Quantifying DNA Damaging Effects of FLASH Irradiation

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Conventional vs. FLASH Radiotherapy

Conventional Radiotherapy (CONV-RT):

- 2 Gy/fraction, 5 fractions/week for several weeks
- Dose rate: 0.01-0.1 Gy/s

FLASH Radiotherapy (FLASH-RT):

- Single fraction
- Dose rate: >40 Gy/s
- **FLASH Effect**: Significant normal tissue sparing while achieving comparable tumor control to CONV-RT

Clinical Potential- First FLASH-RT Patient

Patient:

- 75-year-old male with CD30+ T-cell cutaneous lymphoma

Prior treatments:

- Immunosuppressors, chemotherapy, 110 tumor sites treated by conventional RT

FLASH-RT treatment:

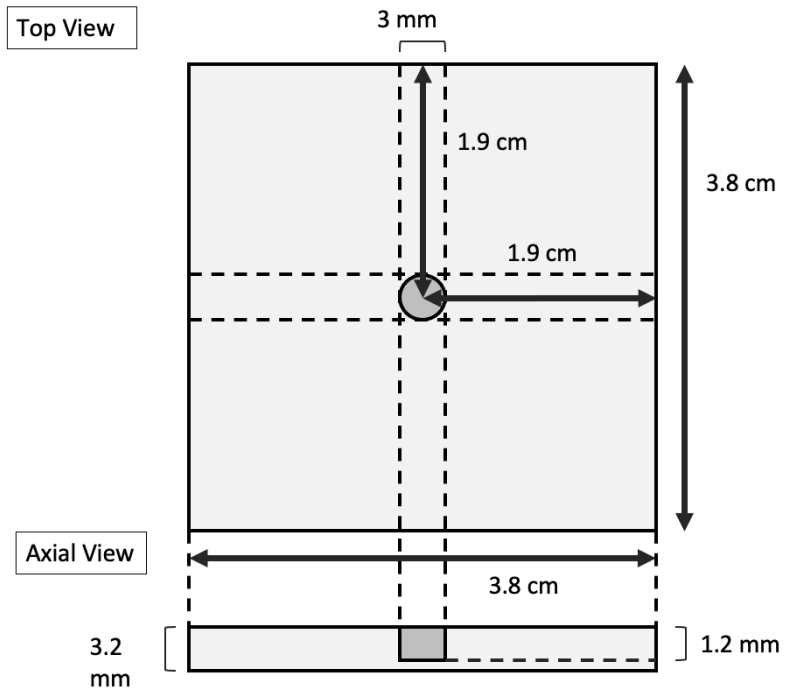
- 1 fraction of 15 Gy delivered in 90 ms

Bourhis et al., 2019

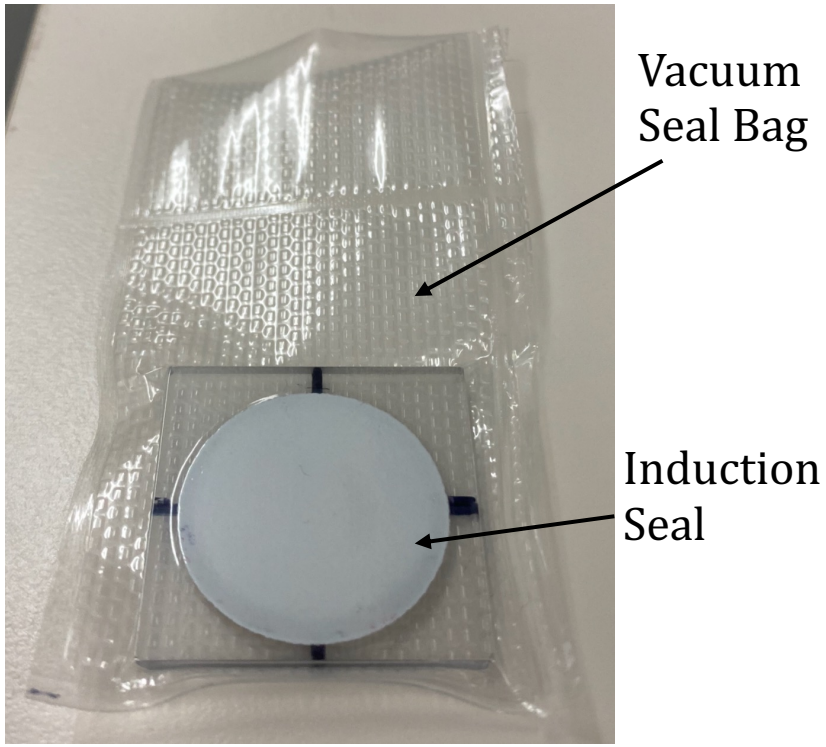
Experimental Design: A Plasmid DNA Study

