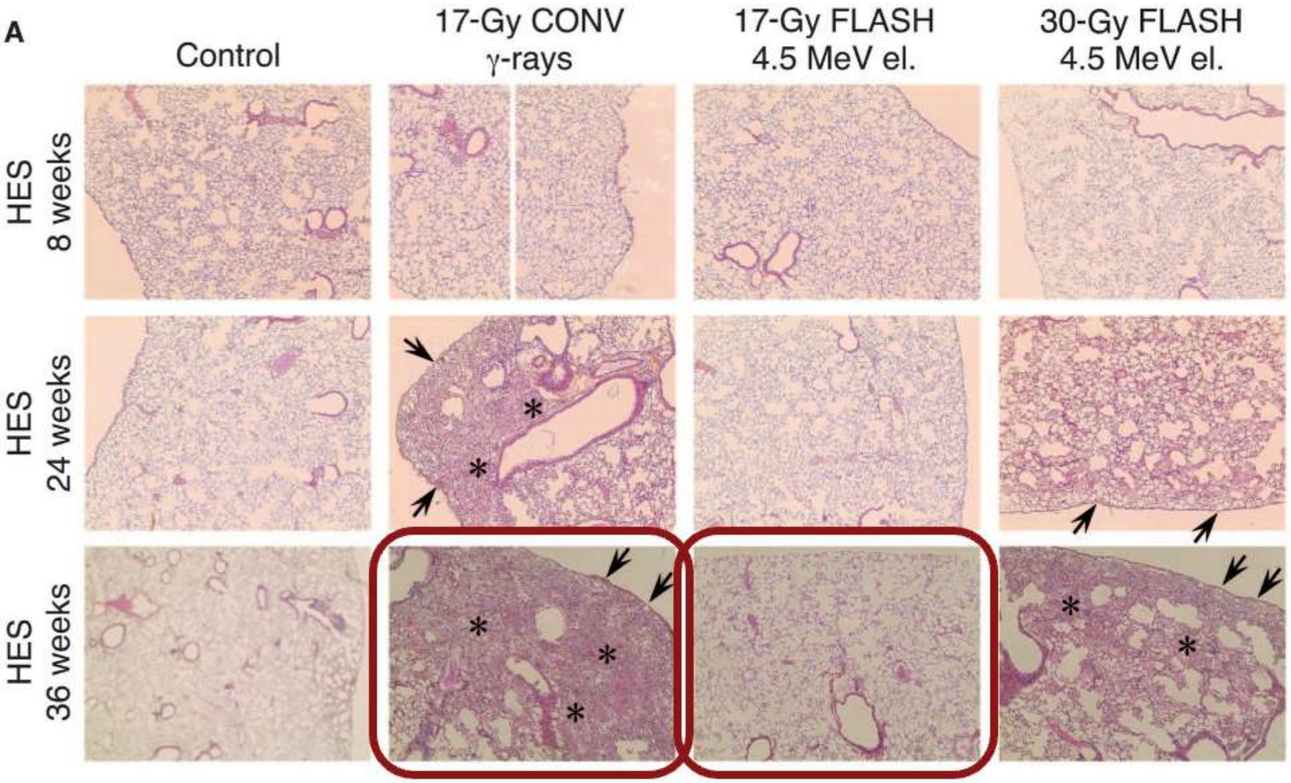
Bortfeld: "The potential of scanned VHEE therapy to deliver dose nearly instantaneously (dose rates of Gy/s) to a treatment volume might be characterized with one word: **scary**"

