Transformative Technology for FLASH Radiation Therapy

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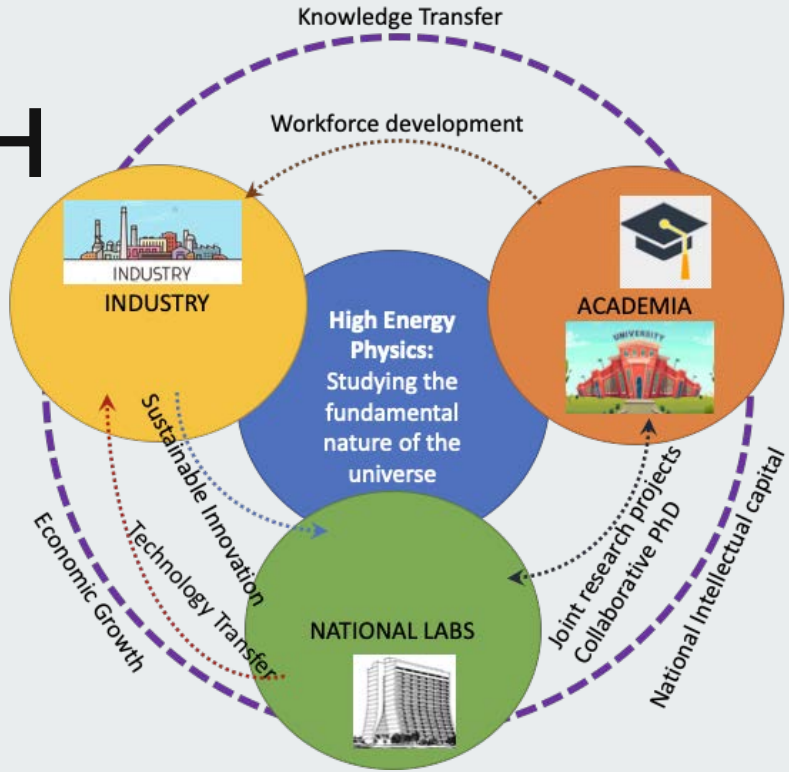

Application and Industry (A&I) working group

Snowmass 2021: Community Engagement Frontier (CEF)

Outline

- FLASH RT Background
- Authors, Participants
- Core idea & Objective
- Areas in AF6 technologies addressing High Energy Physics goals that can help FLASH RT

FLASH Radiation Therapy: Excitement and Recognition

- Special FLASH workshops organized by NCI and DOE
- Increasing number of FLASH sessions at recent ASTRO, AAPM, RRS, ESTRO Annual Meetings
- Special FLASH journal editions of leading Radiation Therapy and Radiation Research Journals
- LOI was readily encouraged by Conveners of CommF1: Applications & Industry Town hall Meeting August 18, 2020

The Significance of FLASH – Therapeutic Index

- FLASH has the potential to shift the normal tissue complication probability vs. dose curve towards higher doses
- The tumor control probability versus dose curve remains unchanged
- This widens the therapeutic index (dose window) and increases tumor control and/or reduces side effects

Holthusen's hypothesis – a universal principle of cancer therapy

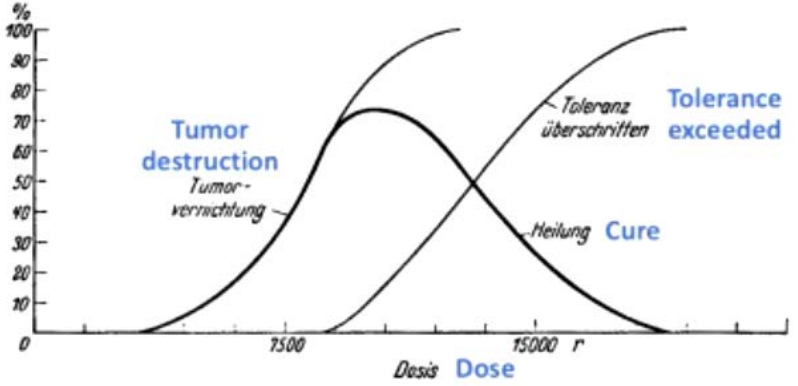

Bild 6.
Holthusen *Strahlenther Onkol* 1936

Summary of Recent Evidence

- Researchers at the Institut Curie in Paris **demonstrate for the first time that pulsed, ultrahigh dose-rate irradiation causes less damage to the healthy lung** than conventional radiation in mouse models and confirmed that FLASH is **equally effective against tumors**; Favaudon, Science Translat Med 2014
- Ultrahigh dose rate FLASH electron beam irradiation caused **significantly less radiation-induced intestinal injury in both healthy and tumor-bearing mice** while **tumors were not spared**; Levy/Natarayan/Wang, bioRxiv 2019
- Single whole-brain dose given at FLASH dose rates **no significant memory deficit and reduced cognitive damage in mice**, Montay-Gruel, Radiother & Oncol, 2017, PNAS 2019
- FLASH showed **large skin-dose sparing but no sparing of tumors was demonstrated in mini-pigs and cats**; Vozenin, Clin Cancer Research, 2018
- **First in human case report** (Bourhis, Radiother Oncol 2019), modified LINAC with high dose-per-pulse electron beam RT; 15 Gy single fraction delivered in 90 ms; **excellent clinical outcome**

