Current Knowledge and Prospective of FLASH Radiotherapy

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Penn Medicine

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Learning Objectives

- **To review current findings in FLASH**
- **To discuss unknowns and challenges in FLASH research**
- **To project potential improvements and directions in future radiotherapy**

Disclosures

- **Research grants: NIH Grant (P01); Sponsored Research Grant from IBA**
- **Speaker Bureau Honorarium: Varian**
- **Consortiums: Varian FlashForward™; IBA ConformalFLASH® Alliance**

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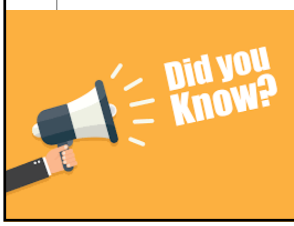
Have you heard about…

FLASH RT



FLASH therapy is one of the hottest topics in radiation therapy!

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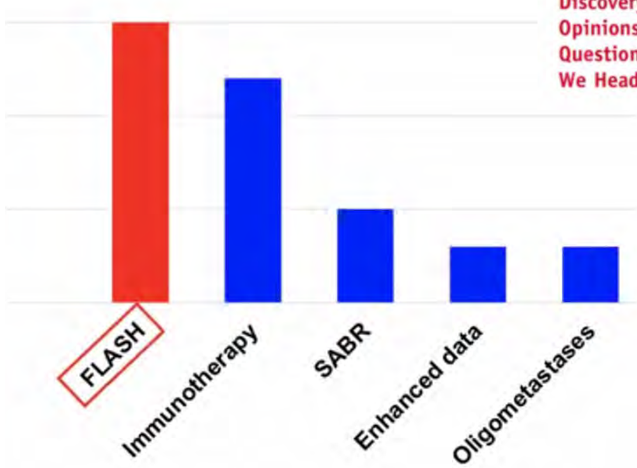
ASTRO Member Survey

International Journal of
Radiation Oncology • Biology • Physics ASTRO

- What is the One Big Discovery that needs to be translated into the clinic RIGHT NOW?



EDITORIAL

Responses to the 2018 and 2019 "One Big Discovery" Question: ASTRO Membership's Opinions on the Most Important Research Question Facing Radiation Oncology…Where Are We Headed?

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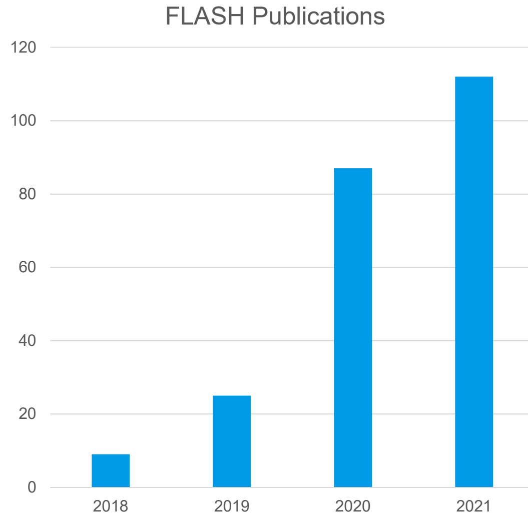
FLASH Related Publications

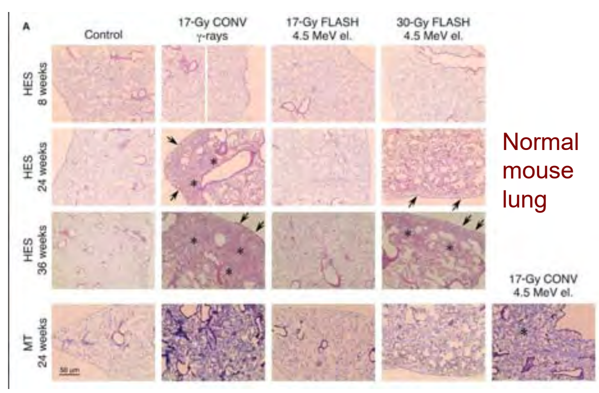
- **1/3 of publications are review articles!**



What is FLASH RT? – Sparing normal tissues

- **It stirred from a major scientific publication using electron beams:**
  - It is ionizing radiation (electron or proton) delivered at ultra-high dose rates (>40 Gy/sec) over a very short duration (less than a second).
  - **FALSH-RT is less toxic to normal tissues while maintaining tumor control**

Professor Vincent Favaudon
Institut Curie, INSERM



Normal mouse lung

Favaudon *et al., Science Transl. Med.*. 2014

What is FLASH RT? – without compromising tumor control

- **It stirred from a major scientific publication using electron beams:**
  - It is ionizing radiation (electron or proton) delivered at ultra-high dose rates (>40 Gy/sec) over a very short duration (less than a second).
  - **FALSH-RT is less toxic to normal tissues while maintaining tumor control**

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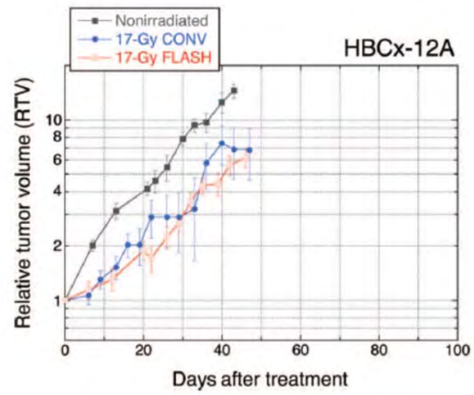


Favaudon *et al., Science Transl. Med.*. 2014

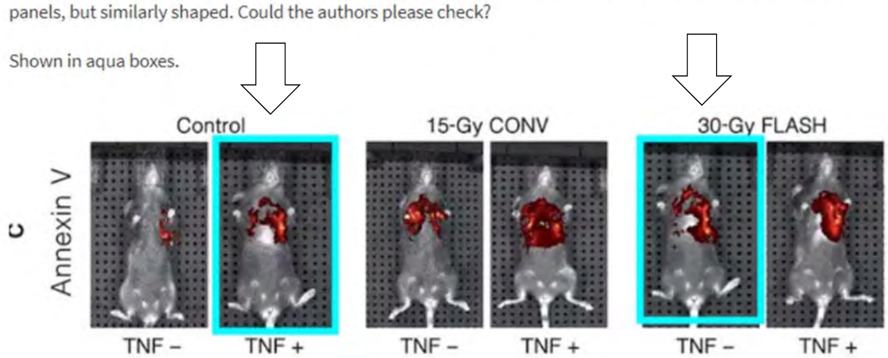
PUBPEER
The online Journal club

https://pubpeer.com **Dr. Elisabeth Bik - Finding Fake Publications**

#1 Elisabeth M Bik commented a year ago

Figure 2C. The same mouse appears to be visible twice. The measured signal is slightly different between the 2 panels, but similarly shaped. Could the authors please check?

Shown in aqua boxes.



Sept 18, 2019

Error was corrected on Dec. 24, 2019

ERRATUM

Erratum for the Research Article: “Ultrahigh dose-rate FLASH irradiation increases the differential response between normal and tumor tissue in mice” by V. Favaudon et al.

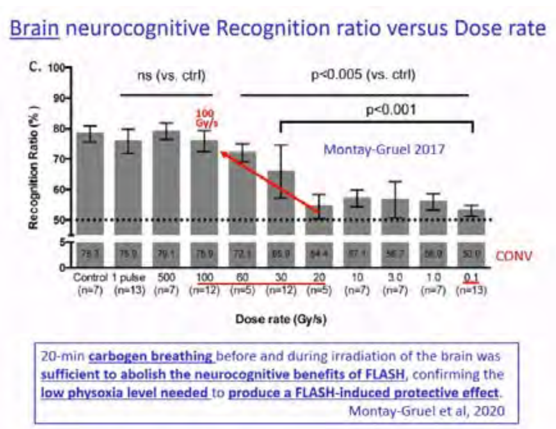
In the Research Article “**Ultrahigh dose-rate FLASH irradiation increases the differential response between normal and tumor tissue in mice**,” IVIS images were presented incorrectly in Fig. 2C and Fig. 4B. The panel [30 Gy FLASH, TNF-] in Fig. 2C has been replaced; the quantification is correct. Panel B in Fig. 4 has been replaced. In the last paragraph of the Results section, the sentence should read “…80% of the mice exposed to 28-Gy FLASH were still alive, and 60% of them were free of tumors at 62 days...” This mistake does not affect the conclusions of the study. The PDF and HTML (full text) have been corrected.

https://stm.sciencemag.org/content/11/523/eaba4525

What is the threshold dose rate for FLASH?

