Spatially Fractionated Radiation Therapy **to optimise LhARA**

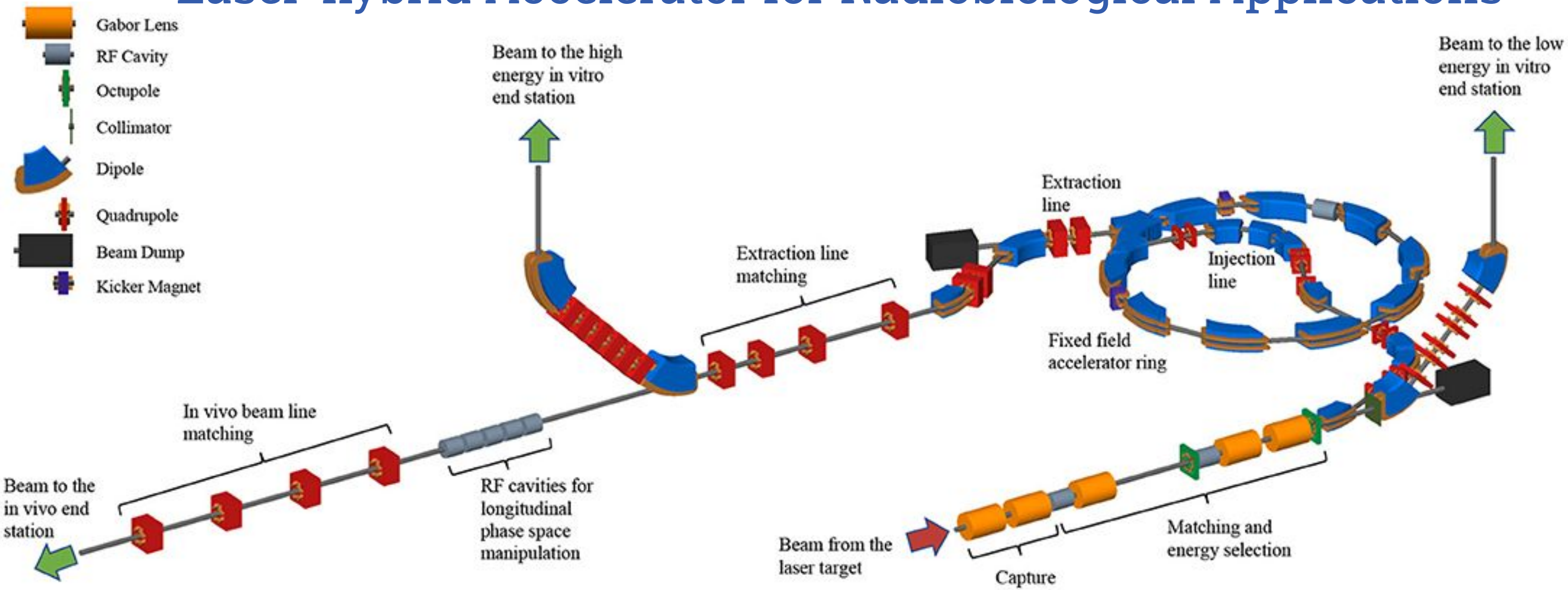
Josie McGarrigle

LhARA
Laser-hybrid Accelerator for Radiobiological Applications

Imperial College London

LhARA

Laser-hybrid Accelerator for Radiobiological Applications



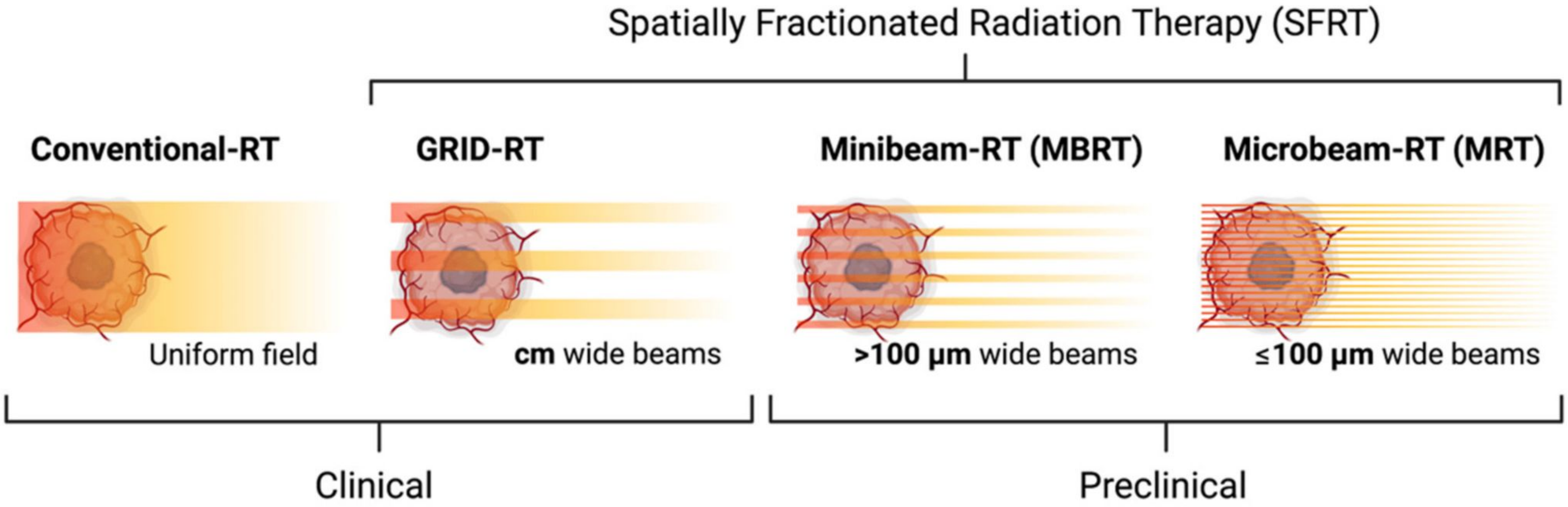
Flexible facility

- dedicated to the study of the biological response to ionising radiation.

Beam sizes

- allow for new radiotherapy modalities e.g. ultra-high dose rates and spatially fractionated radiotherapy delivered in these end stations.

SFRT



SFRT

separates the beam into fractions to minimise the exposure regions, sparing the normal-tissue during treatment.