Papiez, Bortfeld *Med Phys* 2004

Ultra-rapid FLASH biology

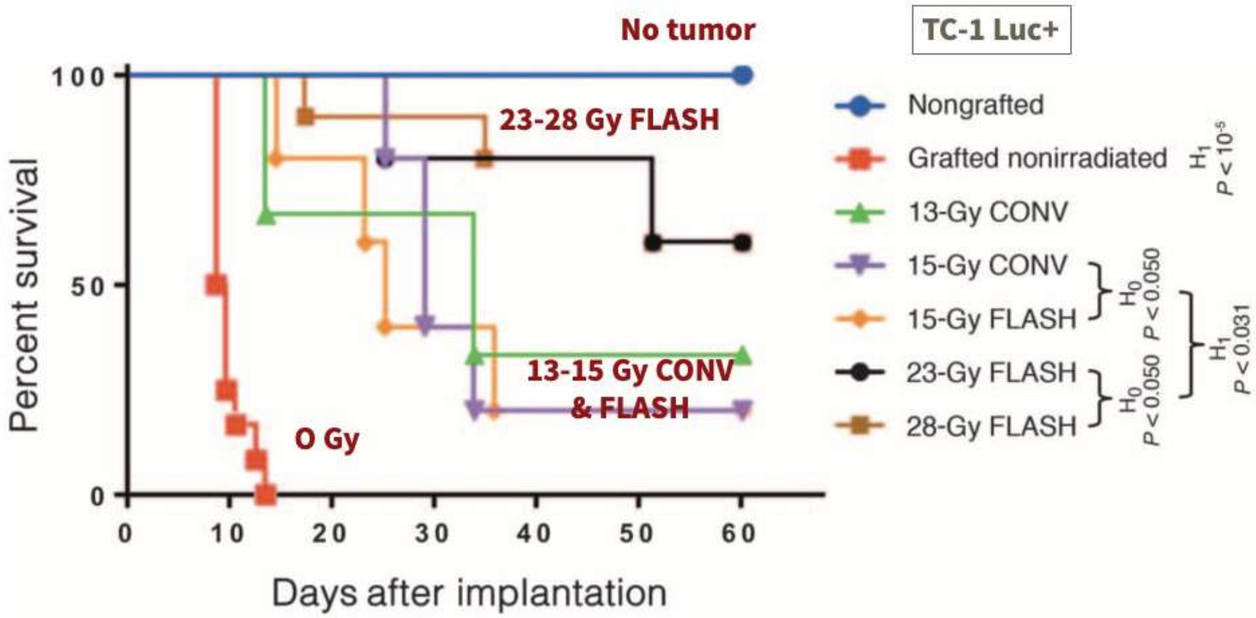
Normal organ sparing

Lung



Tumor control

Orthotopic lung tumors



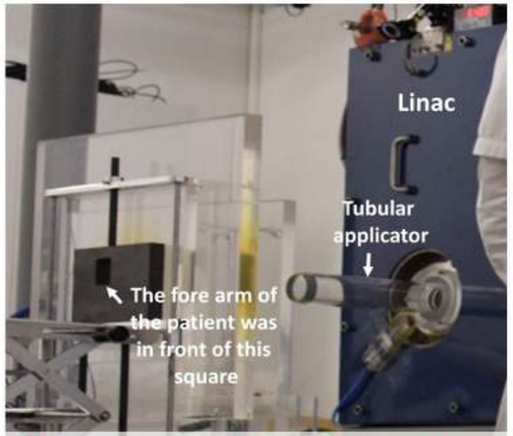
Syngeneic tumors in C57BL/6J mice

Favaudon/Vozenin *Science Translat Med* 2014

The Need for Speed

Clinical electron FLASH has begun

First in human case



15 Gy single fraction delivered in 90 ms

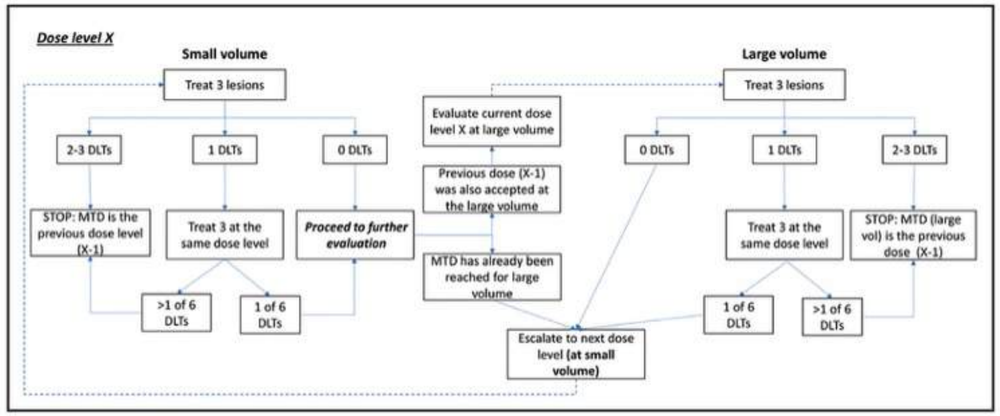
Day 0

5 months

Complete response
No toxicity

Bourhis *Radiother Oncol* 2019

CHUV Impulse phase I melanoma electron trial

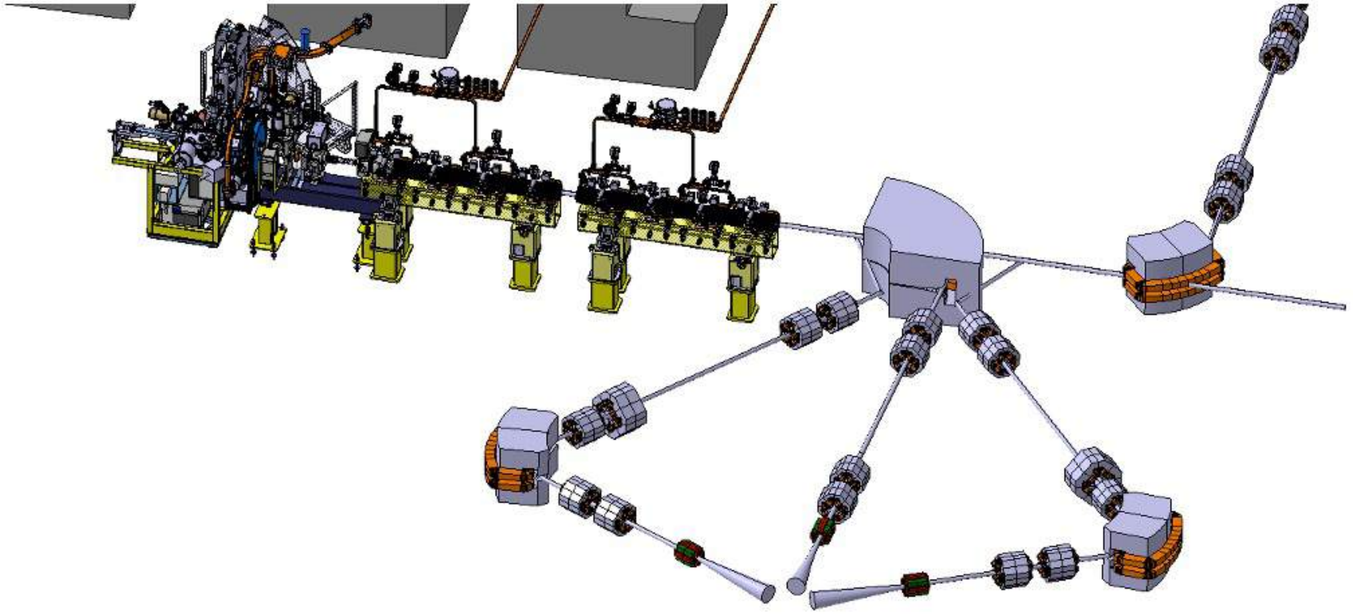


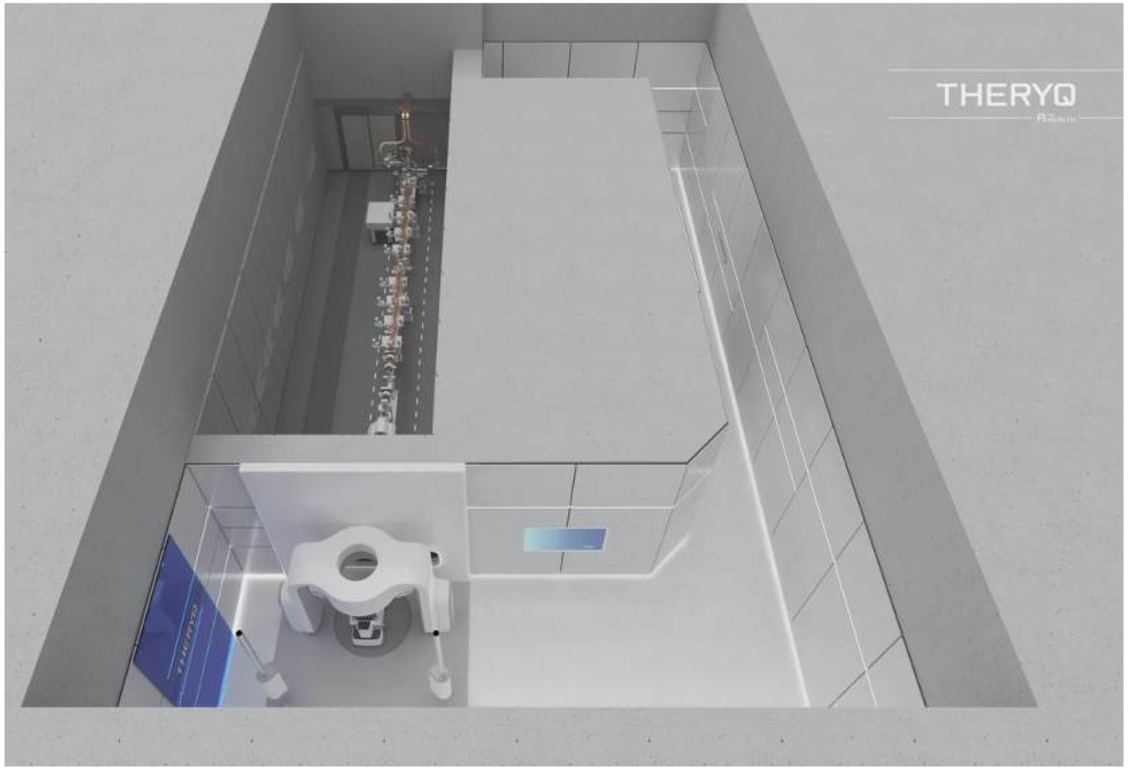
Wu, No *Appl Radiat Oncol* 2021

CERN-CHUV VHEE FLASH project

DEFT (Deep Electrons FLASH Therapy) :