- **It came from a publication using electron beams:**
  - It is ionizing radiation (electron or proton) delivered at ultra-high dose rates (>40 Gy/sec) over a very short duration (less than a second).
  - Brain neurocognitive study in a mouse study
- **Dose rate definition?**

Professor Marie-Catherine Vozenin
University Hospital of Lausanne



Some Reported a threshold and most others did not

Venkatesulu BP, Sharma A, Pollard-Larkin JM, et al. Ultra high dose rate (35 gy/sec) radiation does not spare the normal tissue in cardiac and splenic models of lymphopenia and gastrointestinal syndrome. *Sci Rep 2019;9:17180.*

SCIENTIFIC REPORTS
natureresearch

OPEN

Ultra high dose rate (35 Gy/sec) radiation does not spare the normal tissue in cardiac and splenic models of lymphopenia and gastrointestinal syndrome

Bhanu Prasad Venkatesulu[1,6], Amrish Sharma[1,6], Julianne M. Pollard-Larkin[3], Ramaswamy Sadagopan[3], Jessica Symons[1,4], Shinya Neri[1], Pankaj K. Singh[1], Ramesh Tailor[3], Steven H. Lin[1,2,4*] & Sunil Krishnan[1,2,4,5*]

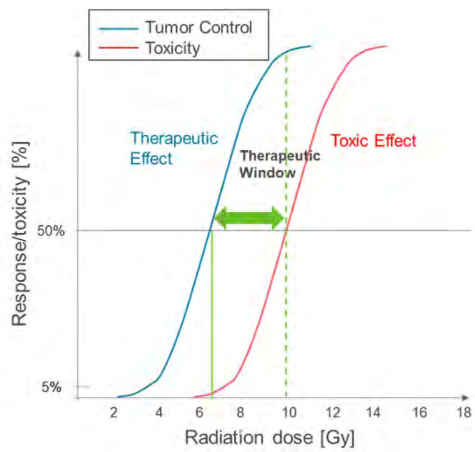
Radiobiological Effects of Ultra-High FLASH Dose Rate Using X-Rays Generated by the Small Animal Radiation Research Platform - John R. Cameron Early-Career

- Denisa Goia etc. to be presented at upcoming AAPM annual meeting (2022)
- Methods: A Small Animal Radiation Research Platform (SARRP) was used to deliver 45 Gy using a Standard dose rates of 0.24 Gy/s and a FLASH dose rate of 45 Gy/s. 9 week old C57BL/6J mice were assigned into groups of 20 to receive 45 Gy to the hind leg.
- Results: The FLASH group showed no difference from Standard group in skin reaction, percent weight change, and skin inflammation at Day 18. The IVIS imaging of the released myeloperoxidase activity by the activated neutrophils gave a similar result at 9, 18, 27, 36, and 72 days post-irradiation. Late effects, such as lymphedema, showed no difference between groups as well.
- Conclusion: Photon FLASH may not have the same thresholding FLASH dose rate as in electrons or protons. More research is needed

General Comments

- **High dose rate effects had been previously reported in early 70's**
  - Roger Berry 1973; Eric Hall 1991
- **Ultra-high dose rate is not readily available until now**
- ***In vitro* studies do not demonstrate the effect unless the cells are already in mildly hypoxic condition (very rare)**
- **Mice experiments were reproduced at different labs around the world by different radiation modalities**
  - Demonstrating an approximately **30%** sparing effects
- **The FLASH mechanism is still unknown!**
  - There have been many theories
- **If this is true, it is a game changer for radiation therapy**

Benefits of Radiation Therapy



[1]Reviewed in Wilson et al Frontiers Oncology 2020

In *vivo* vs. In *vitro* Studies

- **Far fewer evidence of FLASH effects in *vitro***
- **FLASH effects depend on the micro environment of living organs to demonstrate its true efficacy**

Different Hardware Platforms to achieve the FLASH effects

- **Electron FLASH**
  - Benchtop system for research
  - Modified commercial linacs
    - Varian; Elekta etc.
      - Rahman et al. Dartmouth team: ~1 Gy/pulse
  - IORT machines
    - Mobetron, NOVAC 7
  - Very High Energy Electron (VHEE)

Petersson *et al.* 2017
Jaccard *et al.* 2017
Montay-Gruel *et al.* 2017
Jaccard *et al.* 2018
Commercialized as FLASHKNiFE™

Example of FLASH Machine Specifications:

Mobetron™
Moeckli et al. 2021

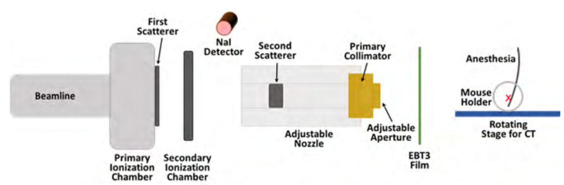
TABLE I. Variable parameters in UHDR mode and their respective range.

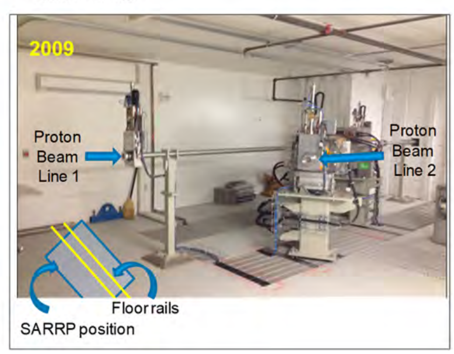
Moeckli et al. Med Phys. 2021

Parameter	Range
Beam energy [MeV]	6 or 9
Pulse width (PW) [µs]	0.5–4
Number of pulses	1–200
Pulse repetition frequency (PRF) [Hz]	5–90
Maximum dose per pulse* [Gy]	>8

Different Hardware Platforms to achieve the FLASH effects

- **Particle FLASH**
  - Diffenderfer et al. IJRBOP 2020 (the first proton FLASH experiments published)
  - Varian FAST01 Trial: pre-commissioned rectangular fields using PBS scanning pattern (56 Gy/s)
  - Darafsheh et al. "Feasibility of proton FLASH irradiation using a synchrocyclotron for preclinical studies" Med Phys (2020).
    - 100-200 Gy/s at center of SOBP
    - ~0.3 Gy per pulse (@4µs pulse width) at 648 Hz
  - Dokic et al. "Carbon Ion FLASH: first investigation in human brain organoids" IJROBP 2021
    - ~40 Gy/s for 7.4 Gy (LETd=12 keV)
    - DNA-damage repair

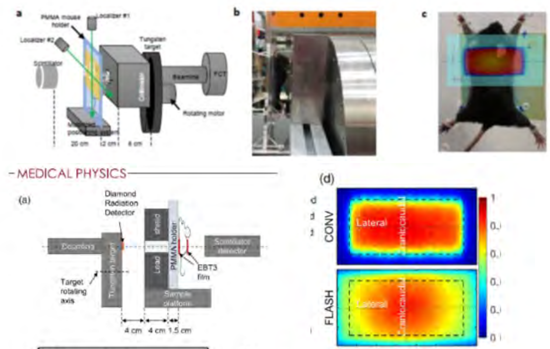
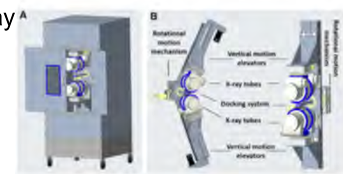
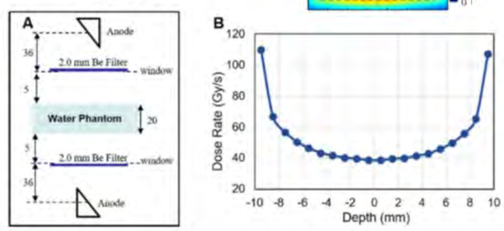




Diffenderfer et al., *IJROBP*, 2020

Different Hardware Platforms to achieve the FLASH effects

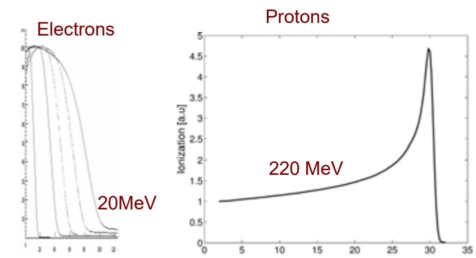
- **Photon FLASH**
  - Gao, Feng, et al. "First demonstration of the FLASH effect with ultrahigh dose rate high-energy X-rays." Radiotherapy and Oncology 166 (2022): 44-50.
    - Industrial electron linac 6-8 MeV at 5mA
    - Mean dose rate ~ 1000 Gy/s
  - H. Zhu et al. "Radioprotective effect of x-ray FLASH" Med. Phys. (49) 2022
    - 6MV x-rays >150 Gy/s (Free electron laser accelerator)
  - Rezaee et al. "Ultrahigh dose-rate x-ray irradiator for pre-clinical lab research" PMB 2021
    - A pair of 150kVp x-ray
    - 40-240 Gy/s

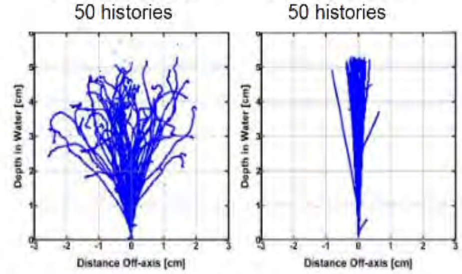




Rezaee et al. PMB 2021

What is the best beam delivery for FLASH effect?

