IMPERIAL

LhARA
Laser-hybrid Accelerator for Radiobiological Applications

EVALUATING NEW MODALITIES IN RADIOTHERAPY

JOSIE MCGARRIGLE

KENNETH LONG

YOLANDA PREZADO

institut Curie

cnrs

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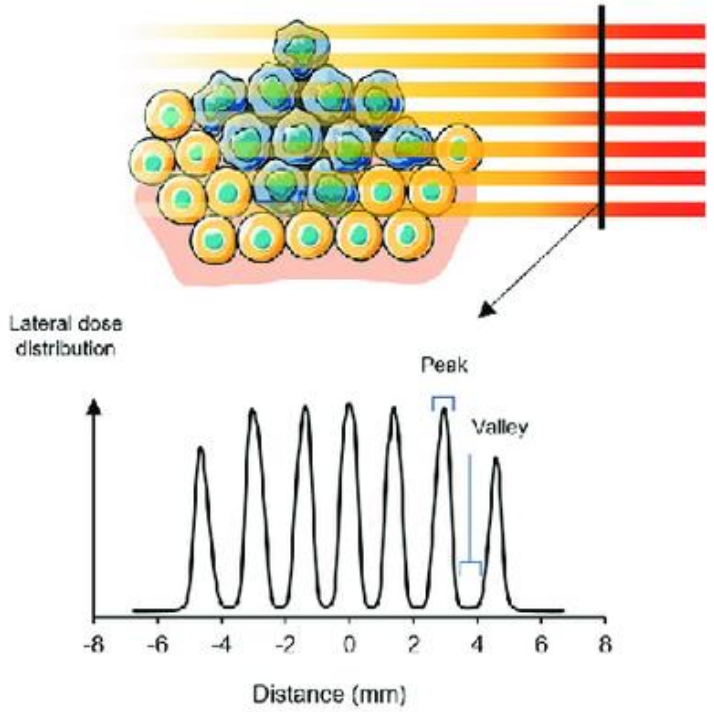
NEW MODALITIES

< 200 ms

$\dot{D}$ ≥ 40 Gy/s (Ultra-High Dose Rate)

Homogeneous dose distribution



FLASH- Ultra-high dose rate radiotherapy

(Time modulation)

- Reduces adverse toxicities than are present in the response to conventional radiotherapy.
- Origin is unknown and the current understanding of the factors that influence the FLASH effect is limited.

SFRT- Spatially Fractionated Radiotherapy

(Spatial Modulation)

- Separates the beam into fractions to, sparing the normal-tissue during treatment.
- MRT, ≤100μm width beamlets, MBRT, >100μm width beamlets.
- Limited knowledge of influences.

FLASH STUDY

ULTRA-HIGH DOSE RATE
RADIOTHERAPY

LITERATURE REVIEW STUDY- FLASH

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EDITED BY
Kevin Prise,
Queen's University Belfast, United Kingdom

REVIEWED BY
Angelica Facoetti,
National Center of Oncological Hadrontherapy, Italy
Ralph Eric Vatner,
University of Cincinnati, United States

*CORRESPONDENCE
Josie May McGarrigle
jmm119@ic.ac.uk
Kenneth Richard Long
k.long@imperial.ac.uk
Yolanda Prezado
yolanda.prezado@curie.fr

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The FLASH effect—an evaluation of preclinical studies of ultra-high dose rate radiotherapy

Josie May McGarrigle[1]*, Kenneth Richard Long[1,2]* and Yolanda Prezado[3,4]*

[1]Department of Physics, Imperial College London, London, United Kingdom, [2]Science and Technology Facilities Council (STFC), Rutherford Appleton Laboratory, Oxford, United Kingdom, [3]Institut Curie, Universite Paris-Saclay, Centre national de la recherche scientifique (CNRS) UMR3347, Inserm U1021, Signalisation radiobiologie et cancer, Orsay, France, [4]Universite Paris-Saclay, Centre national de la recherche scientifique (CNRS) UMR3347, Inserm U1021, Signalisation radiobiologie et cancer, Orsay, France

FLASH radiotherapy (FLASH-RT) is a novel radiotherapy approach based on the use of ultra-high dose radiation to treat malignant cells. Although tumours can be reduced or eradicated using radiotherapy, toxicities induced by radiation can compromise healthy tissues. The FLASH effect is the observation that treatment delivered at an ultra-high dose rate is able to reduce adverse toxicities present at conventional dose rates. While this novel technique may provide a turning point for clinical practice, the exact mechanisms underlying the causes or influences of the FLASH effect are not fully understood. The study presented here uses data collected from 41 experimental investigations (published before March 2024) of the FLASH