VHEE (140 MeV) FLASH therapy facility for large deep seated tumors





Status : construction is ongoing

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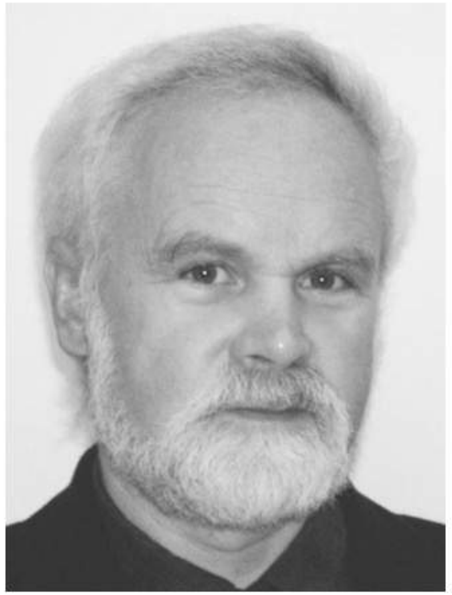

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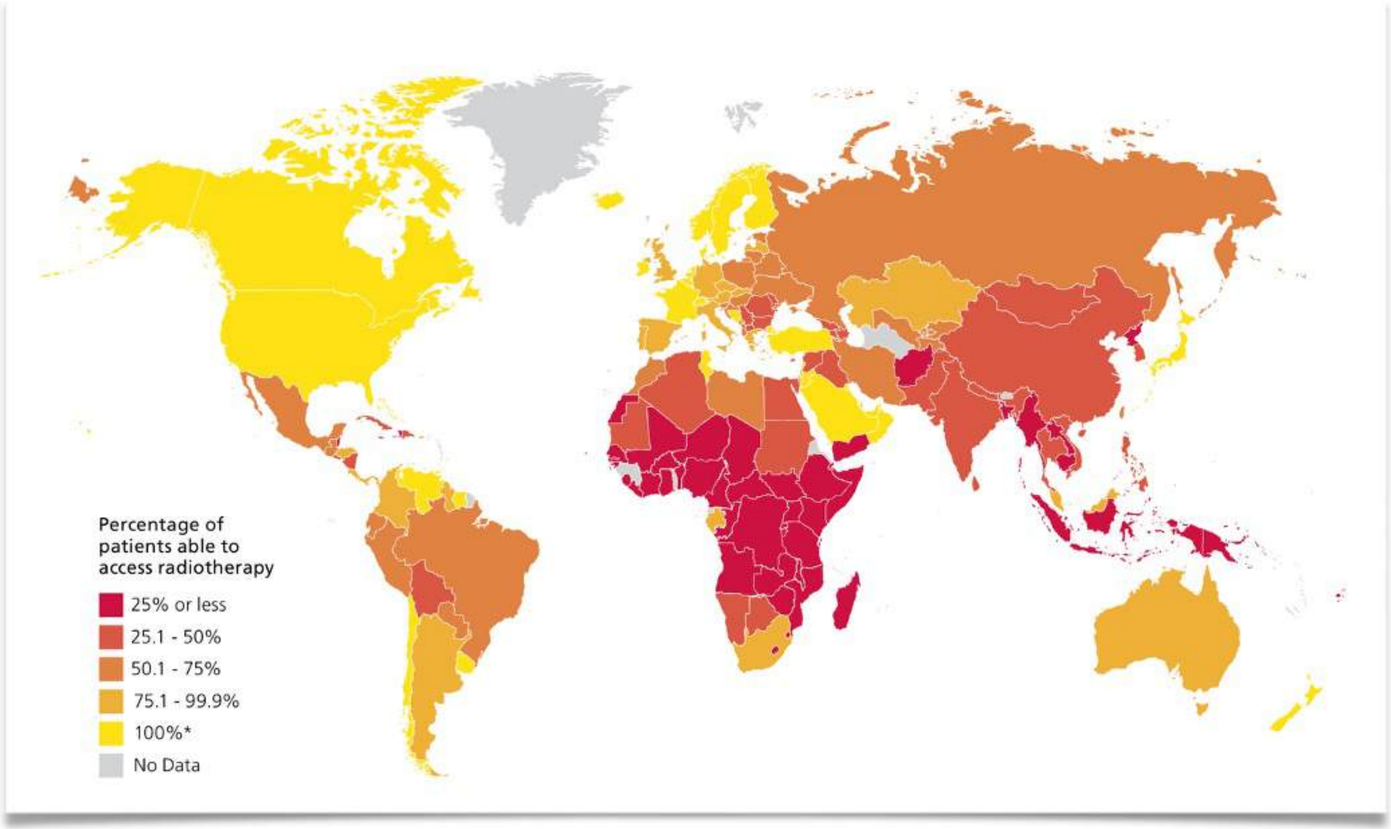
Con

Bortfeld: "One thing that is clear about VHEE is that a clinical treatment machine for 250 MeV electrons would be relatively **bulky and expensive**… It seems to me that VHEE stands primarily for **Very Highly Expensive Electrons**"

Papiez, Bortfeld *Med Phys* 2004

Global access to radiotherapy

! *Only half of patients worldwide who could benefit from RT have any access*



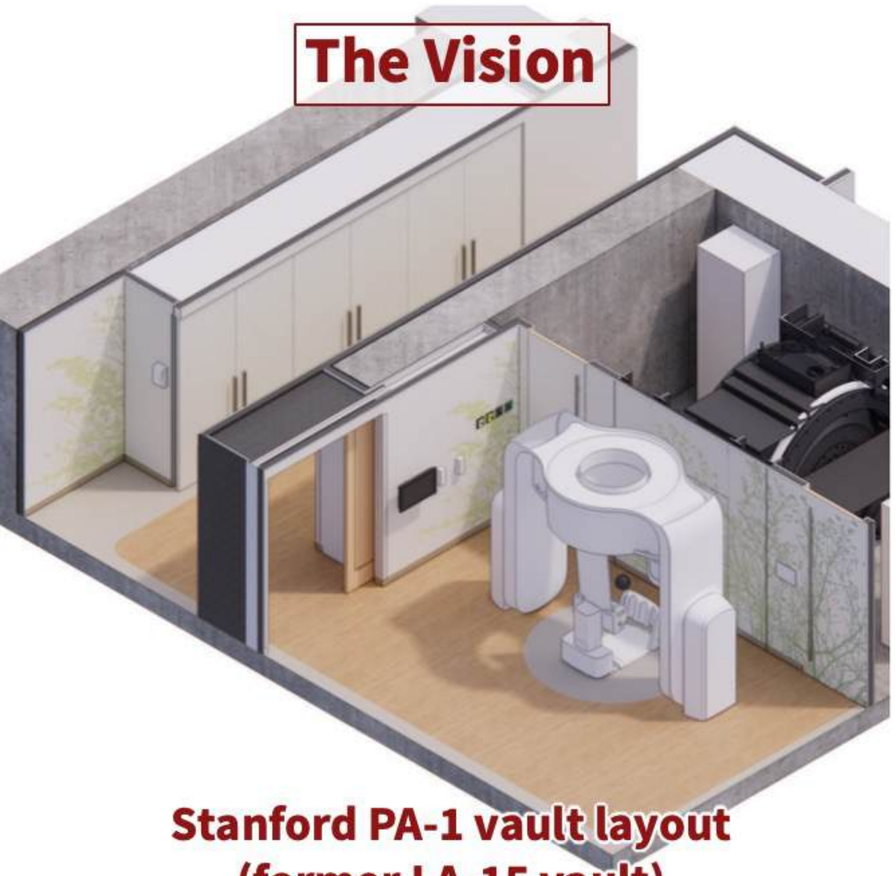
Millions who should be able to receive curative therapy can only get palliative treatment