- **Proton FLASH is promising**
  - Treating deep-seated tumors
- **Better dose conformality (small lateral penumbra)**
- **Easier to upgrade from commercial systems (cyclotron-based)**
  - Already at high dose rate
  - Pencil beam scanning
- **High-energy electron is also possible**
- **It is too early to say, we need to understand the mechanism of FLASH first.**

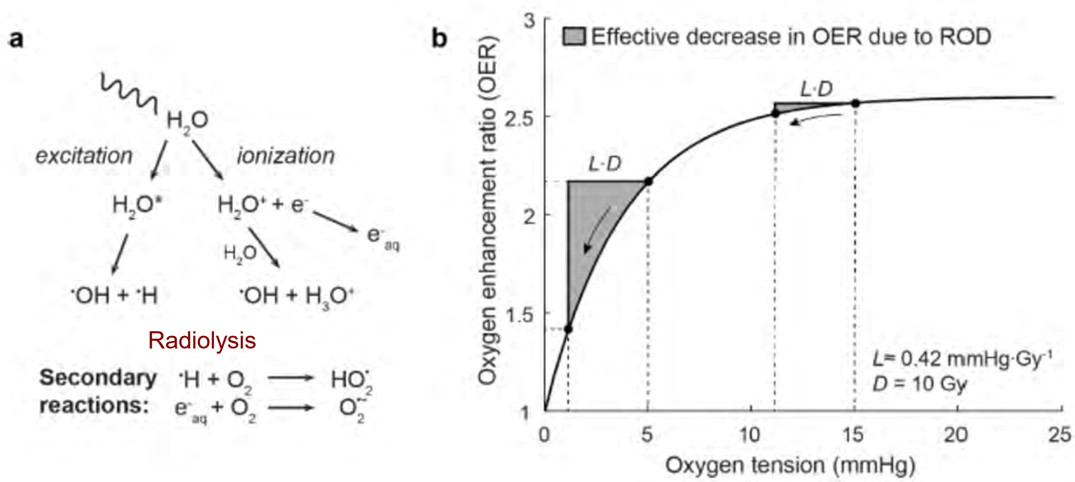




UHDR ≠ FLASH

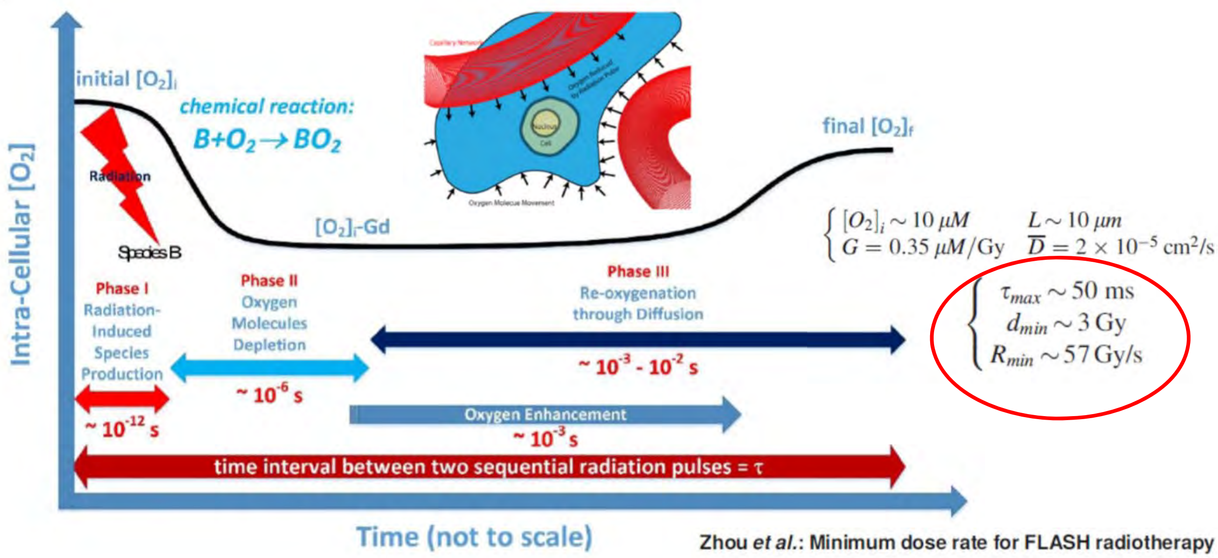
- **Definition: Ultra-High Dose Rate (UHDR) delivery of radiation therapy**
- **FLASH: the normal tissue biological sparing effects under UHDR**
  - FLASH implies UHDR
- **FLASH is biology-based radiation therapy**
- **The fundamental biological mechanism for UHDR is still unknown!**

Pratx & Kapp – an Oxygen Depletion Model during FLASH



Pratx, G. and D. S. Kapp (2019). "A computational model of radiolytic oxygen depletion during FLASH irradiation and its effect on the oxygen enhancement ratio." Phys Med Biol **64(18): 185005.**

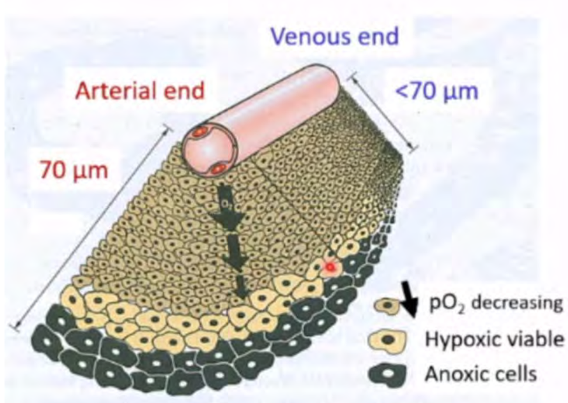
Oxygen Effects in Pulse Radiation and Minimum Dose Rate



Zhou *et al.*: Minimum dose rate for FLASH radiotherapy

Medical Physics, 47 (7), July 2020

Heterogeneity and Dynamic Nature of Oxygen Distribution in Tissues



Diffusion-limited chronic hypoxia

[+Perfusion-limited acute hypoxia]

If oxygen plays a role, the FLASH effects could be tissue-specific or exhibits a partial response

"Radiobiology for Radiologist" – Eric Hall and Amato Giaccia

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Measuring Oxygen Concentration at Ultra-Fast Rates During Proton FLASH Delivery Using Phosphorescence Quenching of Soluble Oxyphor Probes

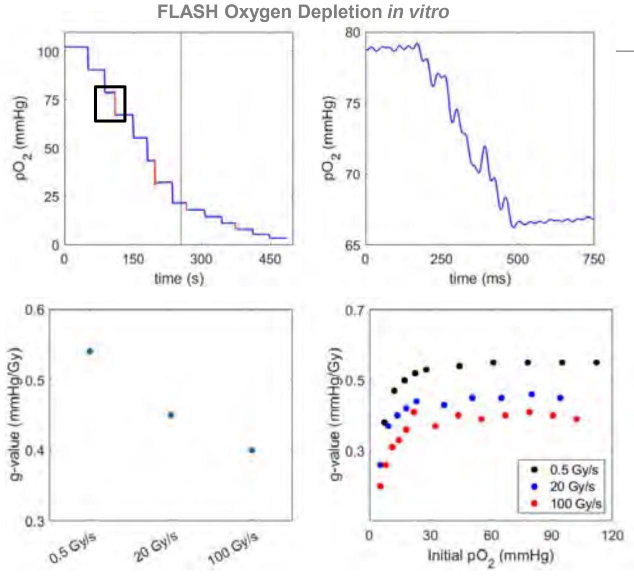
A. L. Van Slyke[1], M. El Khatib[2,3], K. Shoniyozov[1], E. S. Diffenderfer[1], M. M. Kim[1], C. J. Koch[1], S. A. Vinogradov[2,3], and R. D. Wiersma[1]; [1]*Department of Radiation Oncology*, [2]*Department of Biochemistry and Biophysics;* [3]*Department of Chemistry, University of Pennsylvania, Philadelphia, PA*

July 27, 2021

Radiation Research 198 (2) 2022
https://doi.org/10.1667/RADE-21-00232.1

DEPARTMENT OF RADIATION ONCOLOGY AND PROTON THERAPY

FLASH Oxygen Depletion *in vitro*



- FLASH dose rates (~100 Gy/s) depleted ~25% less oxygen per Gray than the conventional dose rate (0.5 Gy/s) in vitro

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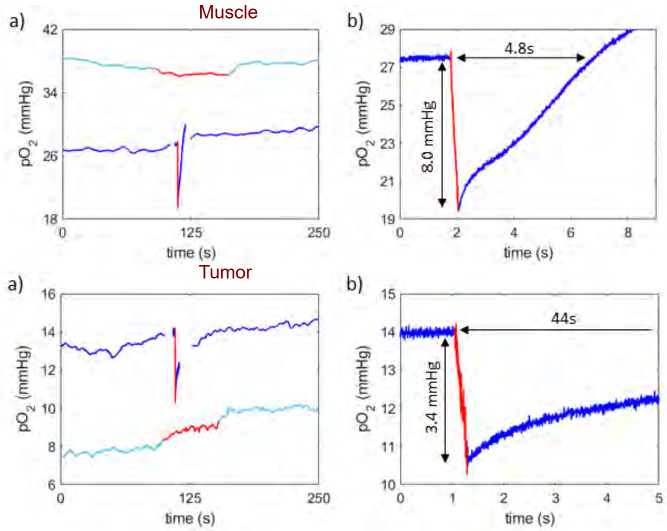
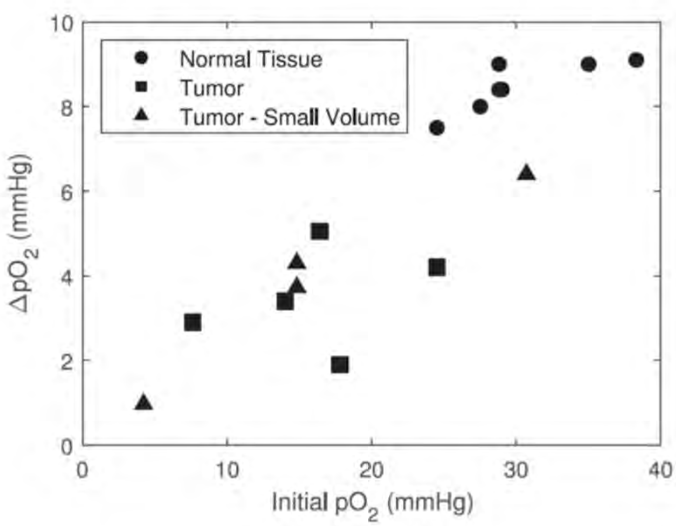
FLASH Oxygen Depletion *in vivo*