In order to explore the influences of different dosimetric parameters on the effectiveness of FLASH, searchable databases were created in order to evaluate:

- Normal-tissue sparing
- Tumour control
- Therapeutic Index
- Increased lifespan
- Survival

LITERATURE REVIEW STUDY- FLASH

Search Criteria

Table 1: Population, Intervention, Comparison, Outcome (PICO) search strategy used to select relevant experiments.

Population	**Intervention**
In-VITRO cells/Small animal *In-VIVO* models	FLASH Radiotherapy
Comparison	**Outcome**
Control group/Pre-radiation	Biological Response Described/Quantified

The parameters identified as potentially correlated with the FLASH effect and considered in this study are:

- Mean Dose Rate (Gy/s)–the average dose rate across the duration of the irradiation;
- Pulse Dose Rate (Gy/s)–the dose rate delivered by each individual pulse, each pulse being composed of a number of bunches from the accelerator;
- Pulse Dose (Gy)–the dose in each pulse;
- Total Dose (Gy)–the total administered dose;
- Pulse Width (μs)–the temporal duration of each pulse;
- Total Duration (s)–the total time taken to administer the full dose;
- Repetition Frequency (Hz)–the frequency at which pulses are delivered; and
- Number of Pulses–the number of pulses delivered.

LITERATURE REVIEW STUDY- FLASH

Evaluation Criteria

Quantitive Scores

Score	Normal-tissue Sparing Score (NTSS)	Tumour Control Score (TCS)
1	No radio-protection	No tumour control
2	Low level of radio-protection	Small amount of tumour control
3	Moderate radio-protection	Moderate tumour control
4	Fair radio-protection	Fair tumour control
5	Great radio-protection	Complete tumour control

Homogeneous Scores

Survival

$$S = \frac{\text{Animals alive } M \text{ months post treatment}}{\text{Animals irradiated}} \times 100$$

Increased Lifespan

$$ILS = \frac{(\text{FLASH}_{MST} - \text{control}_{MST})}{\text{control}_{MST}} \times 100\,;$$