Ultra-compact proton therapy

Stanford MEDICINE | Department of Radiation Oncology

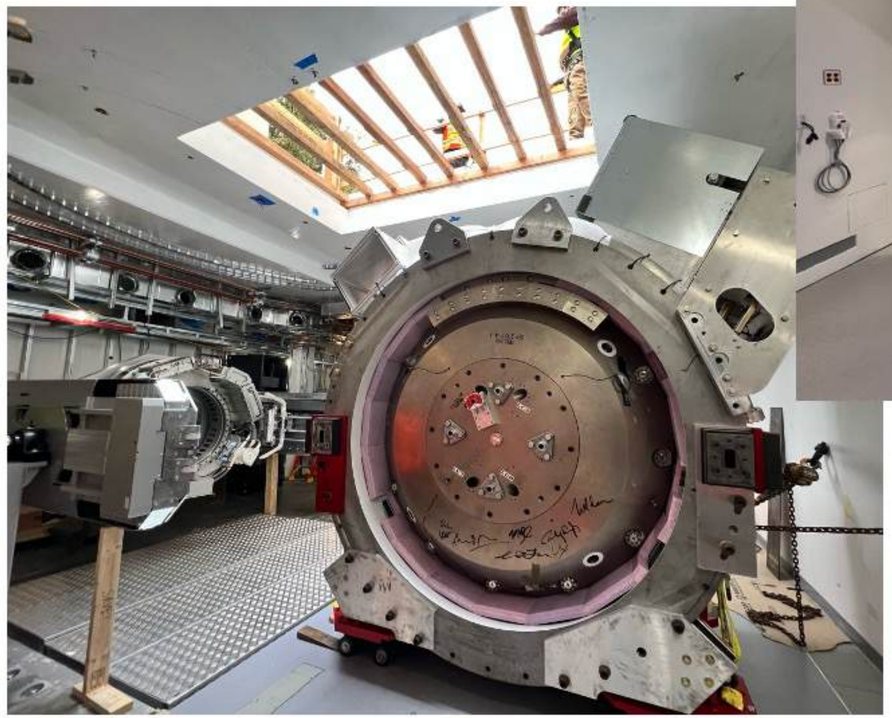
Advanced proton therapy in a standard radiotherapy vault

The Vision



Stanford PA-1 vault layout
(former LA-15 vault)

Realized



Mevion S250-FIT delivered to Stanford
1/19/2025

Installation nearly complete

Treatments to start December 2025

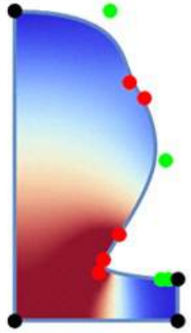
Key to linac performance: efficiency

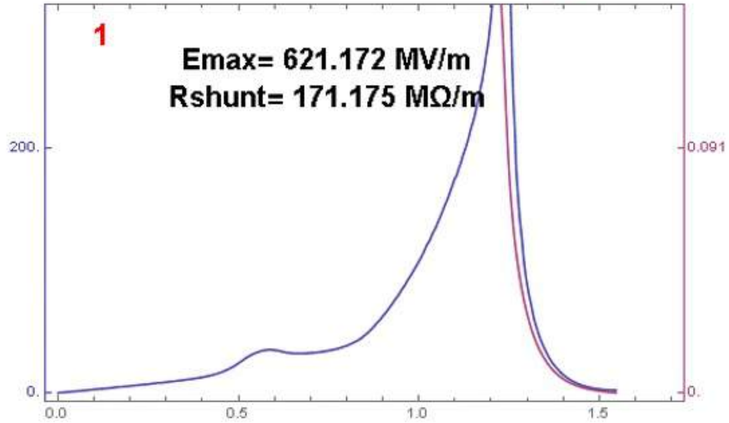
- RF power (from klystron/magnetron) is used to:
  - Establish accelerating gradient (lost as waste heat)
  - Impart energy to electrons in beam
  - Conventional linacs: RF to beam efficiency <20%
- Discovery:
  - Pulsed heating from RF induced surface magnetic fields is major source of energy loss
  - New class of linac with accelerating cells optimized to minimize surface magnetic fields is far more efficient: RF to beam efficiency >80%
- Greater "RF budget" can be used for any combination of:
  - Higher beam current
  - Higher beam energy
  - Higher gradient (more compact structure)