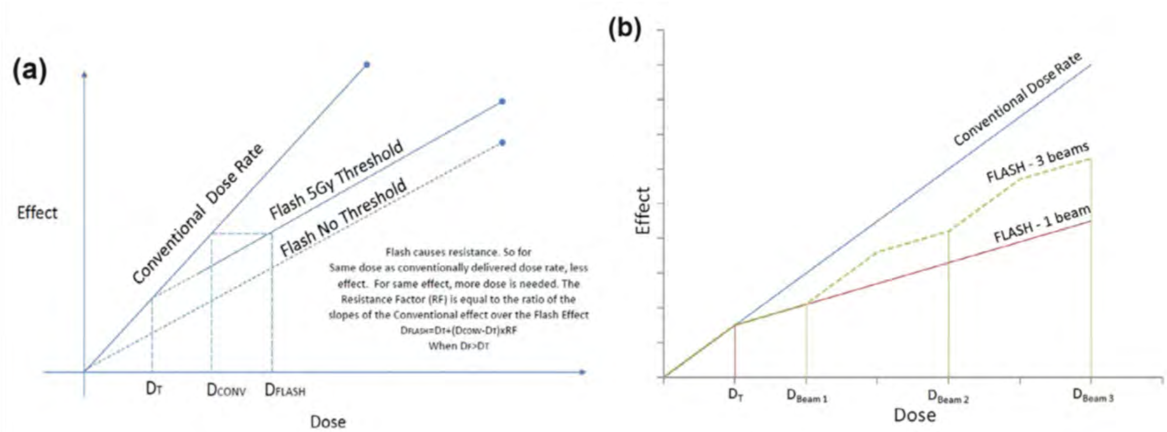


- The pO2 recovery rate was significantly slower in sarcoma tumor tissue (44 seconds vs 5 seconds); normal tissue shows no depletion

Depletion depends on initial pO2 level of the tissue

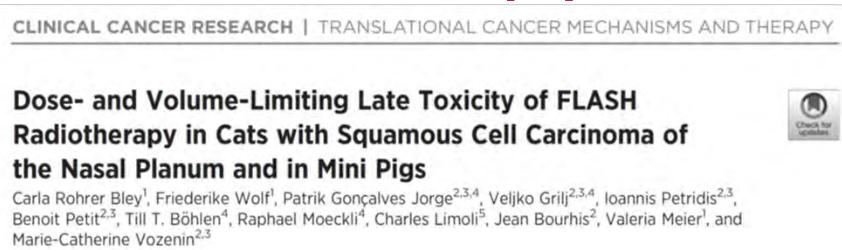


Potential impact of Threshold Dose and Multibeam Delivery



R Mackay et al. Radiotherapy and Oncology 2021

Late Toxicities of FLASH – the jury is out



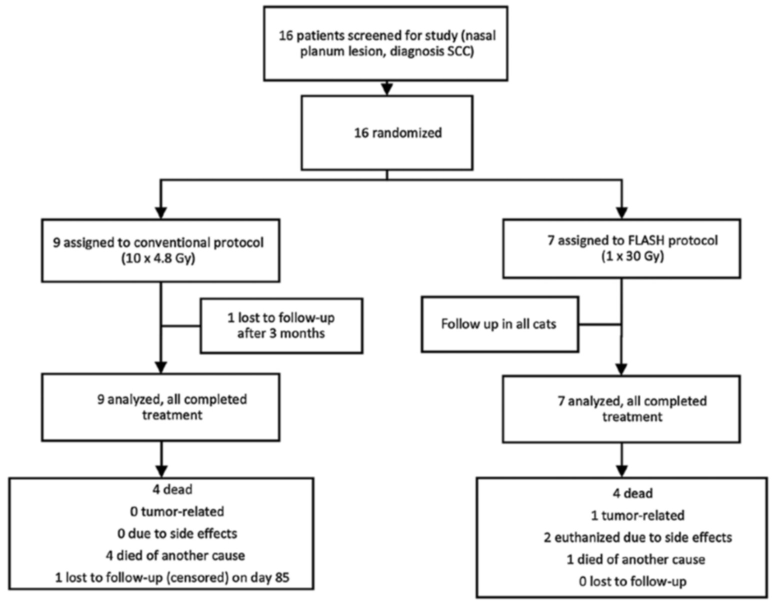
CLINICAL CANCER RESEARCH | TRANSLATIONAL CANCER MECHANISMS AND THERAPY

Dose- and Volume-Limiting Late Toxicity of FLASH Radiotherapy in Cats with Squamous Cell Carcinoma of the Nasal Planum and in Mini Pigs

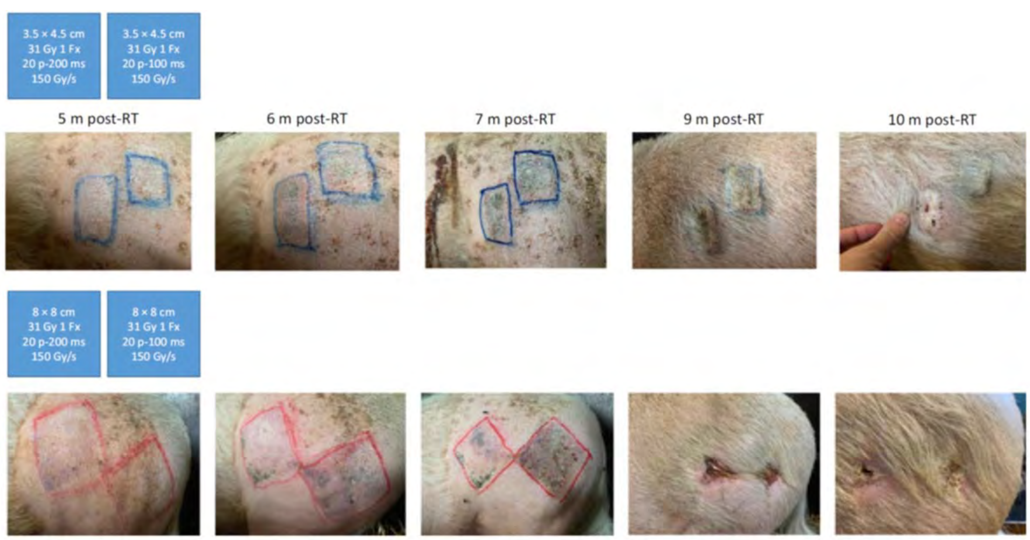
Carla Rohrer Bley[1], Friederike Wolf[1], Patrik Gonçalves Jorge[2,3,4], Veljko Grilj[2,3,4], Ioannis Petridis[2,3], Benoit Petit[2,3], Till T. Böhlen[4], Raphael Moeckli[4], Charles Limoli[5], Jean Bourhis[2], Valeria Meier[1], and Marie-Catherine Vozenin[2,3]

- **Randomized phase III cat patient trial (cats with carcinomas in nasal cavity region)**
  - SoC - 4.8 Gy x 10 fractions vs. FLASH 30 Gy x 1
  - The trial was prematurely terminated due to maxillary bone necrosis from 9-15 months after 3 of 7 cats treated in the FLASH arm vs. 0 of 9 in the SoC arm
  - 1-yr survival free for both arms
  - Late toxicities are similar

Trial Results

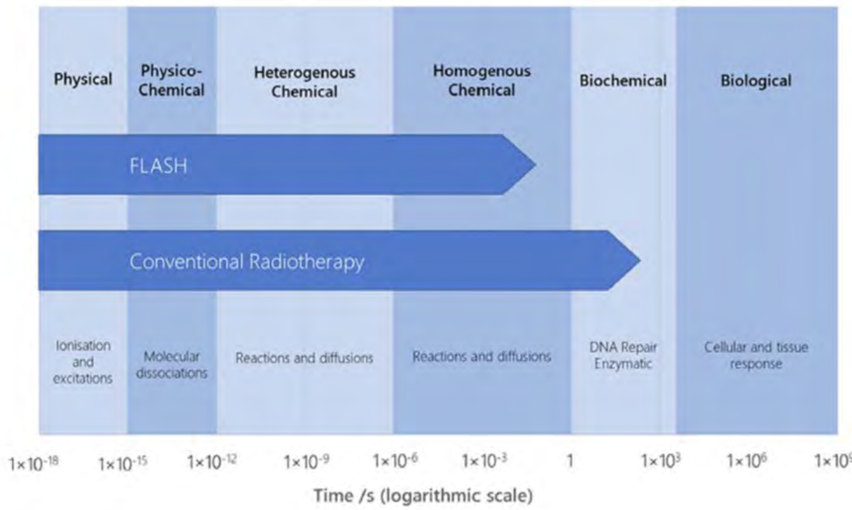


Volume effect of FLASH RT on pig's skin



The Mechanism of FLASH is still unknown

Cause vs. Result – it's challenging to confirm the FLASH mechanism



Vozenin et al. [2019] MacKay [2022]