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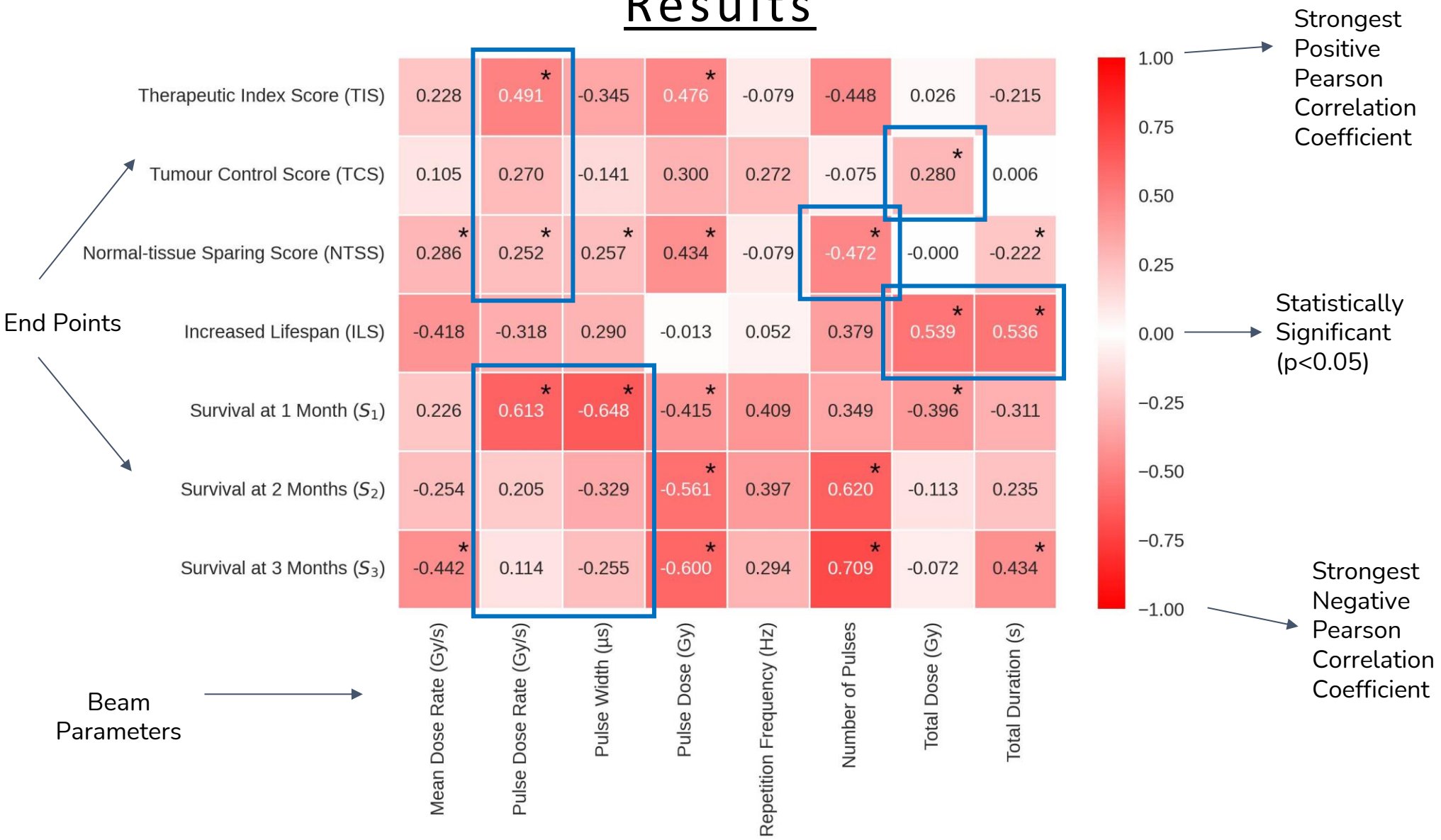
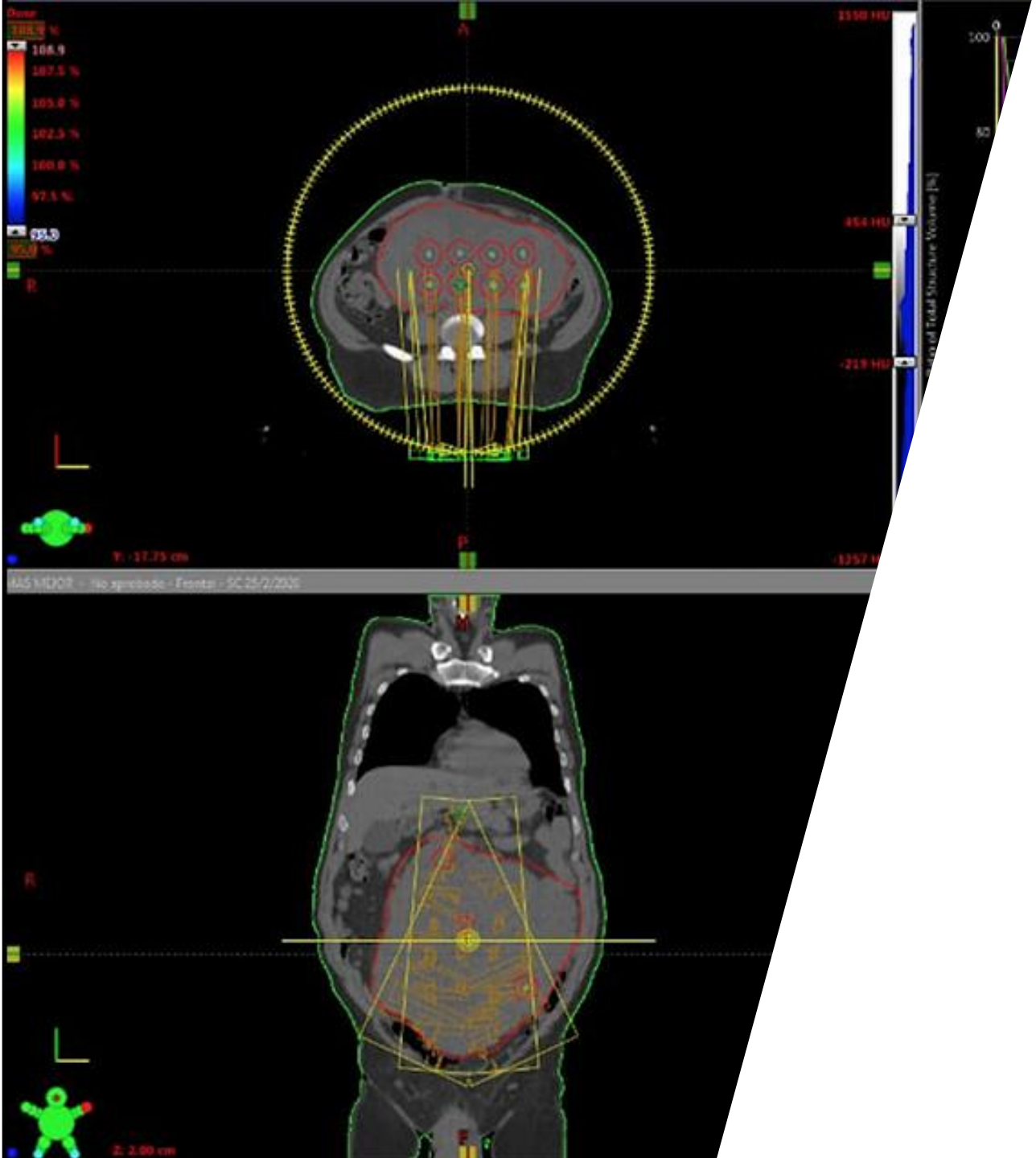
Results





