The Promise of FLASH: Clinical translation

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What are FLASH & PHASER?

FLASH:
Ultra-fast near-instantaneous radiation treatment

PHASER:
Novel technology platform being developed for clinical translation of FLASH RT

Ultra-rapid “FLASH” RT: New biology
FLASH RT biology experiments at Stanford
FLASH total abdomen irradiation

Normal female C57BL/6 mice

Surviving crypts 96 hr post-TAI

Syngeneic orthotopic (peritoneal) ID8 ovarian cancer in C57BL/6

Relative body weight comparison by days post-TAI

24h Stool Weight

Surviving Small Intestinal Crypts

96h Post-Irradiation

Crypts per circumference

Surviving crypts 96 hr post-TAI
FLASH total abdomen irradiation

Syngeneic orthotopic (peritoneal) ID8 ovarian cancer in C57BL/6

Unirradiated  FLASH 14 Gy  CONV 14 Gy

Day 31 solid tumor count

Levy/Rankin, Wang/Loo Unpublished 2019

FLASH total abdomen irradiation

Late cancer induction

Cancer induction @ 1 yr:
Control: 0/5
CONV: 2/8
FLASH: 0/6

Levy/Rankin Unpublished 2018

FLASH: Improved tumor control

Subcutaneous Lewis lung carcinoma in C57BL/6 (syngeneic)

Levy/Rankin - Stanford

Chou, Lartey Unpublished 2017
**FLASH: Decreased metastasis**

Subcutaneous MOC2 in C57BL/6 (syngeneic)

Number: Cao Unpublished 2017

**FLASH – Summary of biological findings**

Compared to conventional dose rate irradiation, FLASH achieves:

- Reduced normal tissue injury
  - Multiple organ systems: lung, brain, intestinal tract, skin
  - Multiple mouse strains, multiple species
- Equal or better tumor killing *in vivo*
  - Multiple tumor models

**Clinical translation of FLASH RT**
75-yr-old with disseminated cutaneous T-cell lymphoma
- Progression through multiple systemic regimens over first 10 years
- Treated with 110 courses of localized RT over last 10 years
- 20-21 Gy in 6-10 fractions
- Good local tumor control, severe acute toxicity taking 3-4 months to heal

1.5 cm symptomatic ulcerated R forearm lesion selected for treatment on protocol

Day 0
Alanine dosimeters

Day 15
Complete response 4 no post dose

3 months
Unirradiated
FLASH
FLASH – Current technology

It is technically feasible to deliver FLASH to patients using modifications of existing clinical/preclinical systems:

- Electron beams: superficial targets
- Proton pencil beams: small volumes from single direction

New technology is needed for FLASH RT to general cancer targets in patients

Precision RT – overcoming a key barrier

Hitting moving targets – current “motion management”

Need for speed: Instantaneous treatment to “freeze” motion

PHASER: Next generation radiation therapy

- 300X faster: Freezes motion, ultimate precision
- FLASH RT: New biological advantages
- Compact & economical: Global access to RT
High-output linear accelerator

- First new design in 60 years
- 3X better power efficiency
- 300X more beam current
- 10X lower manufacturing cost

Maxim, Tantawi, Loo Radiother Oncol 2019

Eliminating slow mechanical motion

RF phased-array power distribution (RAPID) network

Maxim, Tantawi, Loo Radiother Oncol 2019

Eliminating slow mechanical motion

Scanning Pencil-beam High-speed Intensity-modulated X-ray source (SPHINX)

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Integrated rapid volumetric imaging

Conical beam geometry – common isocenter between treatment beams and full ring diagnostic-quality CT imager

Integrated PHASER system
Accelerating clinical efficiency with AI

Automation by machine learning leverages PHASER's imaging & speed capabilities fully to maximize clinical throughput → accessibility in resource constrained regions of world

Vision: PHASER clinical system

Fits in standard ISO 668 cargo container
**Vision: PHASER clinical system**

**Globally accessible curative cancer care**

**FAQs**

• Don't we risk "missing" the tumor in a FLASH?
  – No, integrated rapid volumetric image-guidance is key
  – Rational margin design principles still apply

• Won’t ultra-fast delivery be a nightmare for QA?
  – No, multiple relatively straightforward strategies can be designed up front
Get PHASER to "Cure"

Pluridirectional High-energy Agile Scanning Electronic Radiotherapy (PHASER)