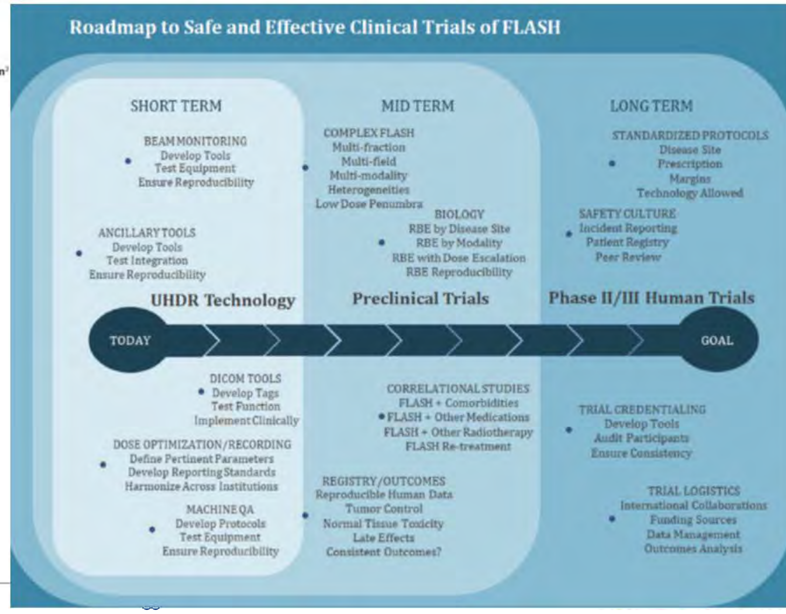
NIH grant support for FLASH Research

SPECIAL ISSUE PAPER

MEDICAL PHYSICS

A roadmap to clinical trials for FLASH

Paige A. Taylor[1] | Jean M. Moran[2] | David A. Jaffray[1] | Jeffrey C. Buchsbaum[3]



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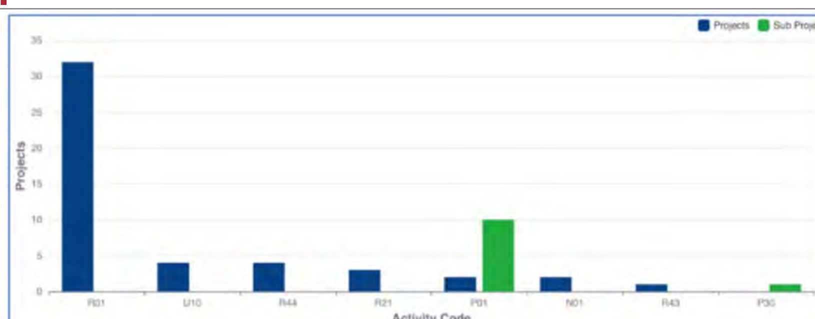
NIH grant support for FLASH Research

- **Funding in 2021**
  - 5 projects
  - $4.7M
- **Funding in 2022**
  - 48 projects
  - $25.8M



Note: Please note that if the hit list contains both a subproject and its parent grant, the subproject funding is already included in the parent project funding amount.

* Funding data available only for NIH, CDC, FDA, AHRQ, and ACF.

Activity Code	Projects	Total Funding	Sub Projects	Sub Project Funding
R01	32	$12,581,618		
U10	4	$3,956,922		
R44	4	$2,556,478		
R21	3	$552,434		
P01	2	$4,236,007	10	$3,591,870
N01	2	$1,683,454		
R43	1	$279,543		
P30			1	$17,316
Total	48	$25,846,456	11	$3,609,186

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FLASH Proton Therapy Research

To achieve a high dose rate to a large treatment field

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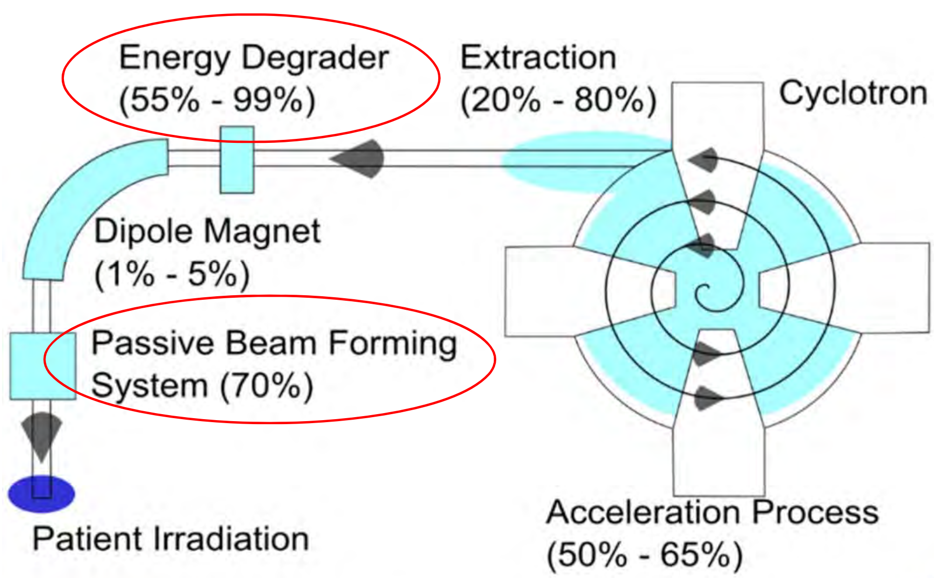
Beam Loss in Typical Cyclotron-based Proton Therapy Systems



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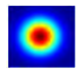
How many protons per second do you need at nozzle?

- **The dose and flux relationship for a thin-buildup geometry**

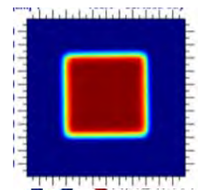
$$D = 1.602 \times 10^{-10} \left(\frac{S(E)}{\rho}\right)_w \phi$$

- **For typical pencil beam ~ 1cm, the general estimate for a single spot at high energy (200 MeV):**
  - 22 nA at nozzle to give 100 Gy/s



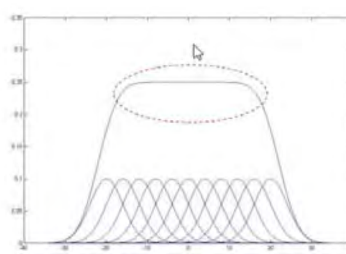
  - 10 Gy requires at least 1.5x10^10 (15Gy/s) protons (~ dose for the size of a pencil beam)

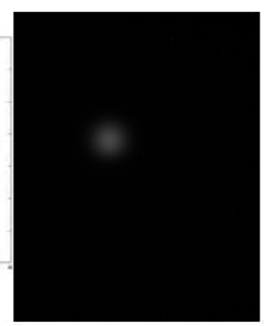
- **Field size could be a strong limitation using current systems**
  - DS/US/PBS to spread beam laterally
  - **5cm x 5cm at 100 Gy/s requires ~600 nA at the nozzle!**

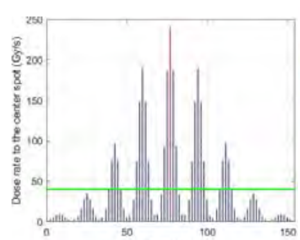


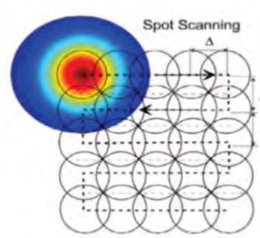
Can you use pencil beam scanning to increase field size?

- **Yes, scanning magnet is very fast!**
  - Spot movement in ~ 5ms
- **PBS creates pulse beam delivery**
  - The voxel dose rate is impacted by both the pencil beam spot and the penumbra
  - Dose rate varies at each voxel
- **It's unclear what is the biological effect of variable dose rate delivery!**







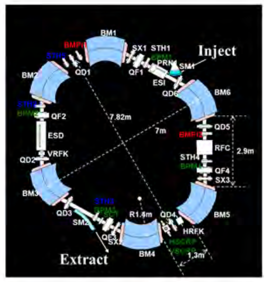


(Zou, 2020)

Beam Delivery Techniques and Timing

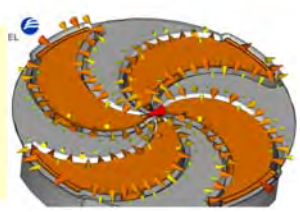
Synchrotron (pulsed beam)

- 7 Mev horizontal multi-turn injection
- 70 – 250 MeV extraction energy
- 0.4 MeV resolution
- 2 – 6.7 sec/cycle
- 0.5 - 5 sec/spill
- > 8 x 10^{10} p/pulse
- 20 nC/p - 2 Gy/min
- pulse to pulse energy change



Cyclotron (microwave frequency)

- Fixed exit extraction energy
- 300 nA – 800 nA
- 72 Mhz – 100 Mhz
- Period: 10-15 ns
- Energy adjustment using degrader



Mevion Synchrocyclotron

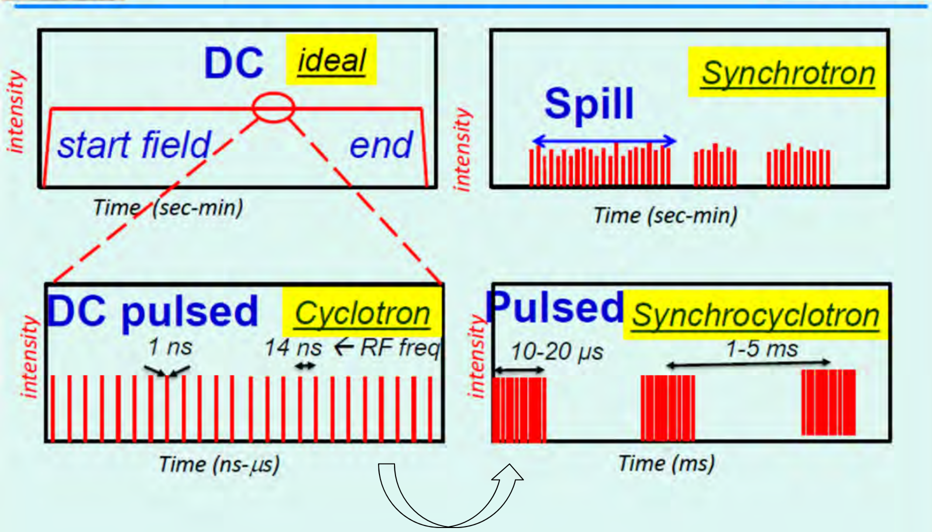
IBA ProteusOne S2C2 model Synchrocyclotron