New class of linear accelerator

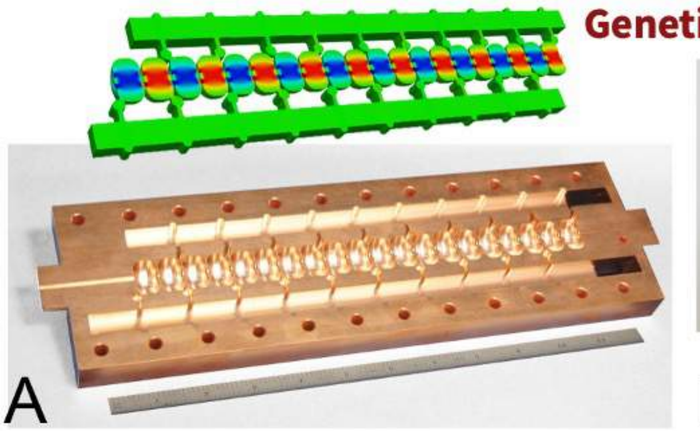
Conventional linear accelerator design

Optimized cell design: minimize peak electric and magnetic surface fields

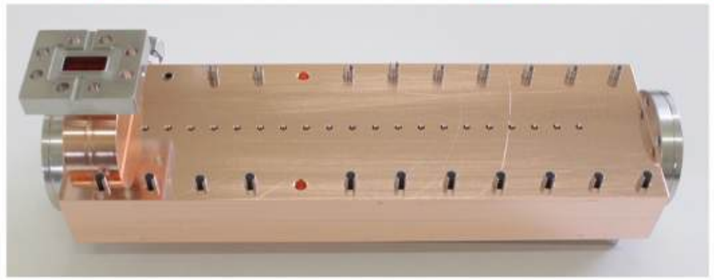




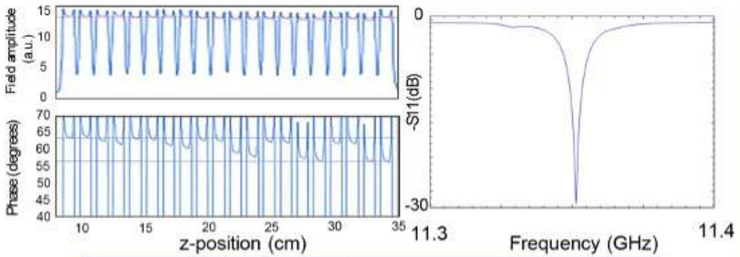
Distributed RF-coupling Architecture with Genetically Optimized cell desigN (DRAGON)