MRT

Microbeam Radiation Therapy:
≤100μm width beamlets

MBRT

Minibeam Radiation Therapy:
>100μm width beamlets

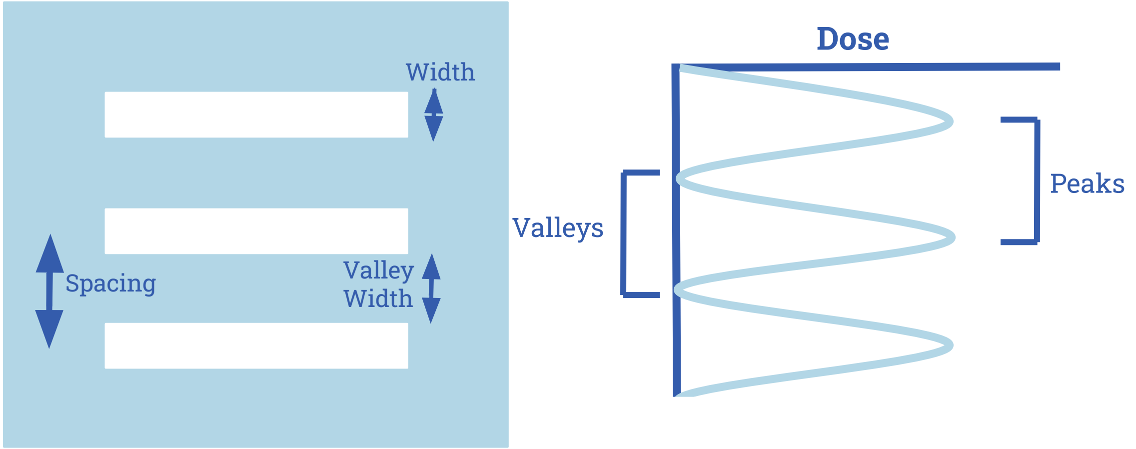
Literature Review Analysis

SFRT parameters:

The Geometric Parameters:
Width (μm)
Spacing (μm)
Valley Width (μm)
% Peak Dose
% Valley Dose

The Dosimetric Parameters:
Volume Average Dose (Gy)
Peak Dose (Gy)
Valley Dose (Gy)
PVDR (Peak-Valley-Dose-Ratio)

3 slit collimator & the associated distribution:

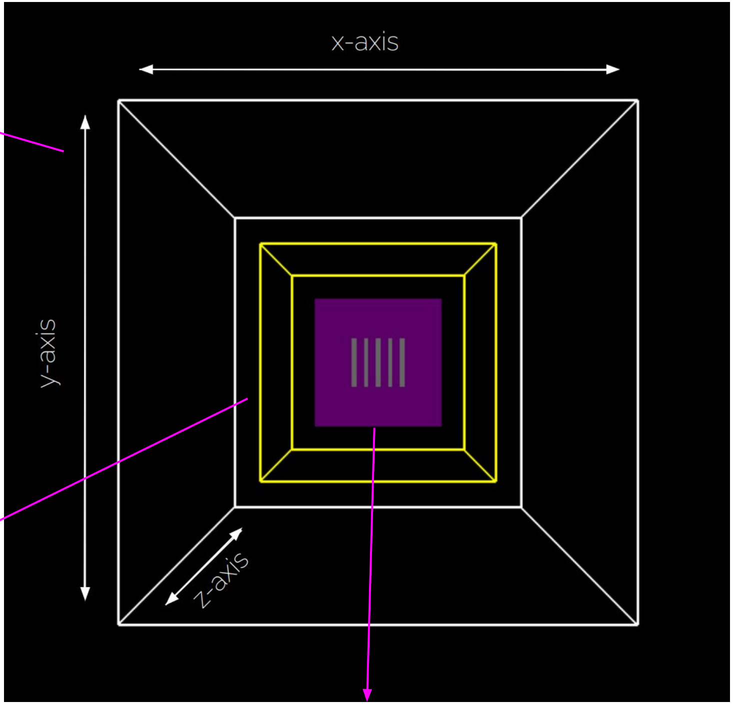


% Valley Dose = 100*(Spacing/Width)

% Peak Dose = 100*(Width/Spacing)

PVDR= 100*(Peak Dose/Valley Dose)

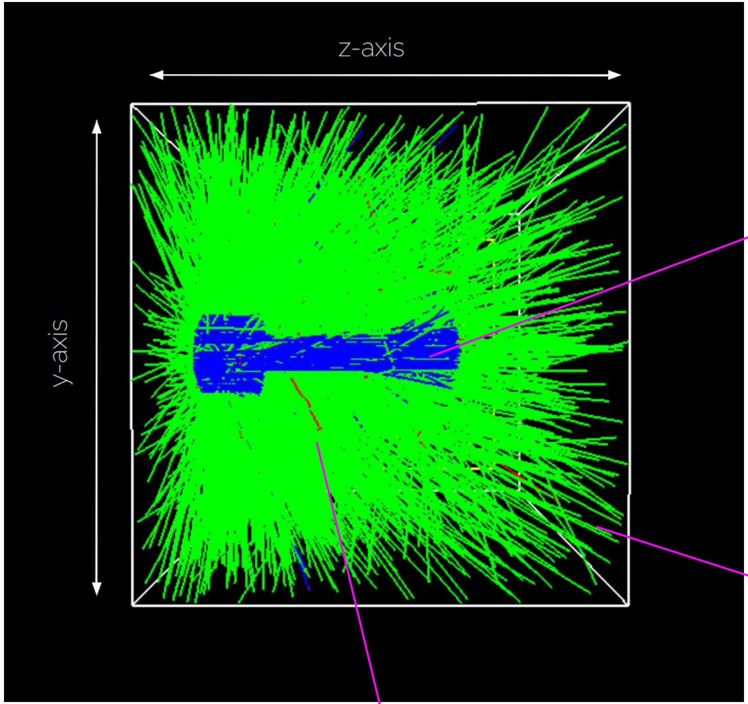
TOPAS Set-Up



‘world’