Proton Linac

S250	MEVION	SC Syn	250 MeV	20 T 1.8 m	- ?	500 Hz period	~ 9 T
S2C2	IBA	SC Syn	230 MeV	<50 T 2.5 m	- ?	1 kHz period	~ 6.56 T

Time structures of beams

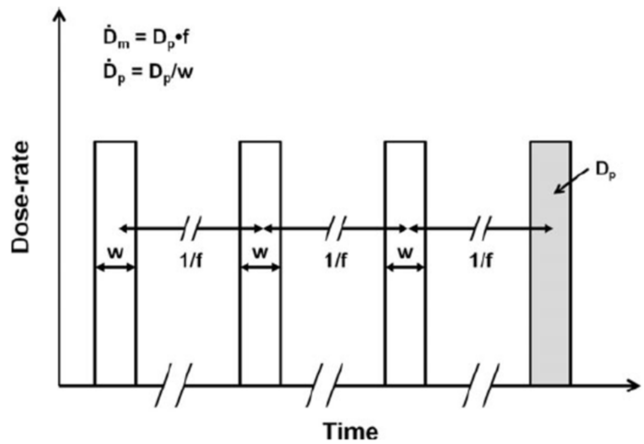
PTCOG PAUL SCHERRER INSTITUT PSI



Marco Schippers - PSI

Physics Challenges – Dose Rate Definitions for PBS

- **Pulse beam delivery**
- **Instantaneous voxel dose rate**
- **Mean voxel dose rate**
  - Average dose rate per field

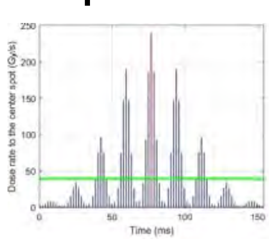


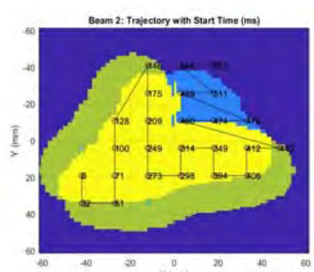
Jaccard et al. Med Phys 45(2) 2018

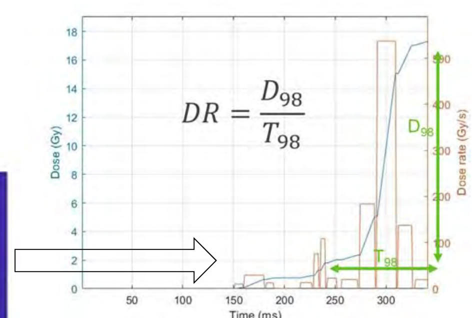
Defining dose rate is a challenge by itself

- **Different dose rate definitions**
  - See some examples to the right
  - None of them correlates with outcome (yet)
- **Pencil beam scanning makes dose rate definition even more complicated**

- **Instantaneous dose rate**
- **Average dose rate per field**
- **Dose-weighted voxel dose rate**







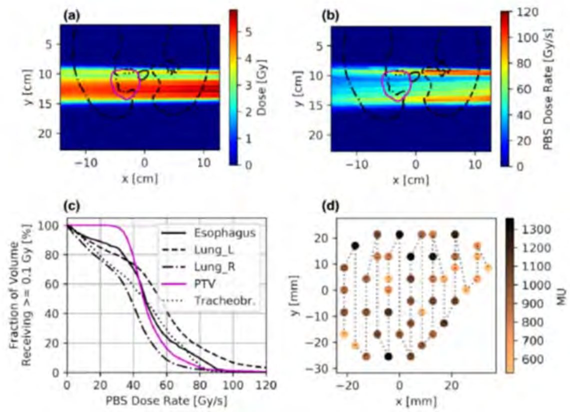
$$\overline{DR} = \frac{1}{N} \sum_{i:D_i \geq D_{min}} \left(\frac{D_{98}}{T_{98}}\right)_i$$

(Zou et al. Radiother Oncol 2020)

Provided by IBA

Physics Challenges – Dose Rate Definitions for PBS

- **Pulse beam delivery**
- **Instantaneous voxel dose rate**
- **Mean voxel dose rate**
  - Average dose rate per field
- **Average dose rate**
- **Effective dose rate**
  - Excluding beam idling time or low dose effect
- **Dose-weighted mean instantaneous dose rate for pencil beam spots**



Folkerts et al. "A framework for defining FLASH dose rate for PBS" Med Phys. 2020

Physics Challenges – Dose Rate Definitions for PBS

- **Pulse beam delivery**
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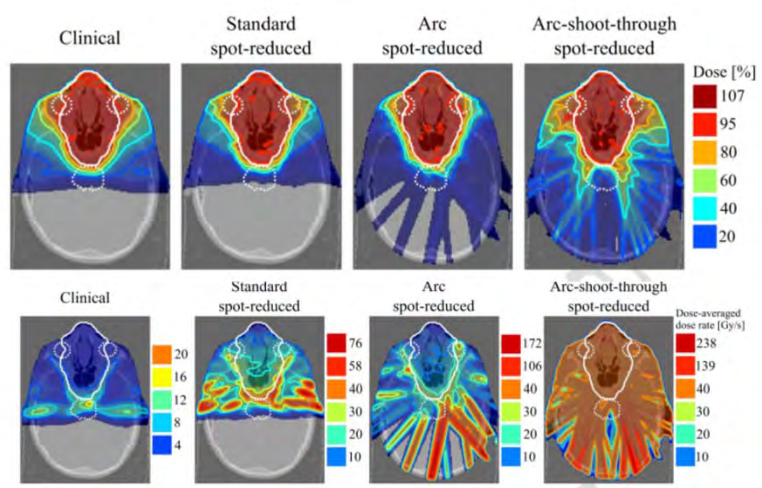
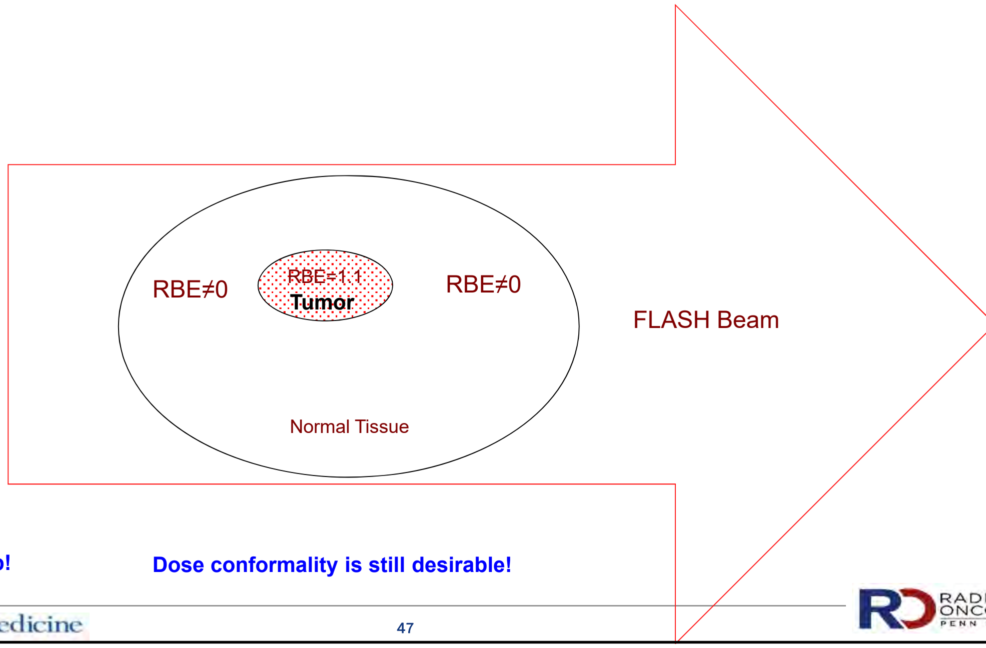


Dose-weighted mean of instantaneous dose rate for all pencil beam spots

- S van de Walter et al. "Towards FLASH proton therapy: the Impact of Treatment Planning and Machine Characteristics on achievable Dose Rates" Acta oncologica 58.10 (2019)

Treatment Planning with FLASH – transmission vs. conformal

Do not have enough protons for treating a large field!



PBS can help!

Dose conformality is still desirable!