SFRT STUDY

SPATIALLY FRACTIONATED
RADIATION THERAPY

LITERATURE REVIEW STUDY- SFRT

To fill the gaps in the SFRT literature, searchable databases were created in order to evaluate normal-tissue sparing for the following parameters:

- The Geometric Parameters (see Figure 1):
  - Width (μm)
    - the width of each beam segment (the collimator gap width);
  - Spacing (μm)
    - the centre-to-centre (c-t-c) spacing between adjacent beam segments;
  - Valley Width (μm)
    - the edge-to-edge spacing between adjacent beam segments;
  - % Peak Dose
    - the percentage of width compared to c-t-c spacing (indicates the % of volume covered by the peak dose):
      % Peak Dose = $\frac{\text{Width}}{\text{Spacing}} \times 100$;
- The Dosimetric Parameters:
  - Volume Average Dose (Gy)
    - the average dose across the tissue volume;
  - Peak Dose (Gy)
    - the dose received in the peaks of the dose distribution;
  - Valley Dose (Gy)
    - the dose received in the valleys of the dose distribution;
  - PVDR (Peak-Valley-Dose-Ratio)
    - the peak to valley dose ratio: PVDR = $\frac{\text{Peak Dose}}{\text{Valley Dose}}$.

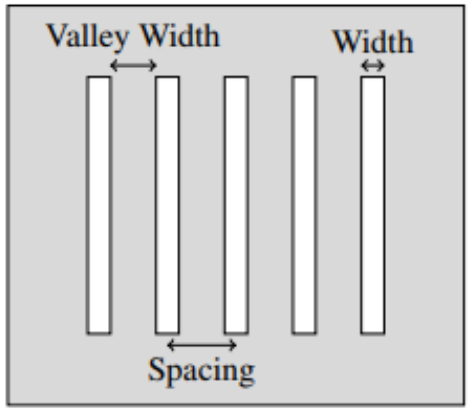


Figure 1: Mechanical collimator diagram annotated with geometric properties.

LITERATURE REVIEW STUDY- SFRT

Search Criteria

- Only a single fraction of unidirectional MRT or MBRT was used in the study
- The study reports Average Dose, Peak Dose, Valley Dose, PVDR, Width, Spacing or Valley Width
- The biological response of normal-tissue to MRT and MBRT is recorded in the study
- Peak dose used in the study is $\leq$ 700Gy
- The experiment in each study was carried out *in-vivo* using small animal models
- MRT or MBRT was exclusively used in each experiment.

Population	**Intervention**
Small animal *in-VIVO* models	Single unidirectional SFRT irradiation (dose $\leq 700Gy$)
Comparison	**Outcome**
Control group/pre-radiation	Biological response described/quantified

Table 2: Population, Intervention, Comparison, Outcome (PICO) search strategy used to select relevant experiments.

LITERATURE REVIEW STUDY- SFRT

Results

THANK YOU

jmm119@ic.ac.uk

FLASH review link