tissue/
tumour

SFRT collimator

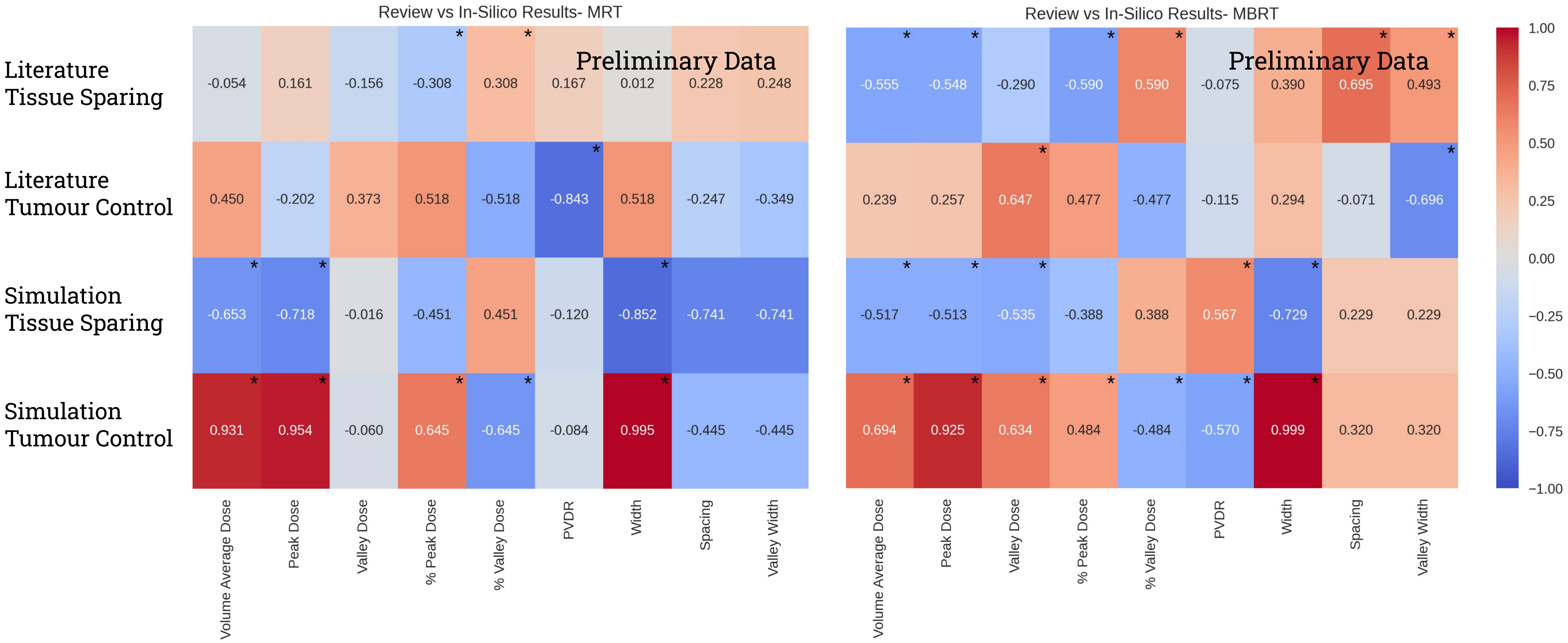


protons

photons

positrons

Literature vs Model correlation coefficients



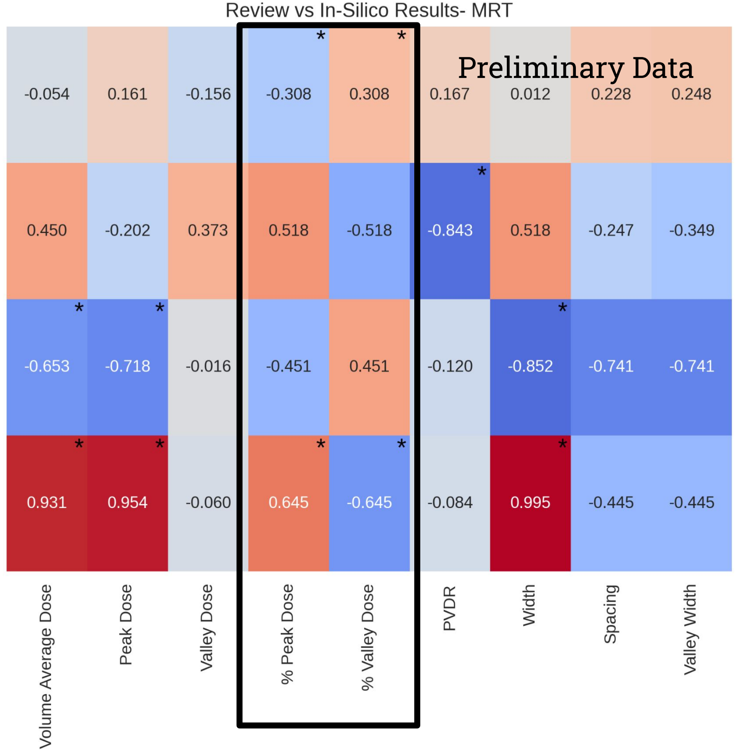
Review vs In-Silico Results- MRT

	Volume Average Dose	Peak Dose	Valley Dose	% Peak Dose	% Valley Dose	PVDR	Width	Spacing	Valley Width
Literature Tissue Sparing	-0.054	0.161	-0.156	-0.308 *	0.308 *	0.167	0.012	0.228	0.248
Literature Tumour Control	0.450	-0.202	0.373	0.518	-0.518	-0.843 *	0.518	-0.247	-0.349
Simulation Tissue Sparing	-0.653 *	-0.718 *	-0.016	-0.451	0.451	-0.120	-0.852 *	-0.741	-0.741
Simulation Tumour Control	0.931 *	0.954 *	-0.060	0.645 *	-0.645 *	-0.084	0.995 *	-0.445	-0.445

Review vs In-Silico Results- MBRT

	Volume Average Dose	Peak Dose	Valley Dose	% Peak Dose	% Valley Dose	PVDR	Width	Spacing	Valley Width
Literature Tissue Sparing	-0.555 *	-0.548 *	-0.290	-0.590 *	0.590 *	-0.075	0.390	0.695 *	0.493 *
Literature Tumour Control	0.239	0.257	0.647 *	0.477	-0.477	-0.115	0.294	-0.071	-0.696 *
Simulation Tissue Sparing	-0.517 *	-0.513 *	-0.535 *	-0.388	0.388	0.567 *	-0.729 *	0.229	0.229
Simulation Tumour Control	0.694 *	0.925 *	0.634 *	0.484 *	-0.484 *	-0.570 *	0.999 *	0.320	0.320

Literature vs Model correlation coefficients



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Preliminary Data

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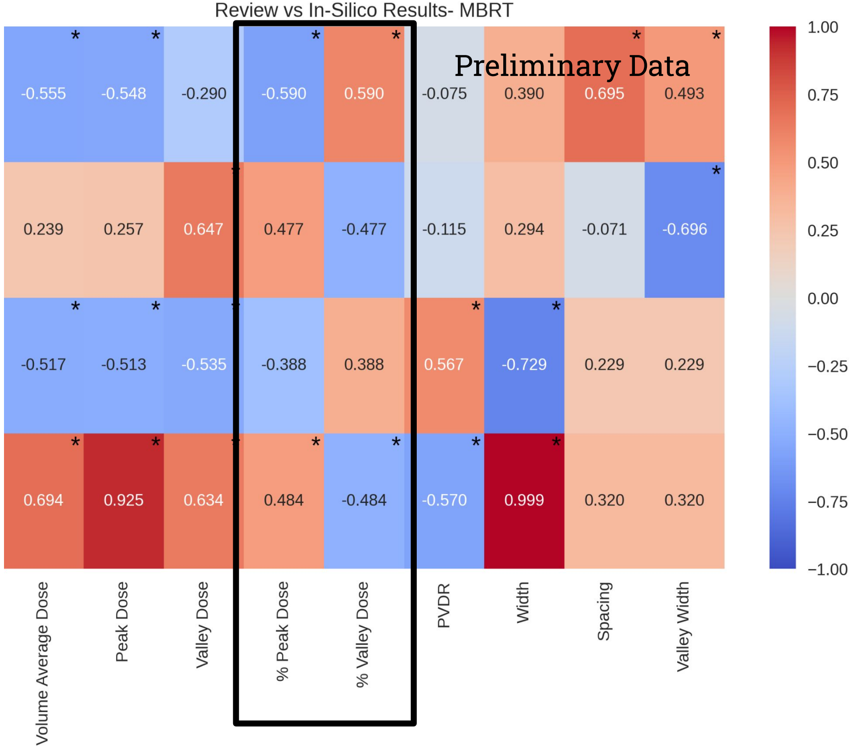