Purpose: To compare the rate of induction of single and double strand breaks with dose delivered at conventional dose rate and FLASH dose rate photons

- **Doses:**
  - 10, 20, 30 Gy
- **Dose Rates:**
  - Conventional: ~0.1 Gy/s
  - FLASH: ~100 Gy/s



Schematic and dimensions of polycarbonate phantom.



Prepared sample sealed with an induction seal and vacuum seal bag.

Radiation Induced DNA Damage Types

Single-strand break (SSB)

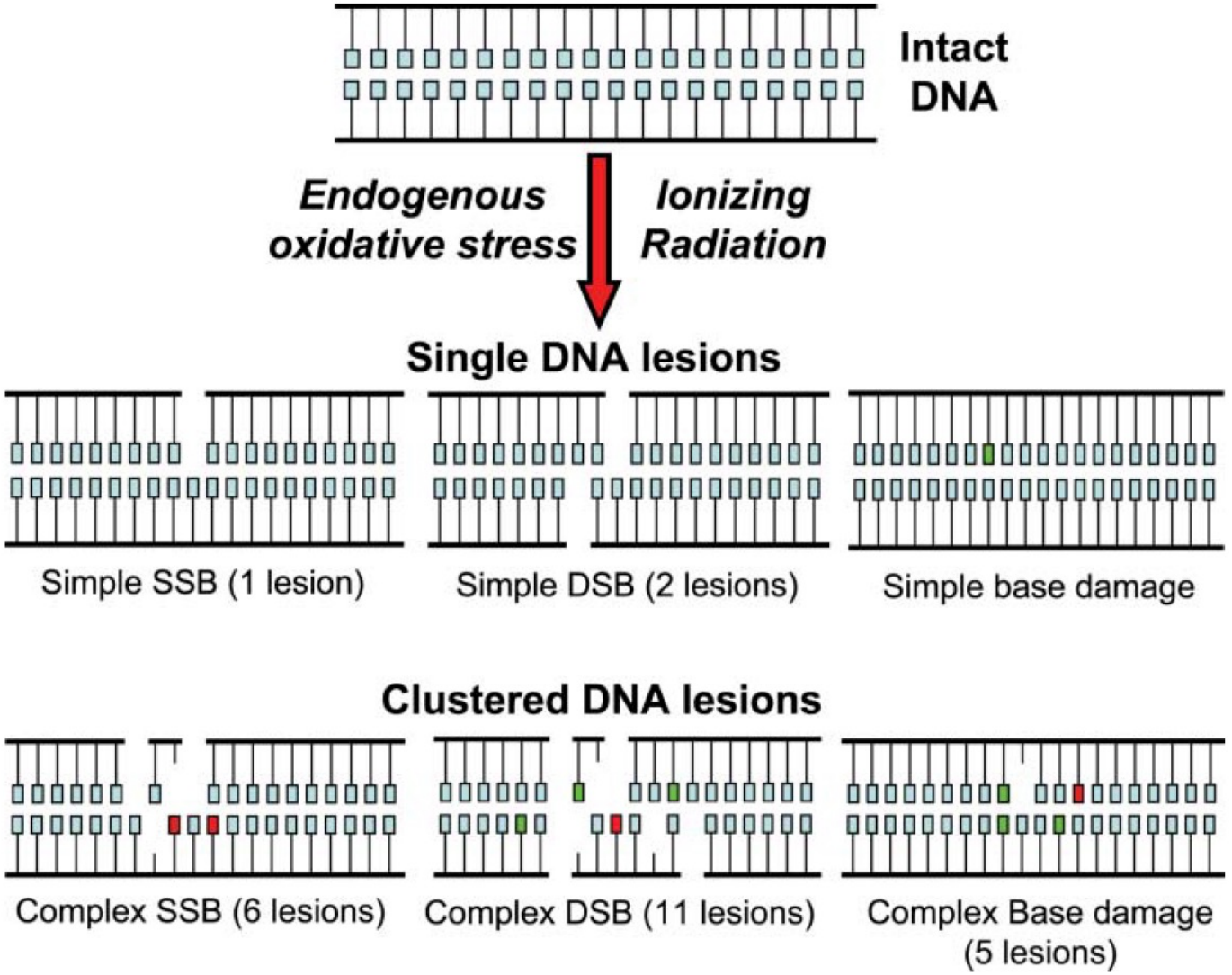
- Chemical break in one strand of the phosphate backbone

