

Stepping Towards Conformal FLASH Delivery: A Murine UHDR Multiple Beam Study

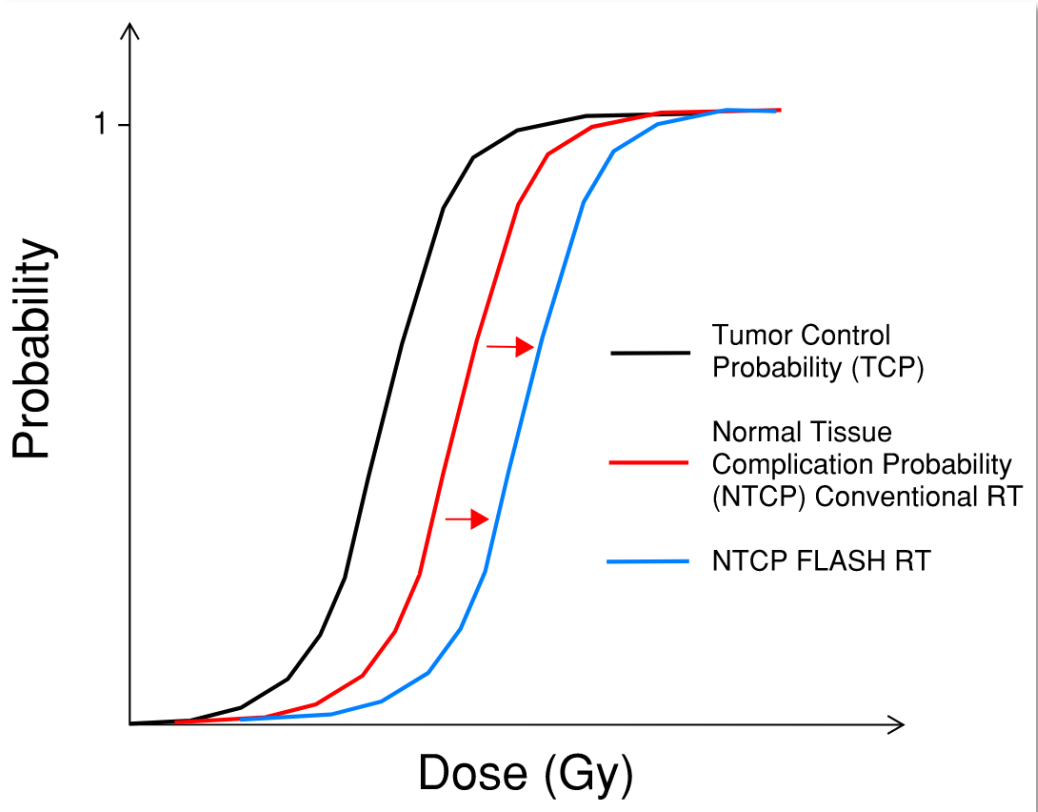
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FLASH Radiotherapy (RT)