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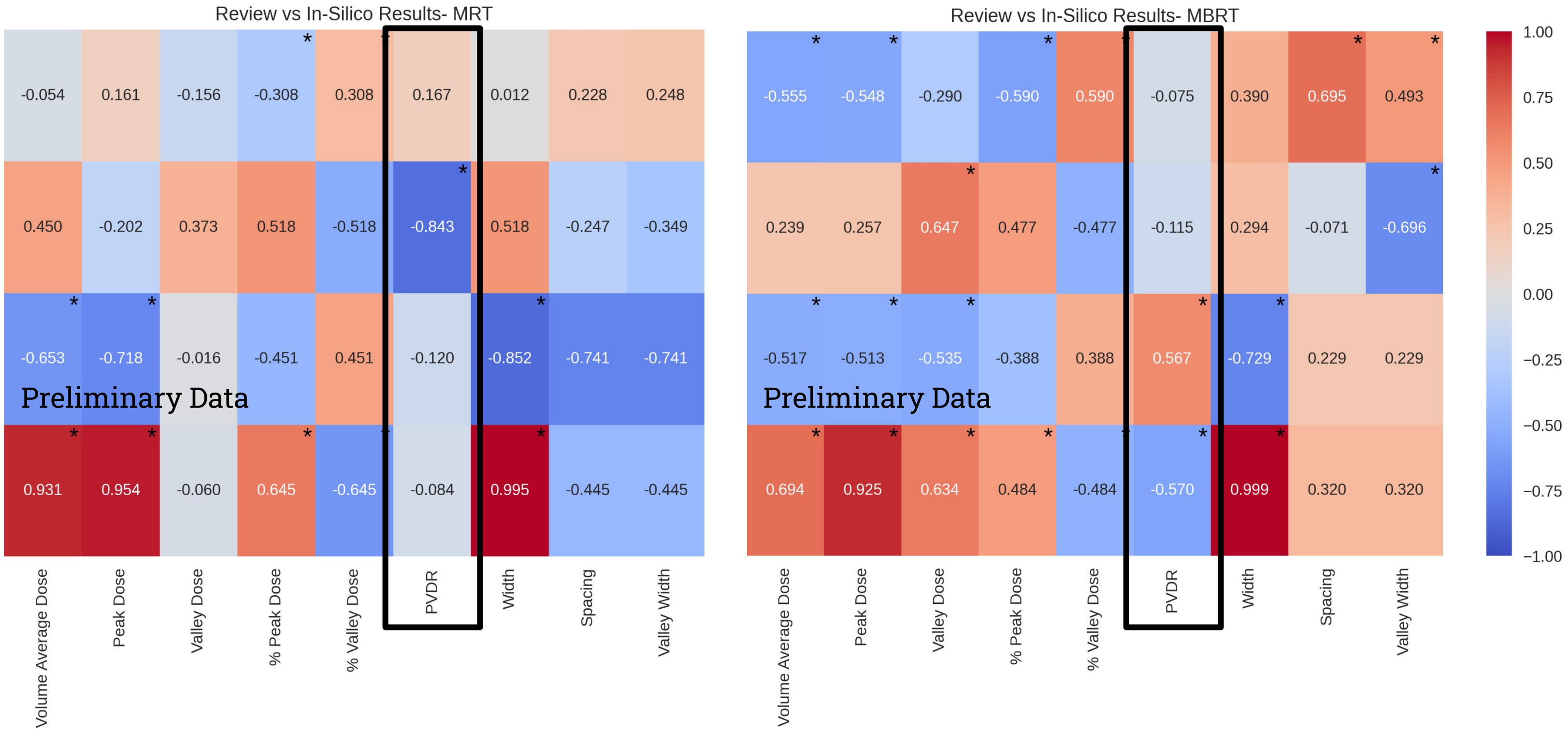

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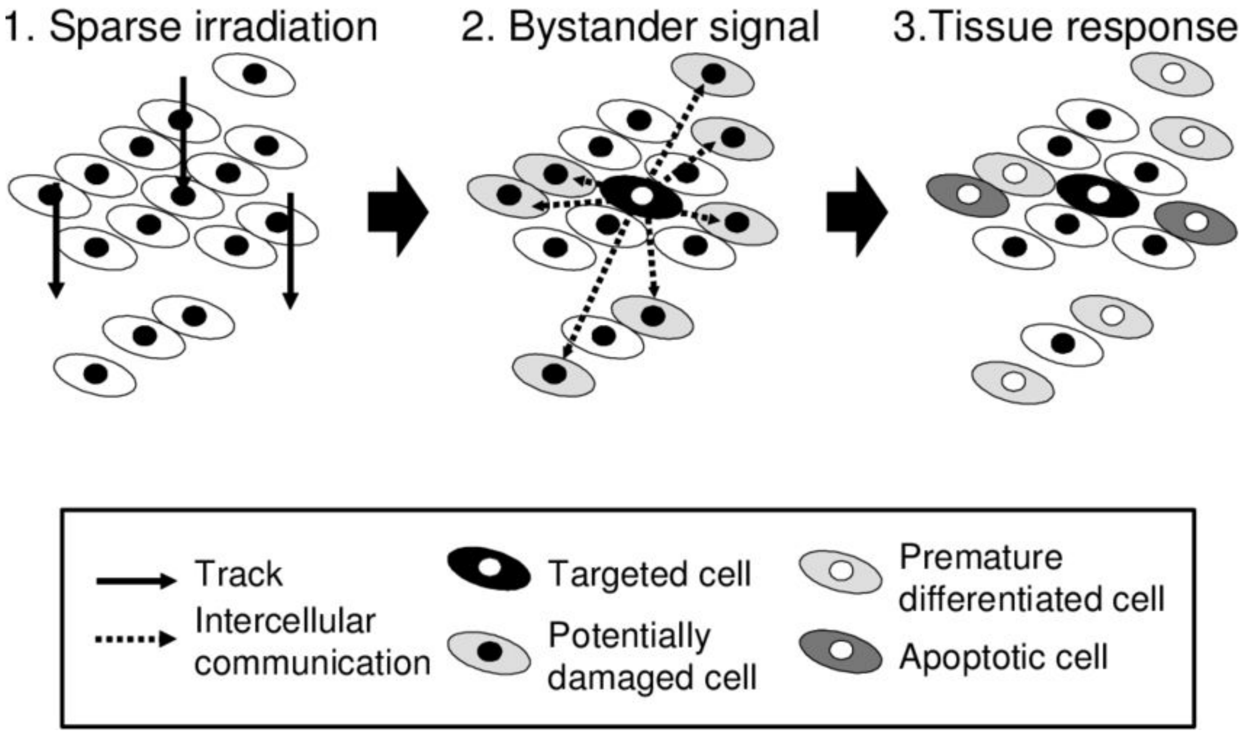
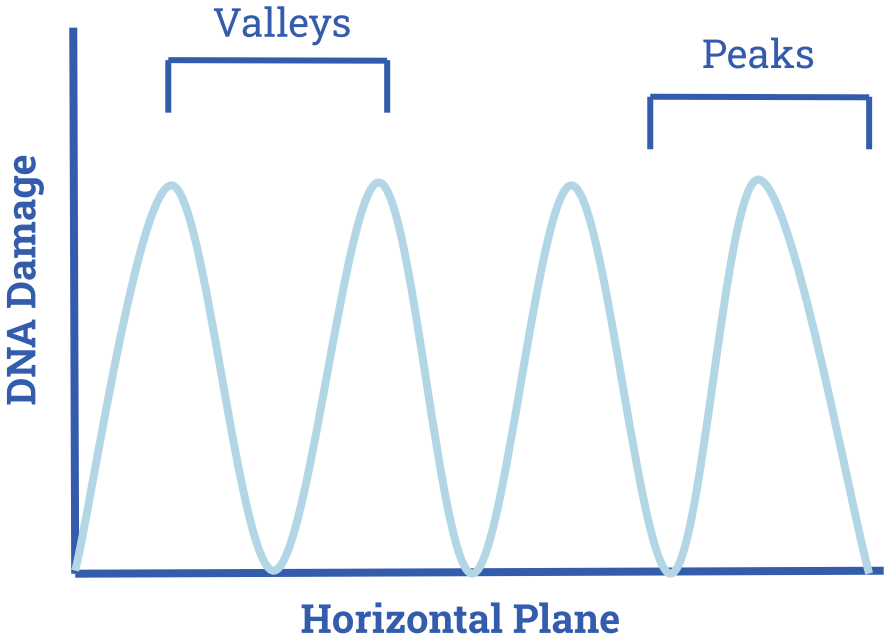
Preliminary Data