Double-strand break (DSB)

- Chemical break is both strands within ~ 10 base pair

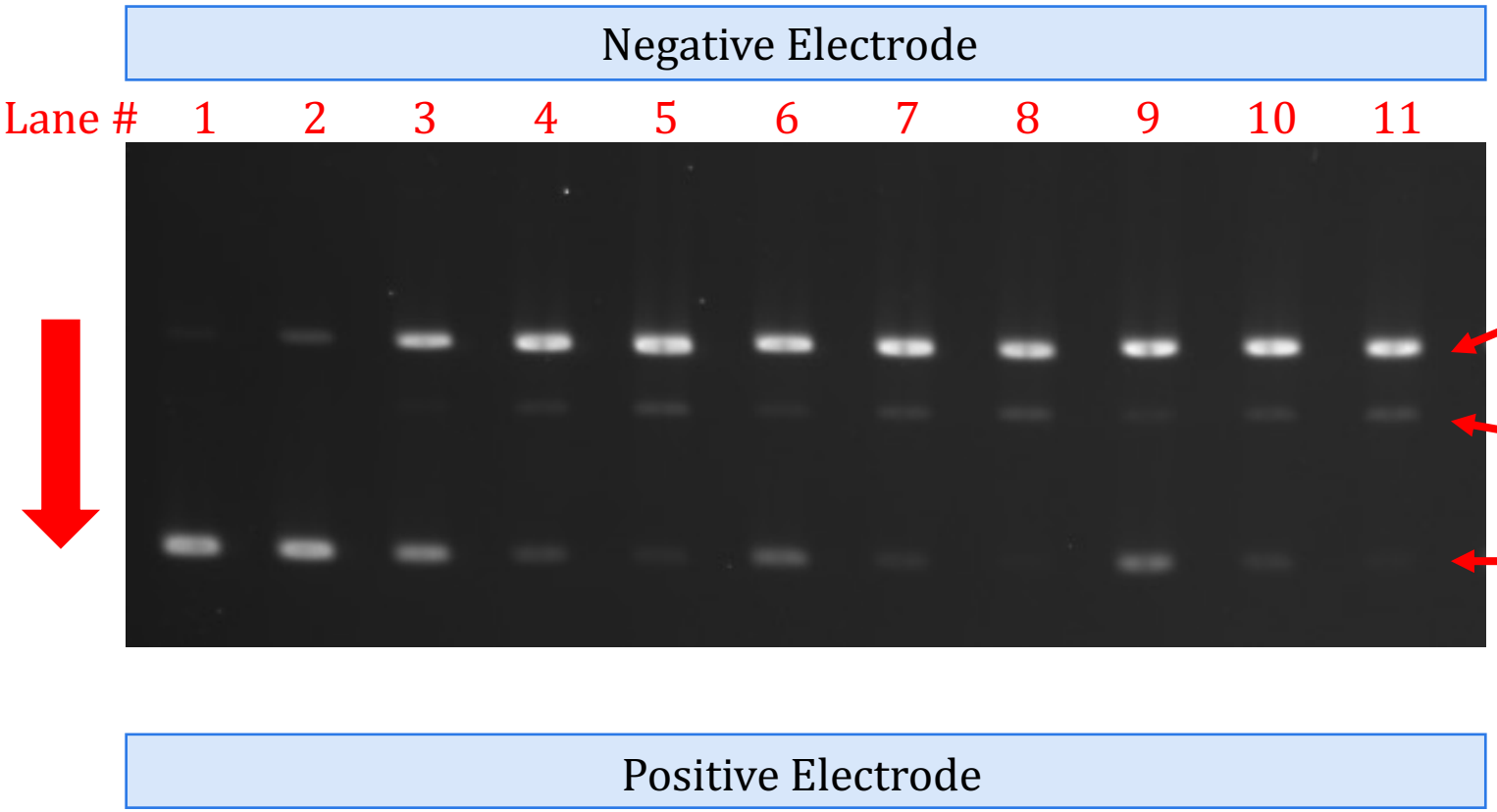
Base damage

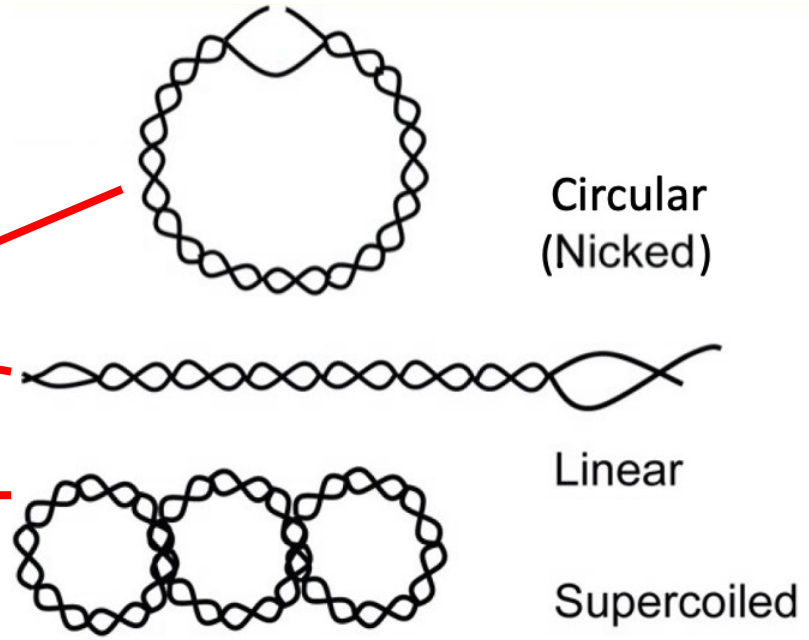
- Isolated or clustered oxidized bases



Alexandros G. Georgakilas (2007)

DNA Damage Analysis: Agarose Gel Electrophoresis





Ziyi Li, Kathryn B. Grant (2016)

McMahon and Currell Fitting Model

Calculated Normalized Yields

$$\boldsymbol{C} = e_{D}^{-\beta_D D}\left(C_0 e^{-\frac{1}{2}\beta_S^2 \rho D^2} + S_0\left(e^{-\frac{1}{2}\beta_S^2 \rho D^2} - e^{-\beta_S D}\right)\right)$$