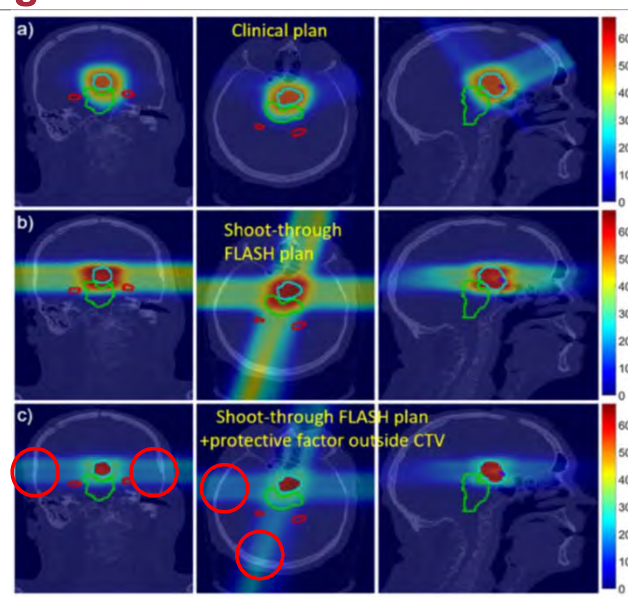
Transmission Beam planning

- **For small targets, the use of high-energy transmission beam technique may be a viable solution for FLASH treatment**
  - Graph assumes 50% sparing

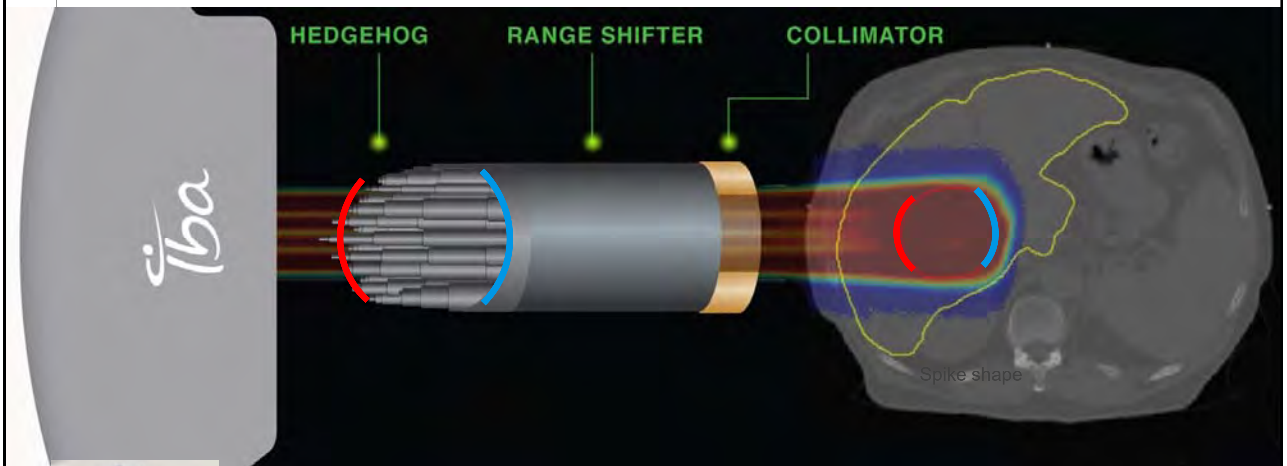
  Frank Verhaegen et al. "Considerations for shoot-through FLASH proton therapy" PMB 2021

- **FLASH spares normal tissue by a factor of only 20-50%.**

  Reviewed in Wilson et al Frontiers Oncology 2020



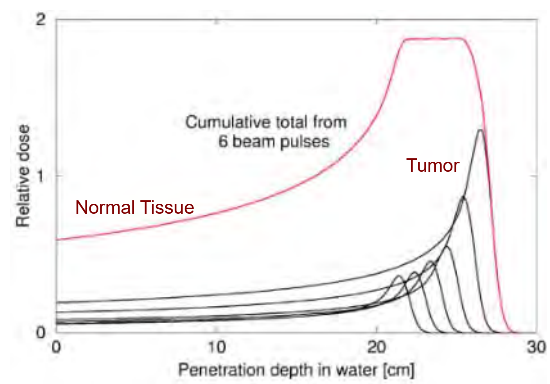
ConformalFLASH® Modulator



- **Control distal surface**
- Control proximal surface
- Control SOBP flatness

Plateau vs. Bragg Peak

- **Bragg Peak**
  - High LET
  - Higher ionization density
  - Is there a FLASH effect at the Bragg Peak as in the plateau region?



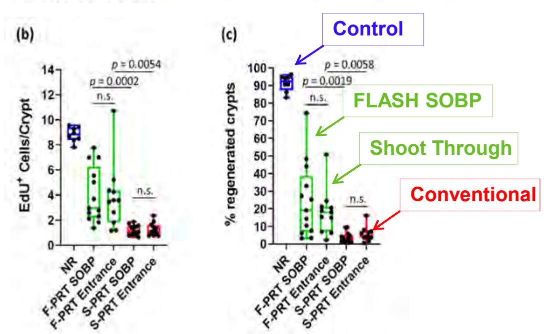
First results of conformalFLASH irradiation on mice at Penn

cancers MDPI

Article

Comparison of FLASH Proton Entrance and the Spread-Out Bragg Peak Dose Regions in the Sparing of Mouse Intestinal Crypts and in a Pancreatic Tumor Model

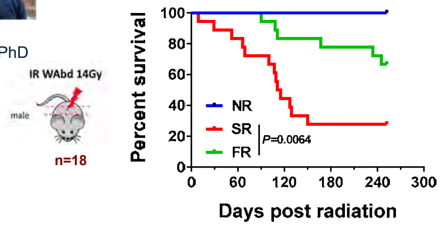
Michele M. Kim †, Ioannis I. Verginadis †, Denisa Goia, Allison Haertter, Khayrullo Shoniyozov, Wei Zou, Amit Maity, Theresa M. Busch, James M. Metz, Keith A. Cengel, Lei Dong, Costas Koumenis and Eric S. Diffenderfer *

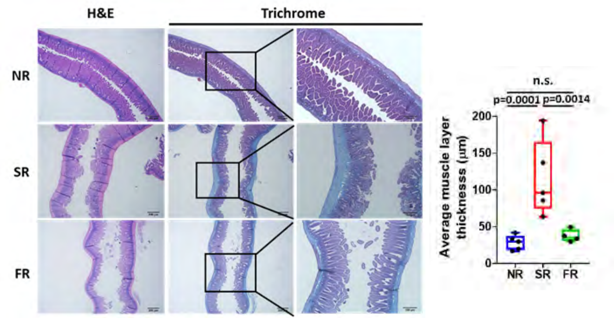


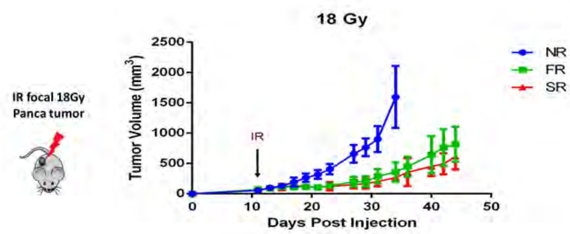
Source: Kim et al. Comparison of FLASH Proton Entrance and the Spread-Out Bragg Peak Dose Regions in the Sparing of Mouse Intestinal Crypts and in a Pancreatic Tumor Model

Focal F-PRT is equipotent with S-PRT on PanCa but reduces intestinal fibrosis

Yiannis Verginadis, PhD







Diffenderfer *et al., IJRBOP; 2020*

Penn Radonc Proton FLASH "Firsts"

Proton FLASH normal tissue sparing


Physics Contribution

Design, Implementation, and in Vivo Validation of a Novel Proton FLASH Radiation Therapy System

Proton FLASH dog trial


CANCER RESEARCH | TRANSLATIONAL SCIENCE

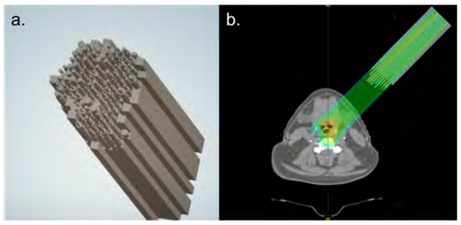
FLASH Proton Radiotherapy Spares Normal Epithelial and Mesenchymal Tissues While Preserving Sarcoma Response

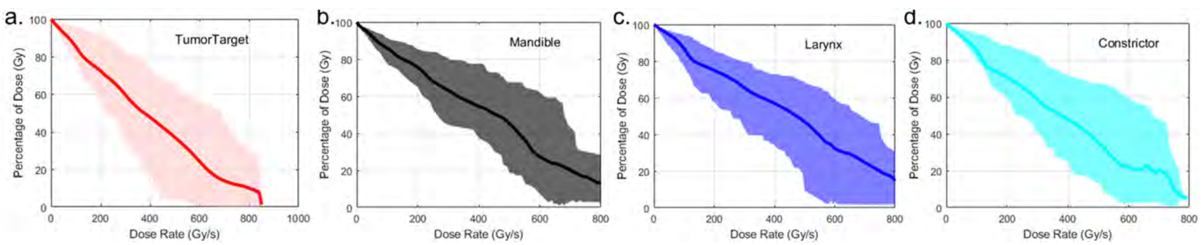
Proton FLASH effect with Bragg Peak


cancers

Comparison of FLASH Proton Entrance and the Spread-Out Bragg Peak Dose Regions in the Sparing of Mouse Intestinal Crypts and in a Pancreatic Tumor Model

Presentation of Treatment Planning Results for FLASH





Dose Rate Histogram

Julia Pakela et al. AAPM Presentation (2022)

Comparing Ultra-High Dose Rate Proton Delivery Techniques From Radiophysical, Radiochemical, and Radiobiological Perspectives – Best of Physics