The Radiation Bystander Effect



Ref: Little et. al (2008) URL: https://tinyurl.com/cx5vakjf

SFRT and the Bystander Effect



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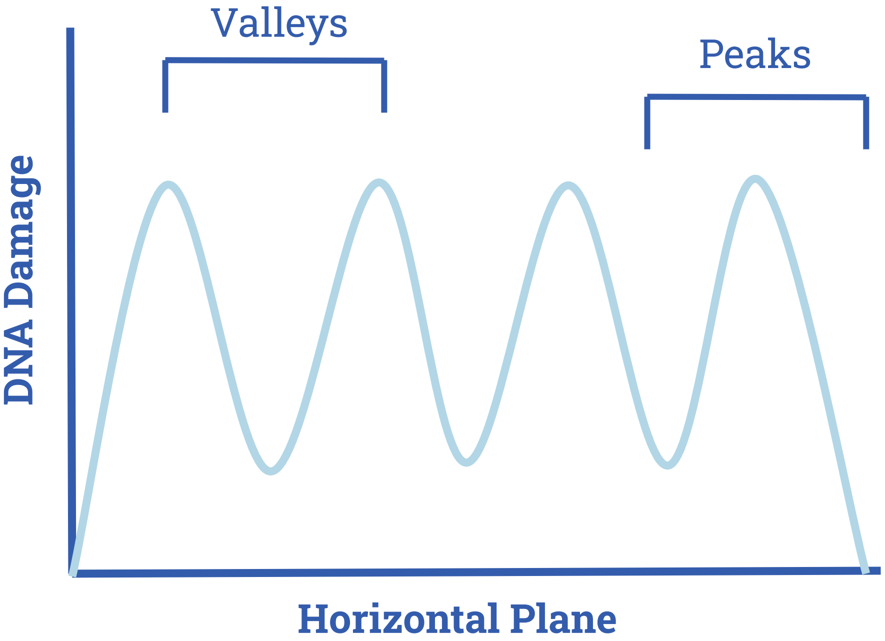
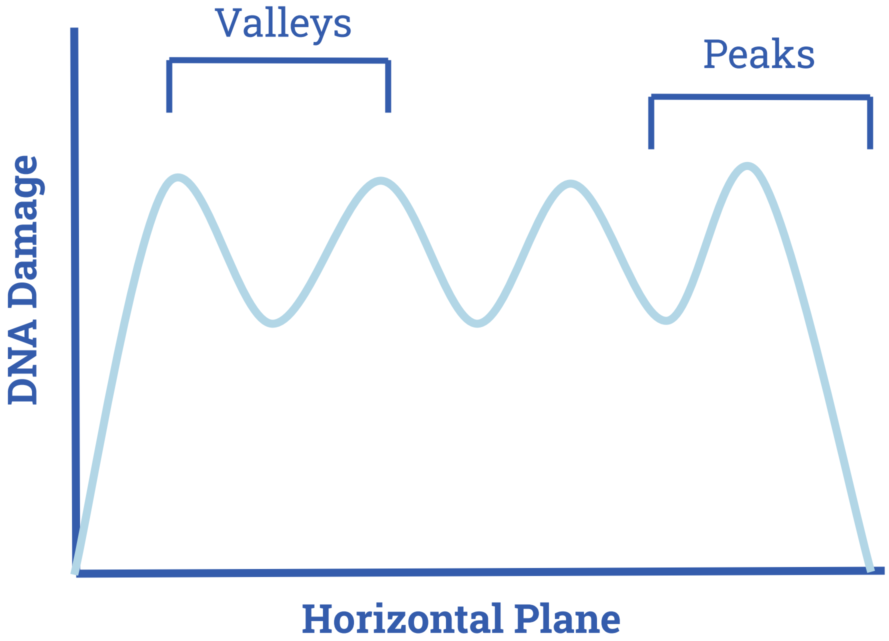
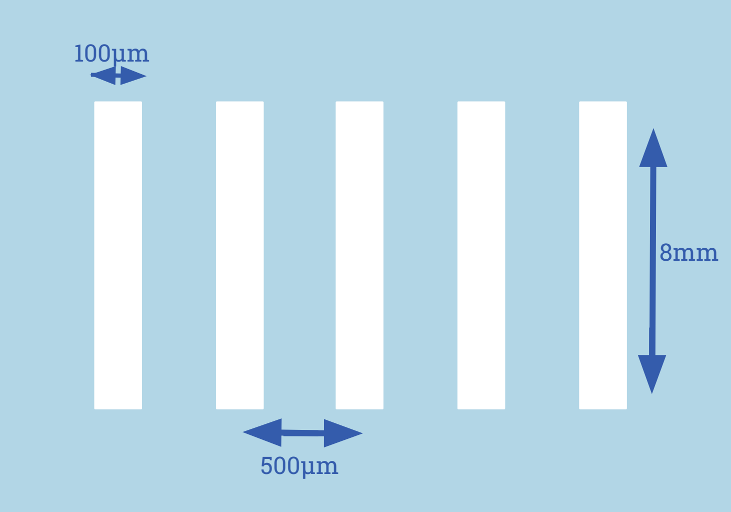