$$\boldsymbol{S} = S_0 e^{-(\beta_S+\beta_D)D}$$

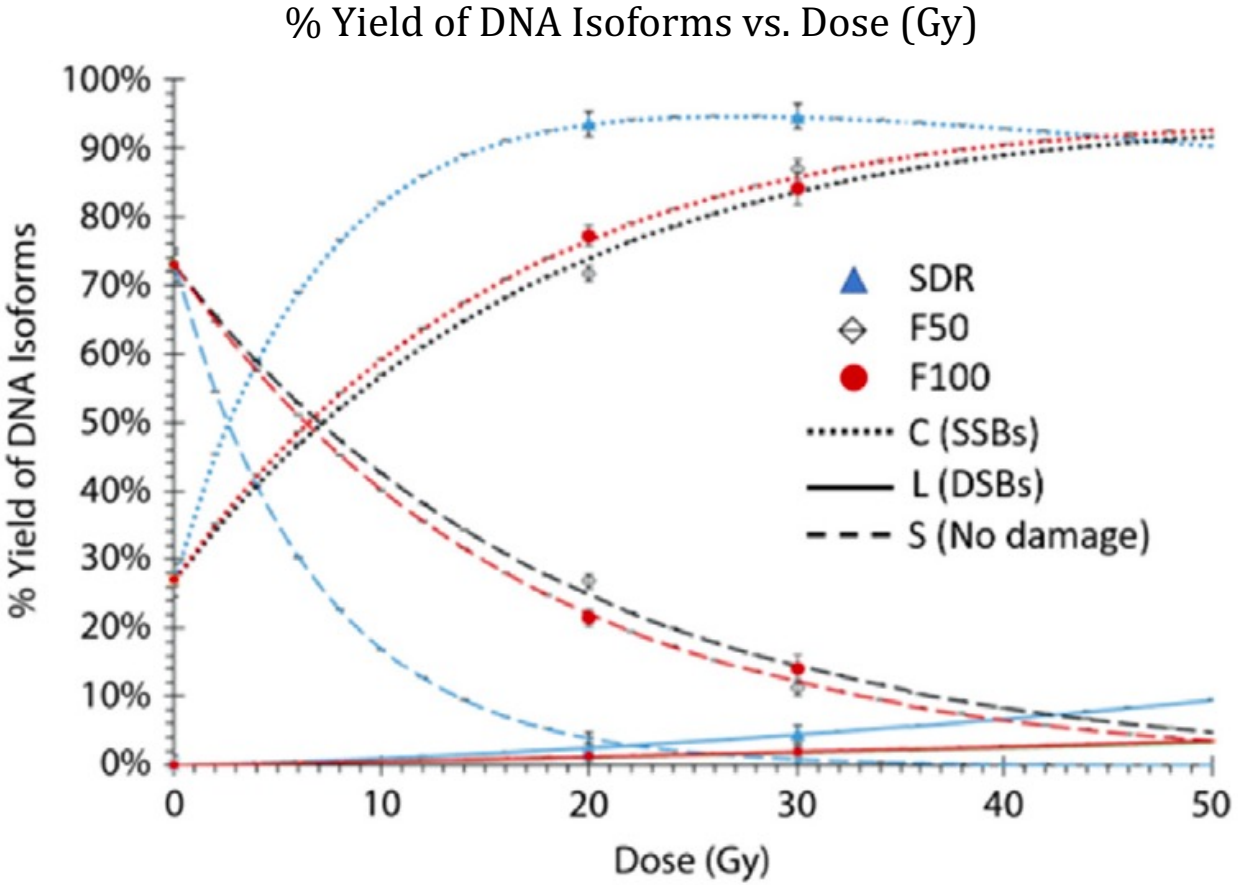
$$\boldsymbol{L} = 1 - (C_0 + S_0)e^{-\beta_D D+\frac{1}{2}\beta_S^2 \rho D^2}$$

Unknown Fitting Parameters

$\boldsymbol{\beta_S}$ = # of single strand breaks induced per Gray

$\boldsymbol{\beta_D}$ = # of double strand breaks induced per Gray

McMahon and Currell model from Electron FLASH study



Perstin et al., 2021

Conclusions

- Our study aims to provide new insight into the DNA damaging effects of photon FLASH irradiation
- FLASH Radiotherapy has the potential to transform the field of clinical radiotherapy
- Further studies are necessary to fully characterize the biological mechanisms contributing to the FLASH Effect

Acknowledgements

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Questions?