A



B

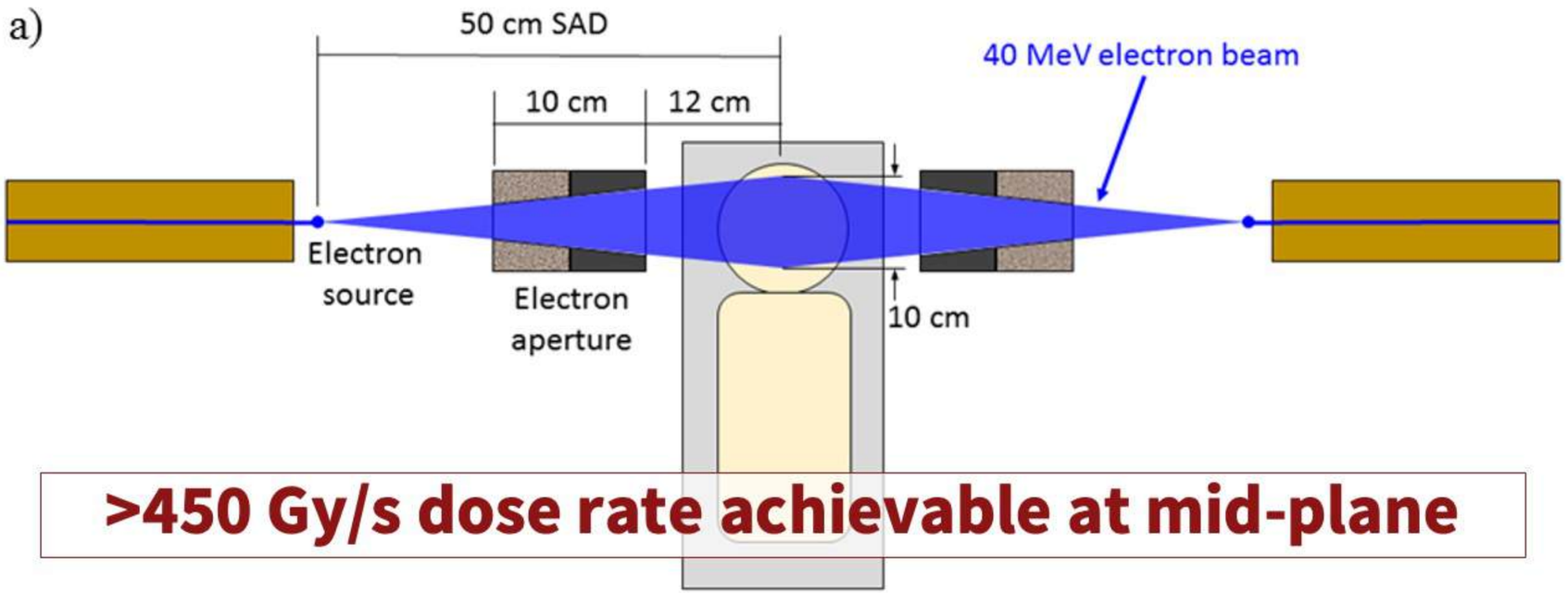


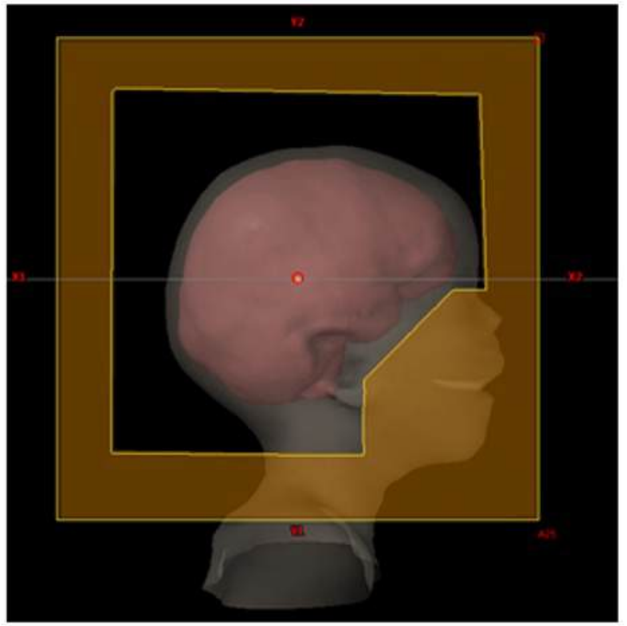
C

Maxim, Tantawi, Loo *Radiother Oncol* 2019; Tantawi *Phys Rev Accel Beams* 2020

Near term clinical FLASH implementation

Feasibility of available linac/klystron for FLASH pediatric WBRT





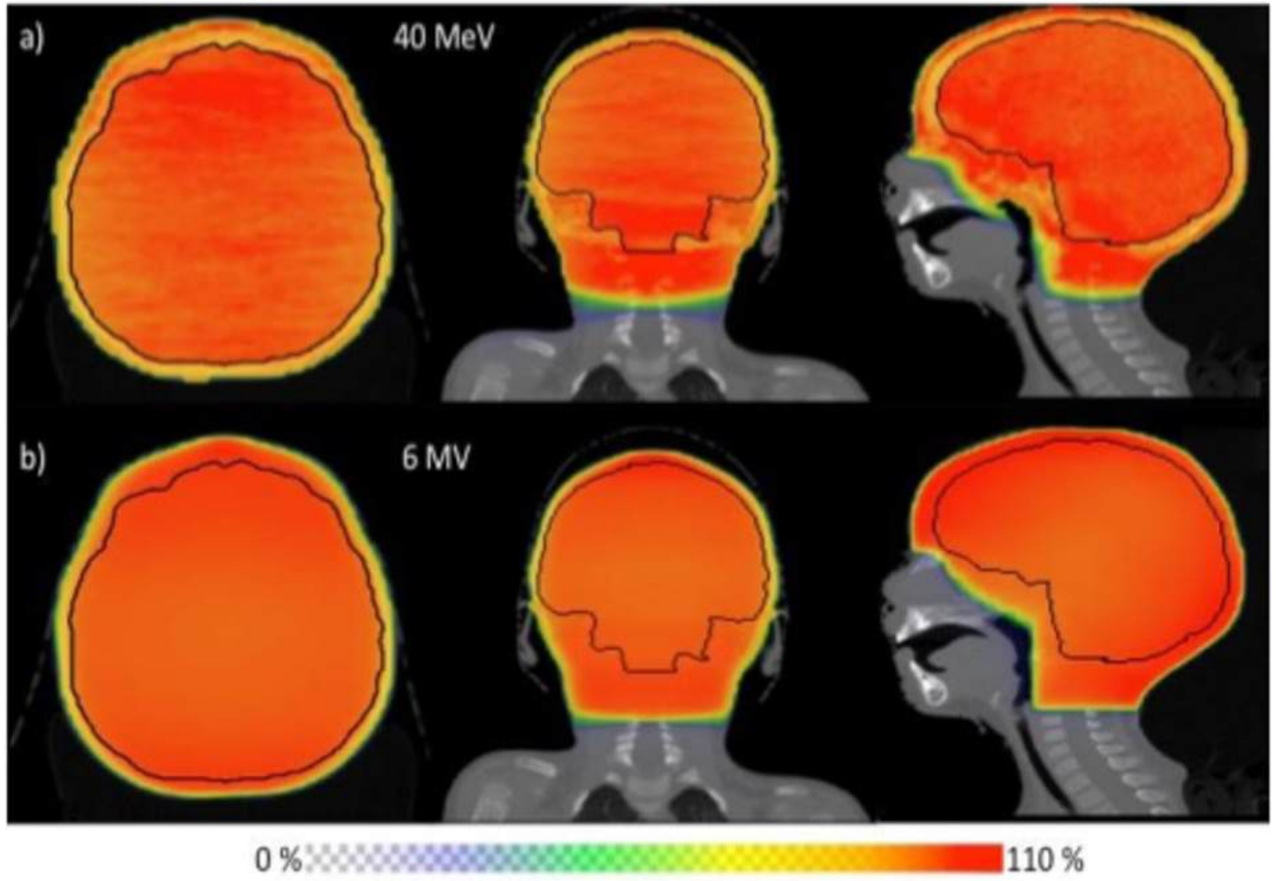
>450 Gy/s dose rate achievable at mid-plane

Breitkreutz *Rad Res* 2020

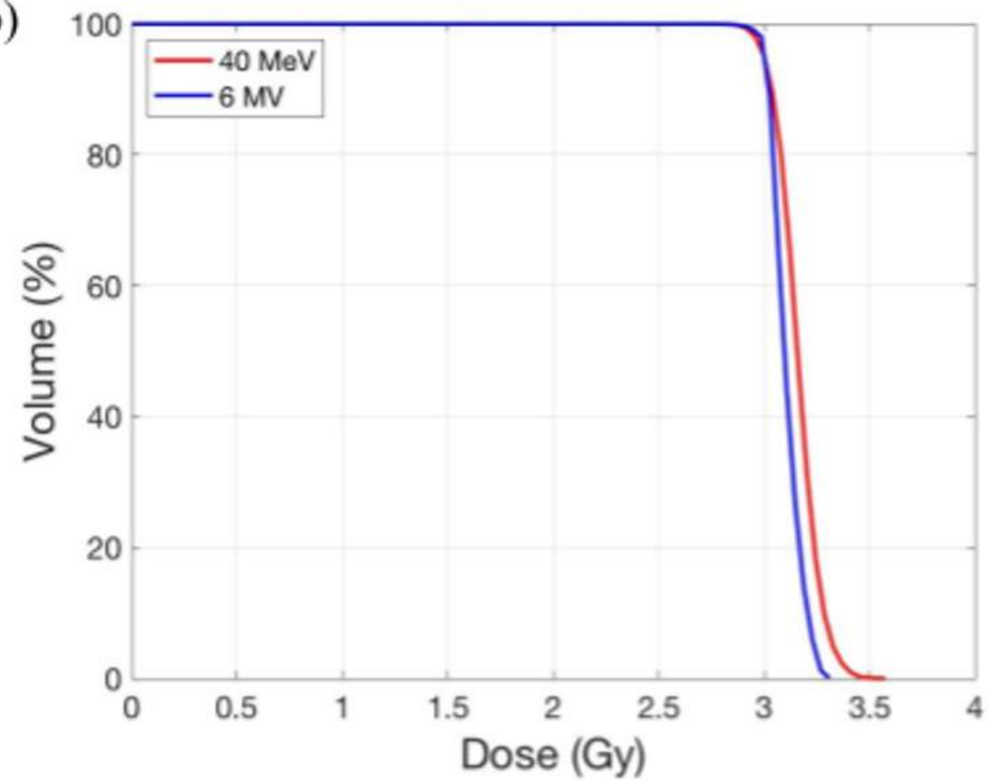
Near term clinical FLASH implementation

Feasibility of available linac/klystron for FLASH pediatric WBRT

a)



b)