- **Ray Yang*, Lei Dong, Eric Diffenderfer**
- **To simulate four distinct spatial-temporal modes of proton FLASH delivery: {Ridge-Filter (RF), Range-Modulated Double-Scattering (RM), Pencil Beam Scanning (PBS), and Hybrid Pencil Beam through Ridge-Filter (PBS-RF)}, using three complementary perspectives to compare surrogate metrics of tissue sparing: {phenomenological oxygen effect, radiochemical kinetics of peroxyl radical recombination, and survival of circulating immune cells}.**

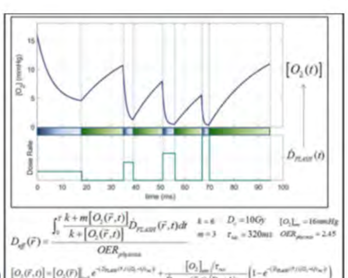
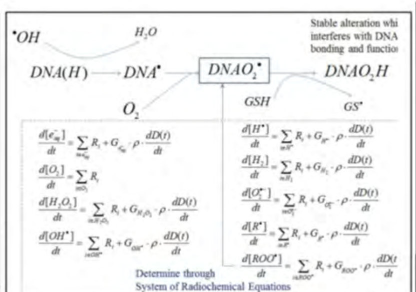


Figure 1: Oxygen depletion mediated radio-sensitization



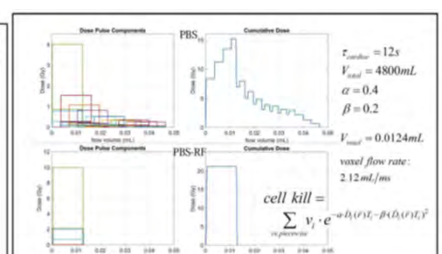
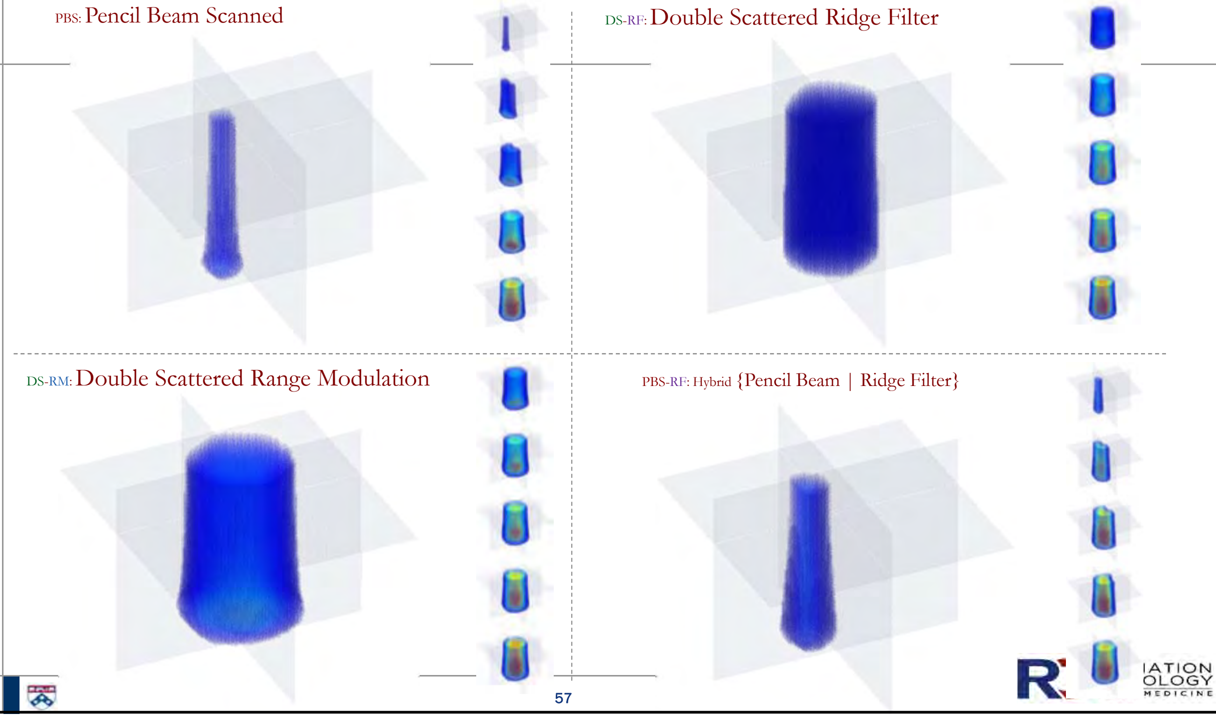


Figure 5: Contrasting dose seen by partial volumes flowing across sample voxel using PBS and hybrid PBS-RF; model parameters for cell kill



Biology-based FLASH Plan Optimization – Ray Yang (AAPM 2022)

- **Each voxel's resulting dose rate sequence feeds into models of (i) oxygen depletion and recovery, mediating radio-sensitization through the OER k-curve, (ii) system of radiochemistry rate equations accounting for organic radicals causing DNA damage fixation, and (iii) survival of blood-pool lymphocytes crossing the radiation field over multiple cardiac cycles.**

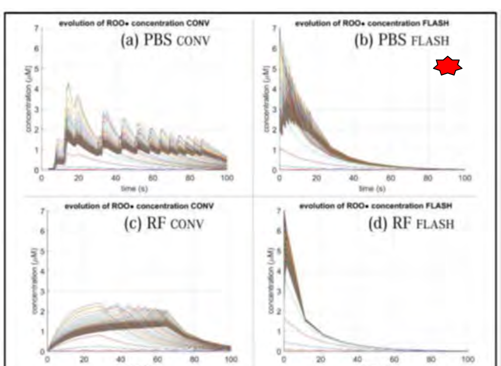


Figure 4: Concentration of organic radicals in central axis voxels during delivery: PBS vs RF at conventional and FLASH dose rates

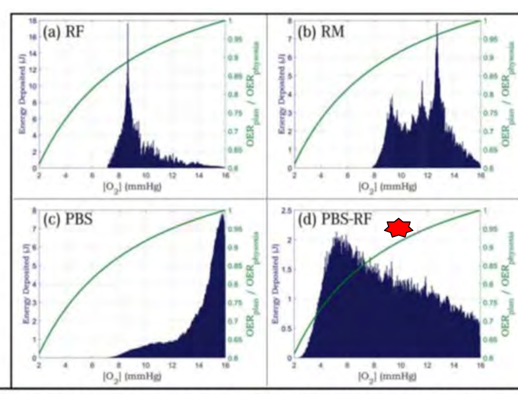


Figure 2: Energy desposition as a function of oxygen concentration for various delivery techniques, superimposed on OER ratio indicating effective sparing

Penn Medicine

RADIATION ONCOLOGY PENN MEDICINE

FLASH is biology-based RT without a well-established theory (yet)

Possible Factors that can directly impact treatment planning:

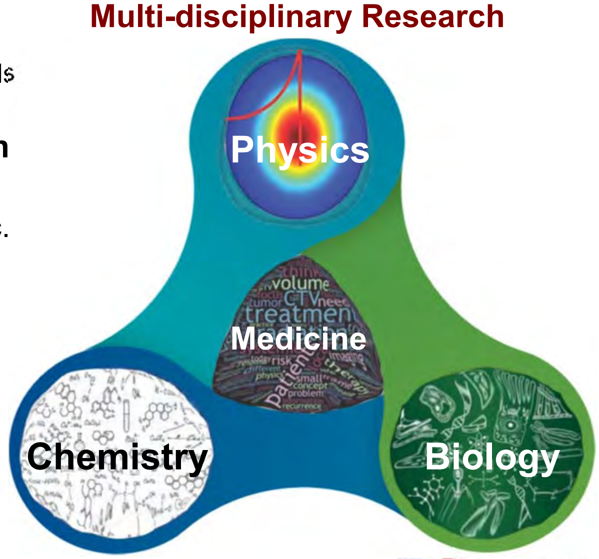
- **Threshold Dose per fraction or per field? (minimum at 5 Gys)**
- **Dose rate threshold? (how to define dose rate?)**
- **Tissue initial oxygen levels (which normal tissue that can benefit the most?)**
- **Repair kinetics?**
- **Biological endpoint (which tissue can benefit most?)**
- **Dose conformality requirement?**

Summary of FLASH Physics

- **FLASH can be realized by different modalities and hardware platforms**
  - Treatment delivery or treatment planning needs to consider hardware implementations
- **Significant progress has been made on dose measurements**
  - Different detectors to measure FLASH etc.
- **It's still too early for some physics tasks; planning studies are useful!**

Possible FLASH Factors:
- Threshold Dose
- Dose Rate(s)?
- Tissue oxygen level
- Repair kinetics
- Biological endpoint
- Document FLASH delivery

Active Participation of Multi-disciplinary Research



Technology has proven translatable to the clinic

- IMRT (dynamic MLC; VMAT; HyperArc etc.)
- IGRT (see picture on the right)
- SBRT (3 x 20Gy etc.)
- Electronic Brachytherapy
- Pencil Beam Scanning (particle therapy)
- Deformable image registration
- On-line adaptive radiotherapy
- Machine Learning (auto-segmentation etc.)
- FLASH (why not?)
- …

FLASH has created a new ecosystem in technology

- Faster control system in the future
- Better dosimetry system to measure high dose rates
- Freezing patient motion
- Faster throughput in treatment…

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