SFRT and the Bystander Effect

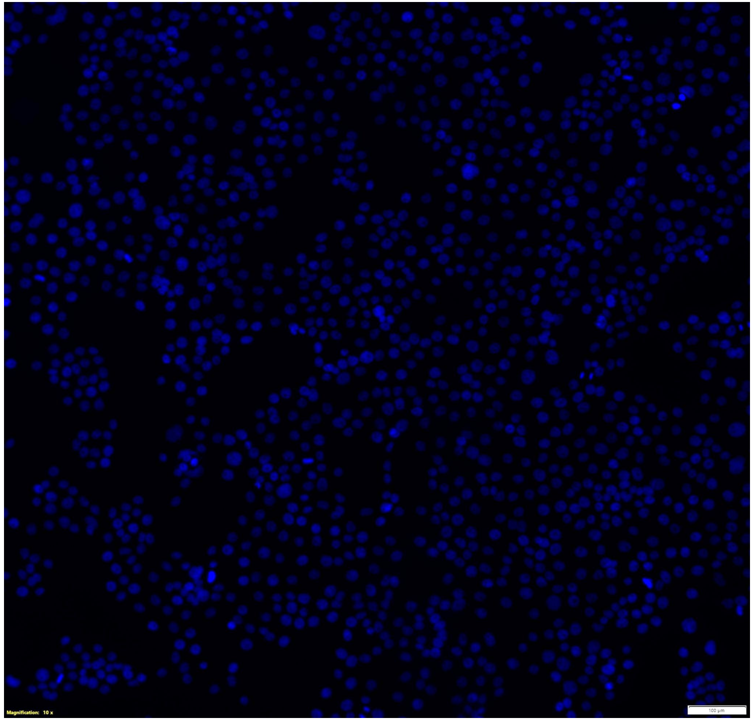


γh2AX Bystander Effect Detection

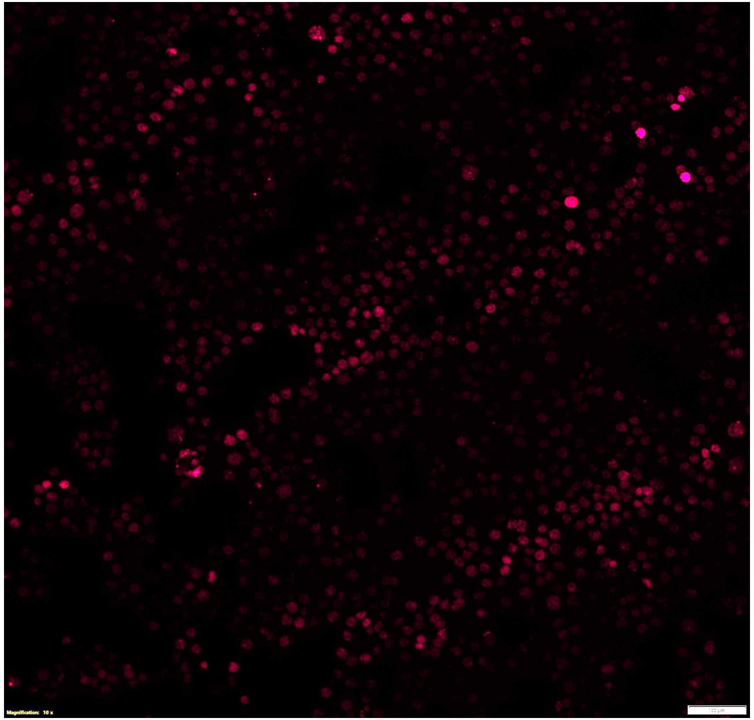


	Dose	4Gy	10Gy
Time post MRT	1 hour	x2	x2
	4 hours	x2	x2
	8 hours	x2	x2
	24 hours	x2	x2

Fluorescent Images

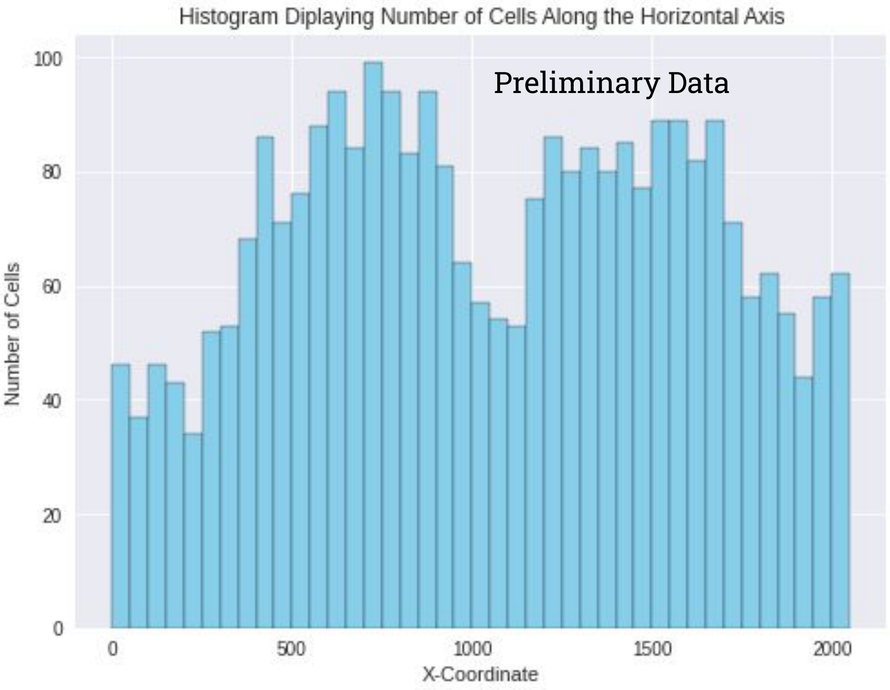


Dapi stain image (all nuclei)

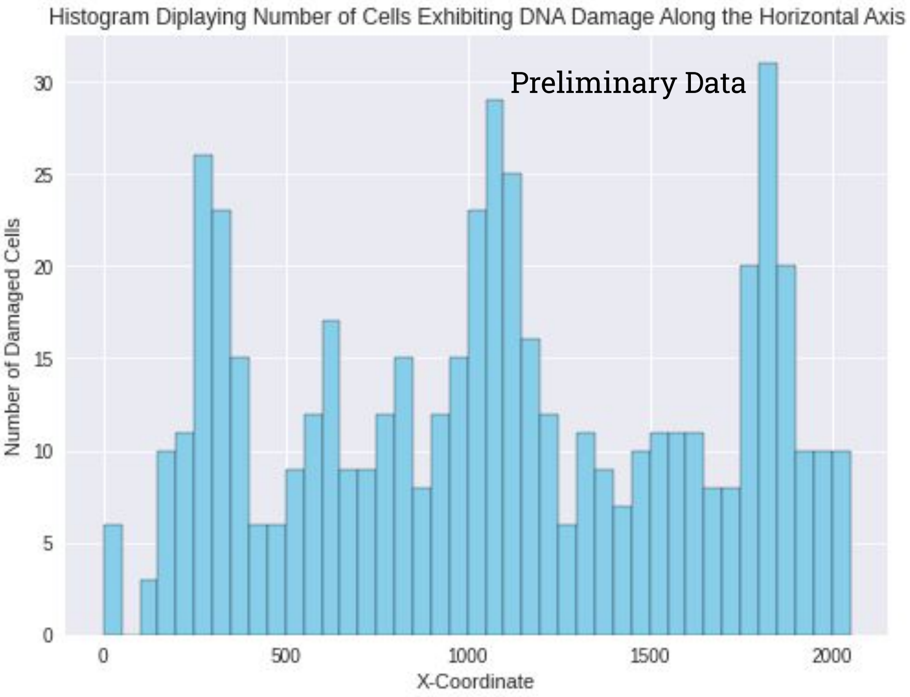


γh2AX stain image (damaged nuclei)