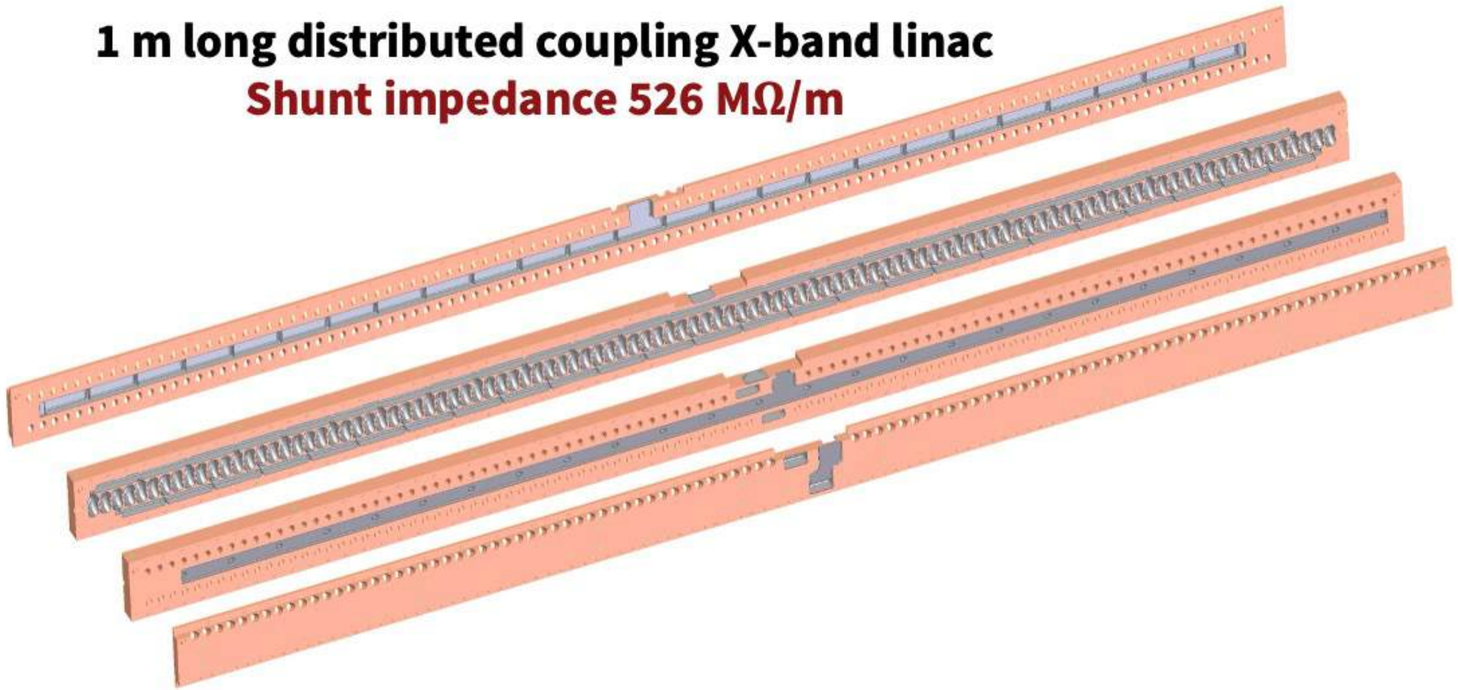
Breitkreutz *Rad Res* 2020

Compact VHEE FLASH technology

100 MeV VHEE linac powered by commercial 6 MW klystron

1 m long distributed coupling X-band linac

Shunt impedance 526 MΩ/m



High efficiency compact cryogenically cooled linac system for very high energy electron radiation therapy