FLASH RT LOI: Authors and Participants

- Reinhard W. Schulte, MD, MS (Physics), Loma Linda University (USA)
- Carol Johnstone, PhD, Fermi National Accelerator Laboratory, (USA)
- Peter S. Friedman, PhD, Integrated Sensors, LLC (USA)

- Vinod Bharadwaj, TibaRay, Inc.,
- Salime Max Boucher, RadiaBeam,
- George Coutrakon, Northern Illinois
- Bruce Faddegon, UCSF
- Peter Friedman, Integrated Sensors, LLC,
- Cameron Geddes, LBNL
- Thomas Kroc, IARC, FNAL
- Brahim Mustapha, ANL
- Emilio Nanni, SLAC,
- Mack Roach III, UCSF
- Keith E. Schubert, Baylor University,
- Ke Sheng, UCLA
- Emma Snively, SLAC
- Sami Tantawi, SLAC
- Miha Ulčar, Cosylab,
- James S. Welsh, Edwards Hines V. A. Hospital

Core Idea and Objectives of our LOI

Core Idea

- To document our desire to develop strategic planning and engagement that will promote applications and technology transfers from the particle physics community to applications with high impact in the field of Radiation Therapy.

Objectives

- Promote applications and technology transfers from the HEP community to applications with high impact in the field of FLASH-RT and other advanced forms of RT
- Enable FLASH-RT, which could revolutionize the treatment of many types of cancer.

Required Application Areas

- Application Area 1: Development of low-cost, compact, and FLASH-capable accelerators for cancer cure
- Application Area 2: Expanded operational parameters for ultra-high dose rate delivery
- Application Area 3: Development of improved large-area, ultrafast radiation detectors for real-time FLASH-dose monitoring and FLASH imaging
- Application Area 4: Development of improved beam-shaping and -modulating technology
- Application Area 5: Optimization and development of treatment planning and delivery control systems to allow for real-time biologic and volumetric treatment adaptation

Department of Energy. 2019. “Basic Research Needs Workshop on Compact Accelerators for Security and Medicine Report of the Department of Energy Office of Science https://science.osti.gov/-/media/hep/pdf/Reports/2020/CASM_WorkshopReport.pdf?la=en&hash=AEB0B318ED0436B1C5FF4EE0FDD6DEB84C2F15B2

FLASH – Example for Clinical Translation at SLAC

- PHASER - Pluridirectional High-energy Agile Scanning Radiotherapy – Maxim, Radiother Oncol 2019

  - Next generation RT with FLASH dose-rate capability
  - 400X faster: freezes motion, ultimate precision
  - Compact & economical, global access to FLASH RT https://biox.stanford.edu/research/seed-grants/pluridirectional-high-energy-agile-scanning-electron-radiotherapy-phaser-novel https://www6.slac.stanford.edu/news/2018-11-28-future-fighting-cancer-zapping-tumors-less-second.aspx
- Near-term clinical FLASH implementation – Breitkreuz, Radiation Research 2020
  - Feasibility of available linac/klystron for FLASH pediatric WBRT
  - Using PHASER under development and commercial klystron, 40 MeV electron beam, >450 Gy/s achievable

Other Examples for Clinical Translation of FLASH

- Making proton therapy more agile - $1.7 million grant from the DOE Office of Science Accelerator Stewardship to SLAC, LLU, and Varian
  - https://www6.slac.stanford.edu/news/2018-11-28-future-fighting-cancer-zapping-tumors-less-second.aspx
- IntraOp and Ohio State University Announce Collaboration in FLASH - confirmed capabilities of delivering dose rates of over 600 Gy per second delivered in 6 and 9 MeV
  - https://cancer.osu.edu/news/intraop-and-ohio-state-announce-collaboration-in-flash
- CERN accelerator technology to underpin FLASH radiotherapy facility - high-performance electron accelerator components and simulation tools originally designed for CERN's Compact Linear Collider
  - https://cancer.osu.edu/news/intraop-and-ohio-state-announce-collaboration-in-flash

LOI Take Home Points (Summary)

- Ultra-rapid FLASH has shown the potential for increased therapeutic index for cancer therapy in multiple preclinical models
- Clinical translation of FLASH and human data are on the horizon for selected clinical scenarios
- Radically new accelerator & ancillary technologies need to be co-developed to deliver FLASH RT
- There is much more to be studied biologically, technologically, and clinically but all needs to come together in a concerted effort