Binning Dapi and γh2AX Images



Dapi co-ordinate histogram (all nuclei)



γh2AX co-ordinate histogram (damaged nuclei)

Gaussian Fitting

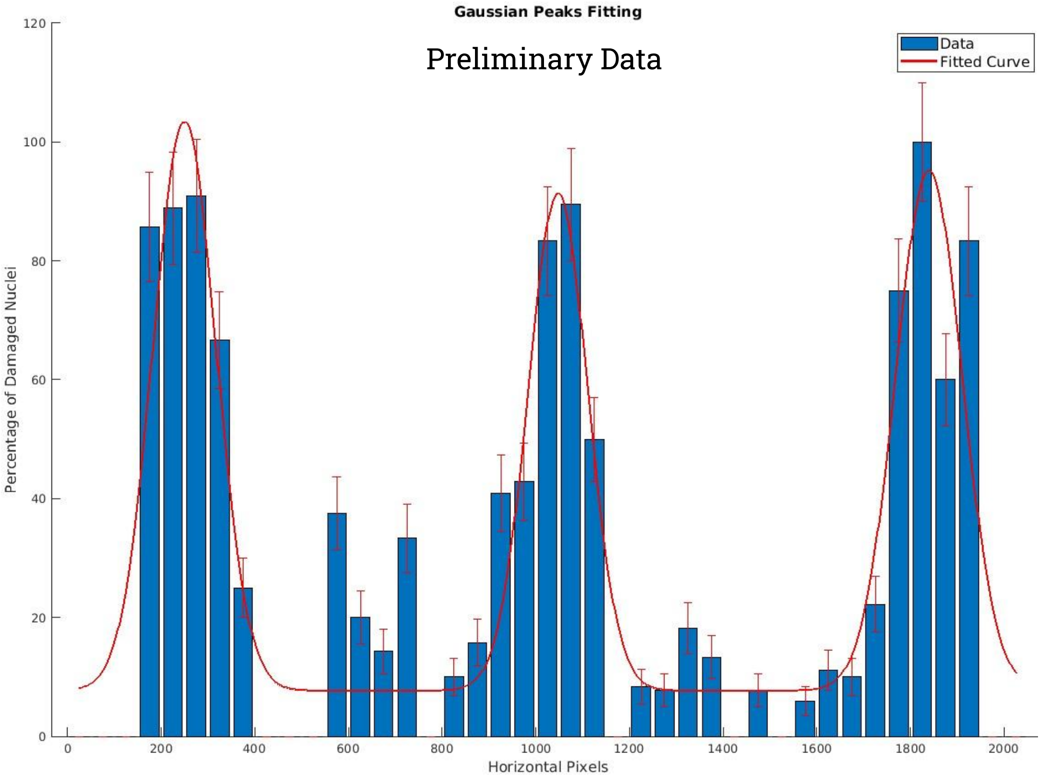
Bin calculation:

$$\% \text{ damaged cells} = \left(\frac{\# \text{ damaged cells}}{\# \text{ total cells}}\right) \times 100$$

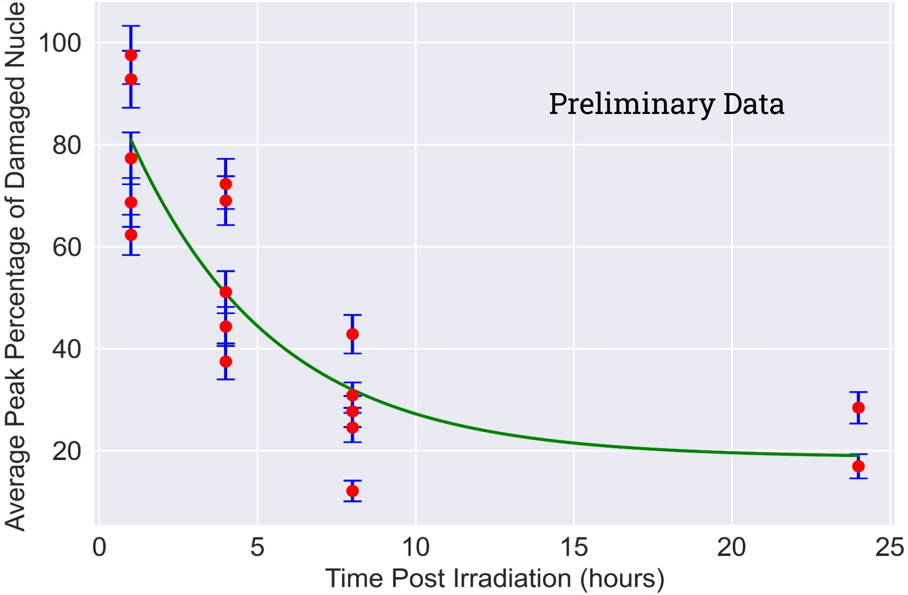
Gaussian Fitting:

$$f(x) = A_1 \cdot e^{-\frac{(x-\mu_1)^2}{2\sigma_1^2}} + A_2 \cdot e^{-\frac{(x-\mu_2)^2}{2\sigma_2^2}} + A_3 \cdot e^{-\frac{(x-\mu_3)^2}{2\sigma_3^2}}$$

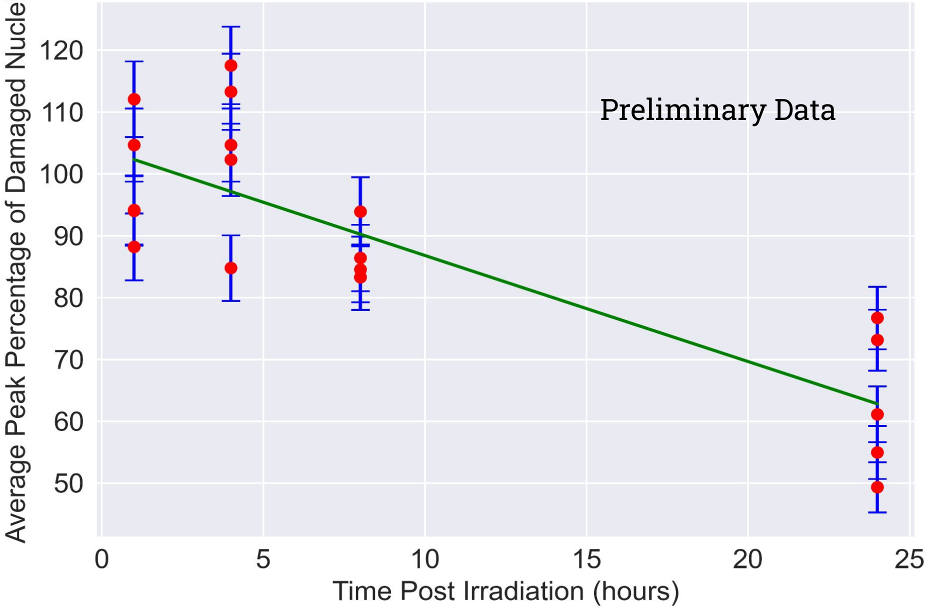
- $f(x)$: The function describing the three-peak Gaussian curve as a function of x.
- x: The independent variable (input) at which the function is evaluated.
- A_i: Amplitude of the i^{th} Gaussian peak, controlling the height of each peak.
- μ_i: Mean or center of the i^{th} Gaussian peak, specifying its position along the x-axis.
- σ_i: Standard deviation of the i^{th} Gaussian peak, determining its width or spread.