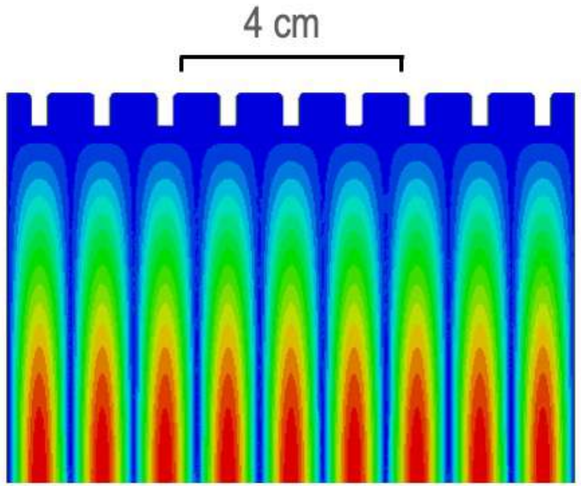
Accelerator Stewardship Program

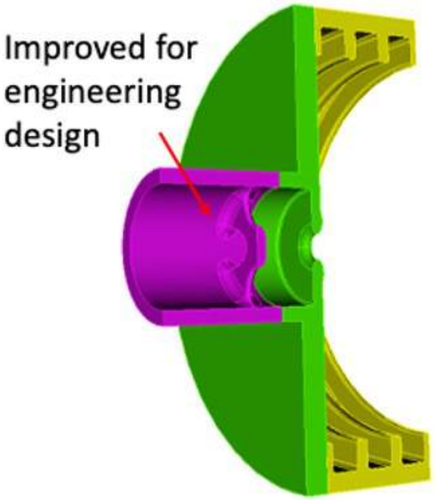
Compact RF pulse compression

Powering the FLASH VHEE linac

K200 Solid State Modulator System from ScandiNova

- 11.424 GHz
- Peak power 6 MW
- Pulse length 4 μs

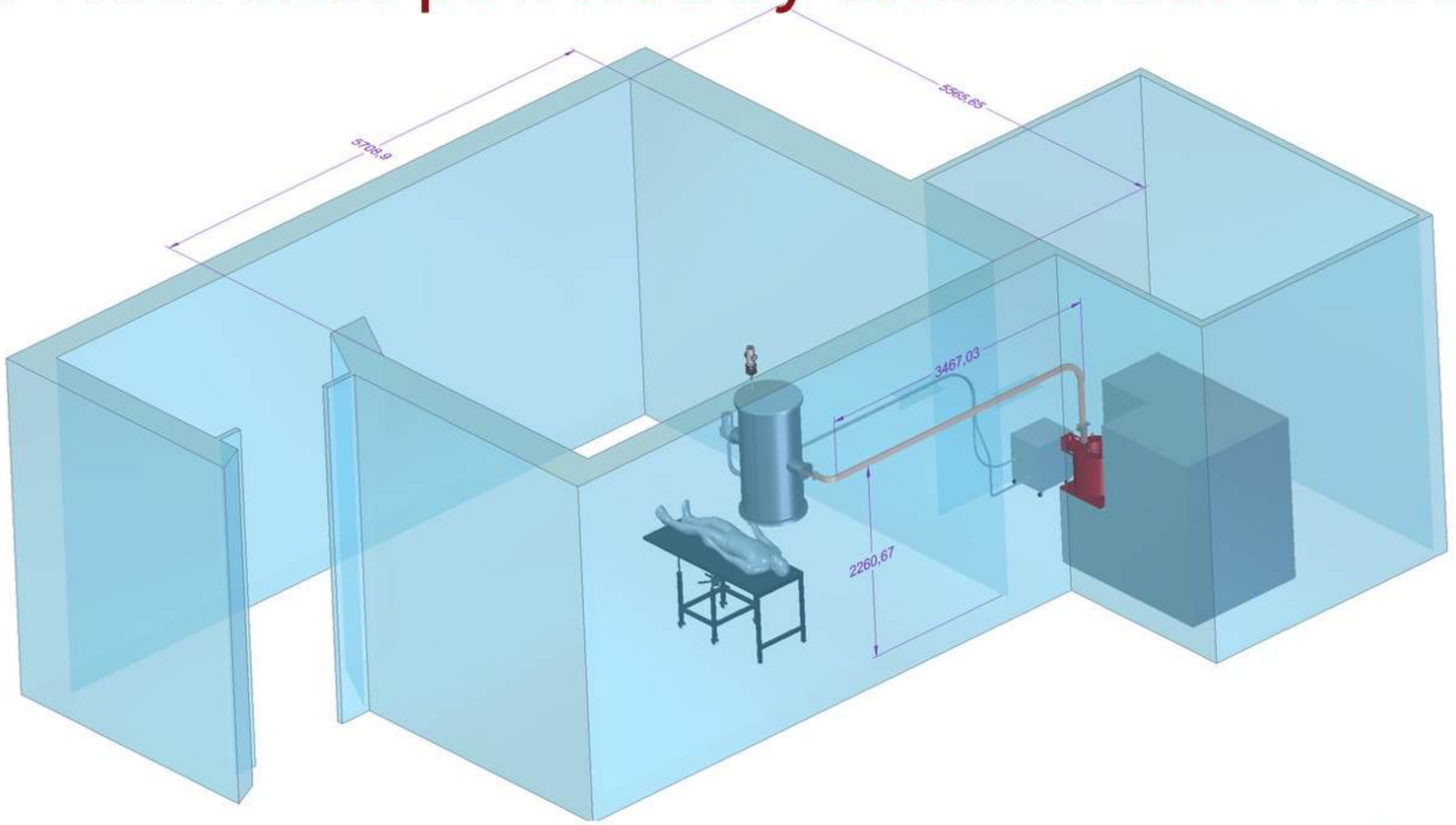




Compressed pulse reaches 19 MW peak power in a 200 ns flattop

Compact VHEE FLASH implementation

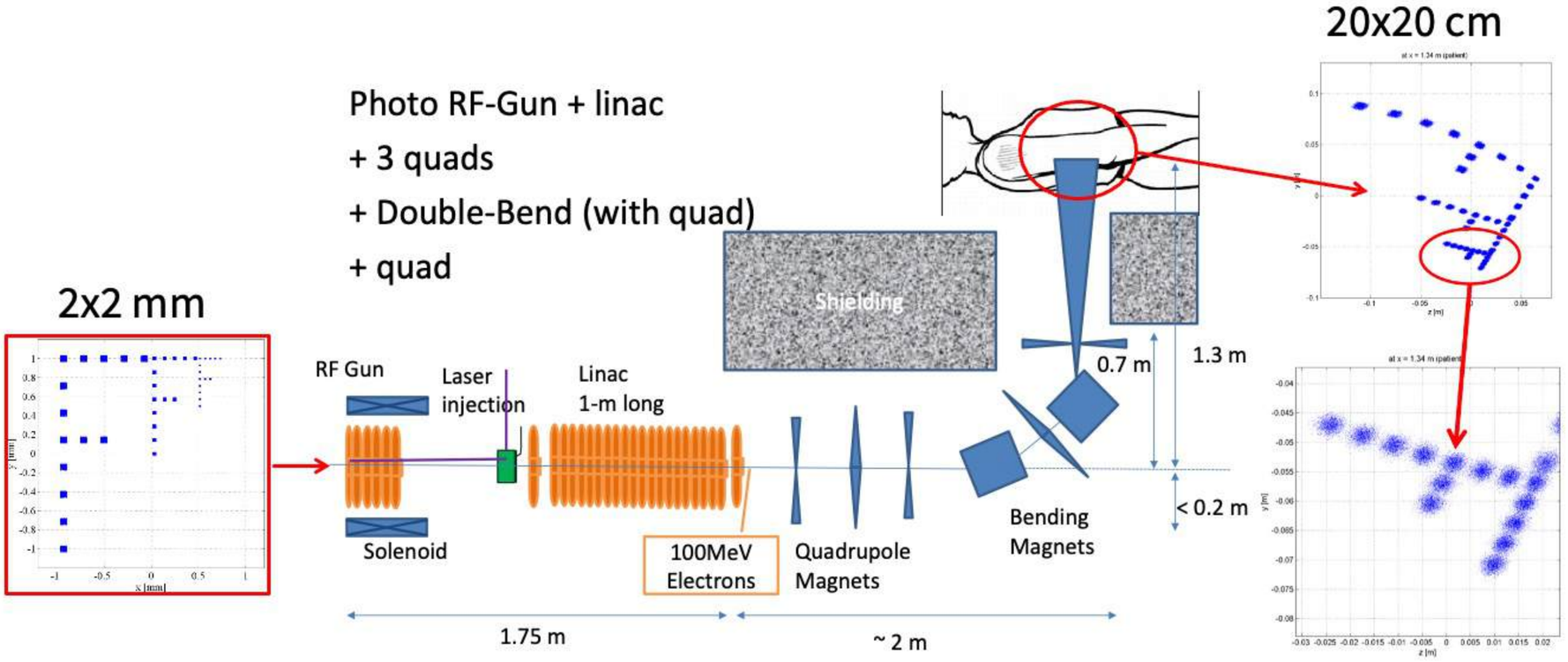
100 MeV VHEE linac powered by commercial 6 MW klystron

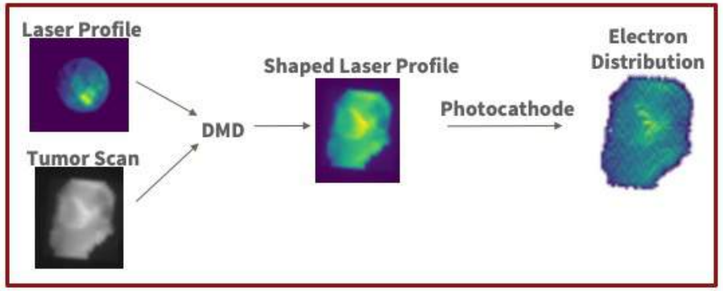


Accelerator Stewardship Program

Novel VHEE intensity modulation

Unique 100 MeV compact electron beamline optics design to **accelerate & project electron "image"** from source to patient





C Recker, N Neveu, E Snively – SLAC

Maxim, Tantawi, Loo *Radiother Oncol* 2019

Conclusions

- Compared to x-rays, VHEE provides
  - Dosimetric advantages
  - Faster delivery
    - Motion mitigation
    - Potential to leverage FLASH effect
- These may provide the improved therapeutic precision needed to increase the impact of radiotherapy on *clinical outcomes & cure*
- Advances in accelerator/RF science underly the *clinical practicality* of these solutions – power efficiency, compactness, economy

FLASH sciences lab @Stanford

biology+physics+engineering | PI: B Loo

Stanford MEDICINE

SLAC NATIONAL ACCELERATOR LABORATORY

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Duaa Al Rawi
Ramish Ashraf
Dylan Breitkreutz
Suparna Dutt
Michael Dworkin
Aaron Garza
Vedika Grover
Byunghang Ha
Naviya Kapadia
Nikita Katila
Anna Kim
Ryan Ko
Fred Lartey
Brianna Lau
Reagan Lee
Kaitlyn Liang
Aaron Libed
Rakesh Manjappa
Stavros Melemenidis
Josh No
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Peter Maxim
Christina Huang
Masha Servati
Brian Thorndyke

Rankin Lab:
Erinn Rankin
Stephanie Chow
Joshua Eggold
Karen Levy
Phoebe Loo
Suchitra Natarajan
Hussein Shehade

Graves Lab:
Ted Graves
Oscar Cortez

Comparative Med:
Kerriann Casey

Le Lab:
Quynh Le
Hongbin Cao
Dhanya Nambiar

Immunology:
Ed Engleman
Sam Strober

Longo Lab:
Frank Longo
Danielle Simmons

MDACC:
Albert Koong
Chih-Chien Chou

Seoul National Univ:
G-One Ahn
Hak Jae Kim

SLAC:
Sami Tantawi
Matt Franzi
Mark Kemp
Chris Nantista
Muhammad Shumail
Aaron Tremaine
Brandon Weatherford
Sayed Rokni
Andrew Rosenstrom
Mario Santana

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