Peak Migration (prelim data)

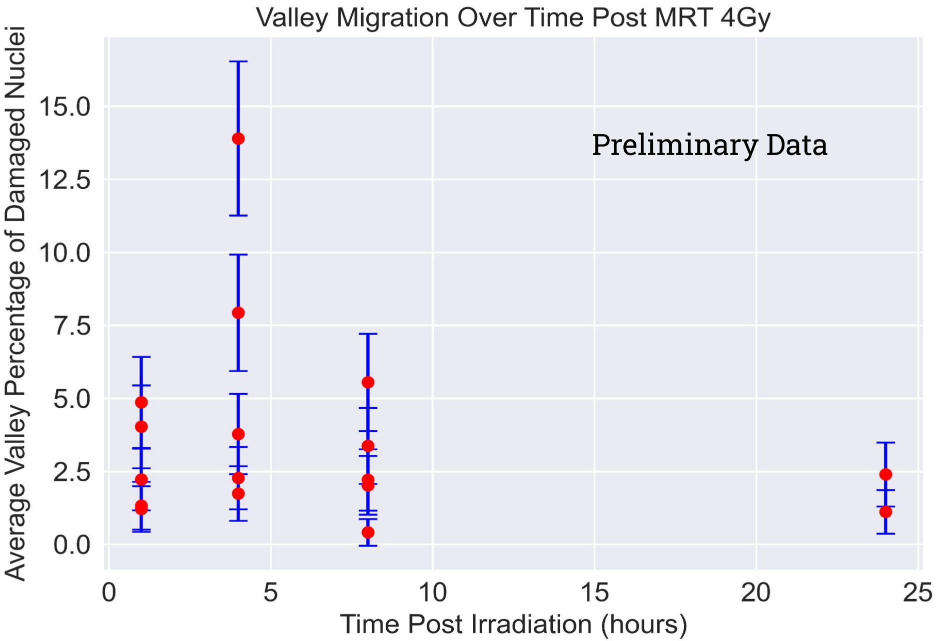

Peak Migration Over Time Post MRT 4Gy

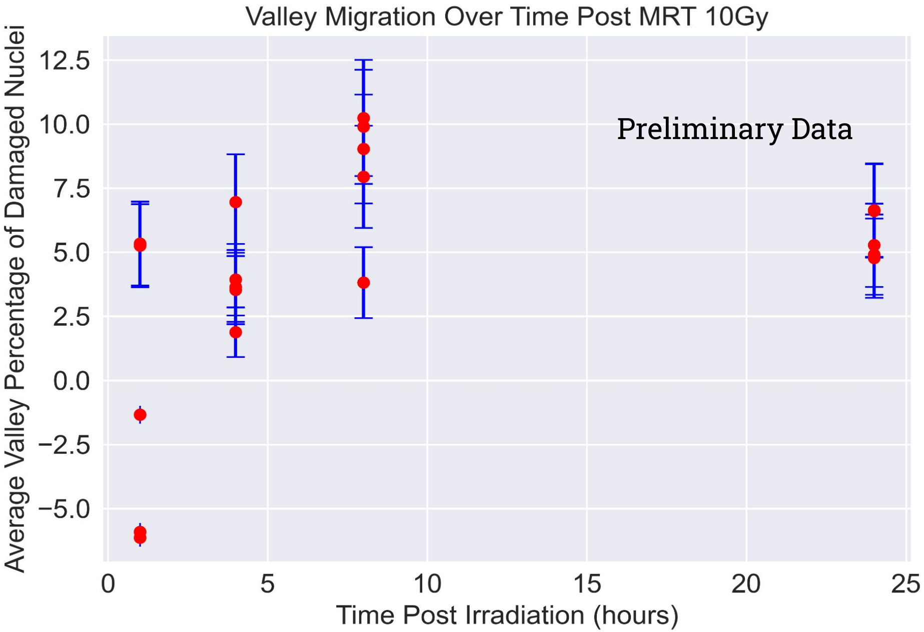
Preliminary Data


Peak Migration Over Time Post MRT 10Gy

Preliminary Data

Valley Migration (prelim data)





Conclusions

Literature Review

Emphasis on geometry- %Peak Dose/ % Valley Dose statistically significant for both SFRT modalities, indicator for magnetic focussing at LhARA.

Literature vs simulation

PDVR was different across both modalities, suggesting a linear model not suitable for predicting tissue effects for SFRT specifically when it comes to PDVR.

In Vitro Bystander Experiment

Peaks decreased over time as damage repaired, whereas Valleys stayed stagnant.

Thanks!

For further questions:

jmm119@ic.ac.uk

SCAN ME

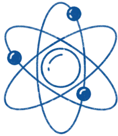
UNIVERSITY OF BIRMINGHAM

- Jason Parsons (and team)
- Tony Price (and team)
- University of Birmingham MC40 specialists

institutCurie

- Yolanda Prezado (and team)

- Kenneth Long



LhARA

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Back-up

Literature Review Analysis

In order to explore the influences of different dosimetric parameters on the effectiveness of MRT and MBRT, searchable databases were created in order to evaluate normal-tissue sparing, tumour control and survival post irradiation with each modality.

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

In-Silico Models

Both the TCP and NTCP models used by TOPAS are EUD-based modifications of the conventional Linear-Quadratic model.

Tumour Control Probability (TCP)

The likelihood of a tumour being effectively controlled or eradicated by a radiation treatment.

$$TCP = \frac{1}{1 + \left(\frac{TD_{50}}{EUD^{Slope_{50} \cdot \gamma_{50}}}\right)}$$

$$EUD_T = \left(\sum_{i=1}^{n} v_i \cdot D_i^{\frac{1}{Slope_{50}}}\right)^{Slope_{50}}$$

Normal-tissue Complication Probability (NTCP)

The likelihood that normal tissue will experience complications due to radiation exposure during treatment.

$$NTCP = \frac{1}{1 + \left(\frac{TD_{50}}{EUD^{m \cdot \gamma}}\right)}$$

$$EUD_N = \left(\sum_{i=1}^{n} v_i \cdot D_i^{1/m}\right)^{m}$$