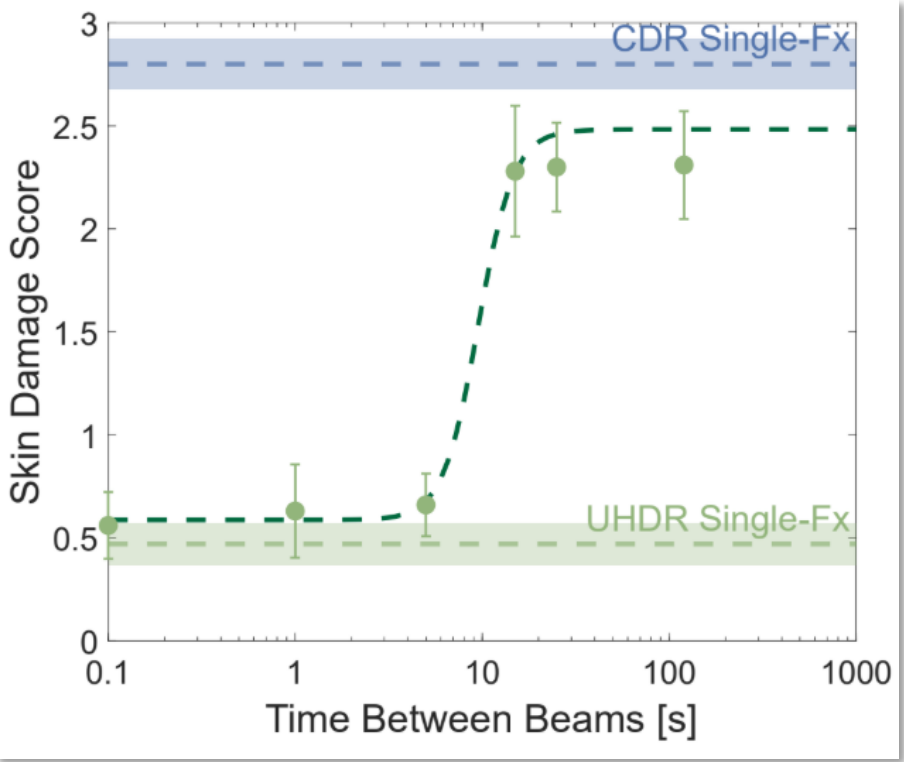
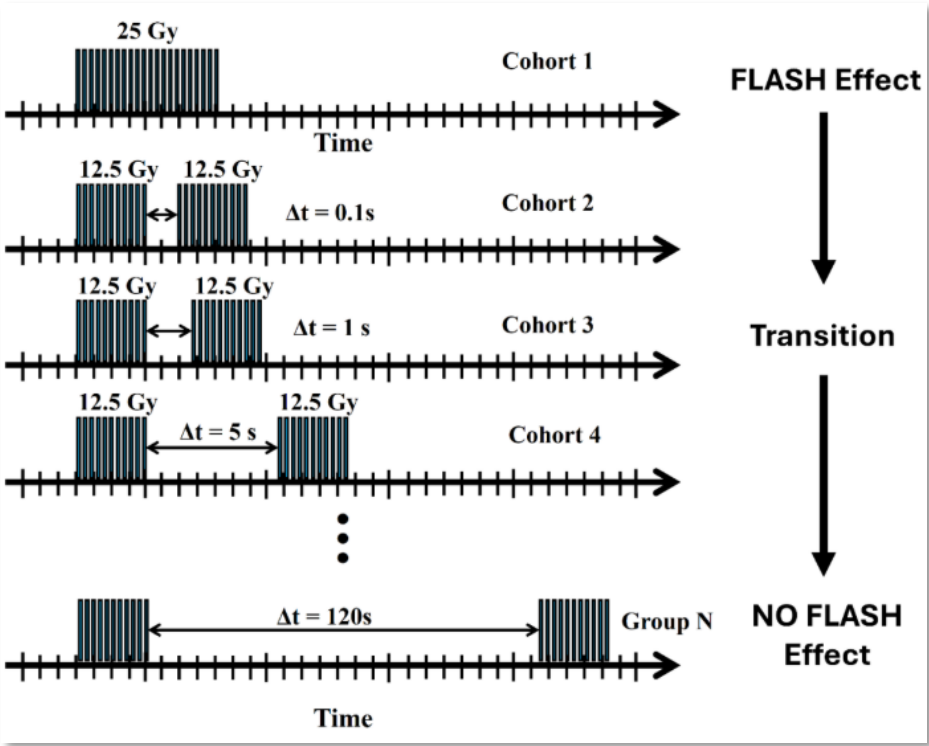
- **The FLASH effect:** increased normal tissue sparing with equal tumor control when compared to conventional RT.
- How to elicit the FLASH effect?
 - Increase dose rate.
 - **Conventional RT:** $\dot{D}_m \approx 0.1 \text{ Gy/s}$
 - **FLASH RT:** $\dot{D}_m \approx 40 \text{ Gy/s}$.

FLASH RT and the Therapeutic Window



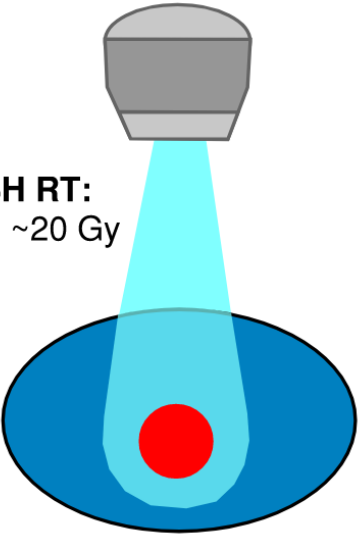
40 Gy/s: Useful Metric or Oversimplification?

- A recent study showed that the FLASH effect is preserved when a total dose of 25 Gy is delivered in 5 seconds or less

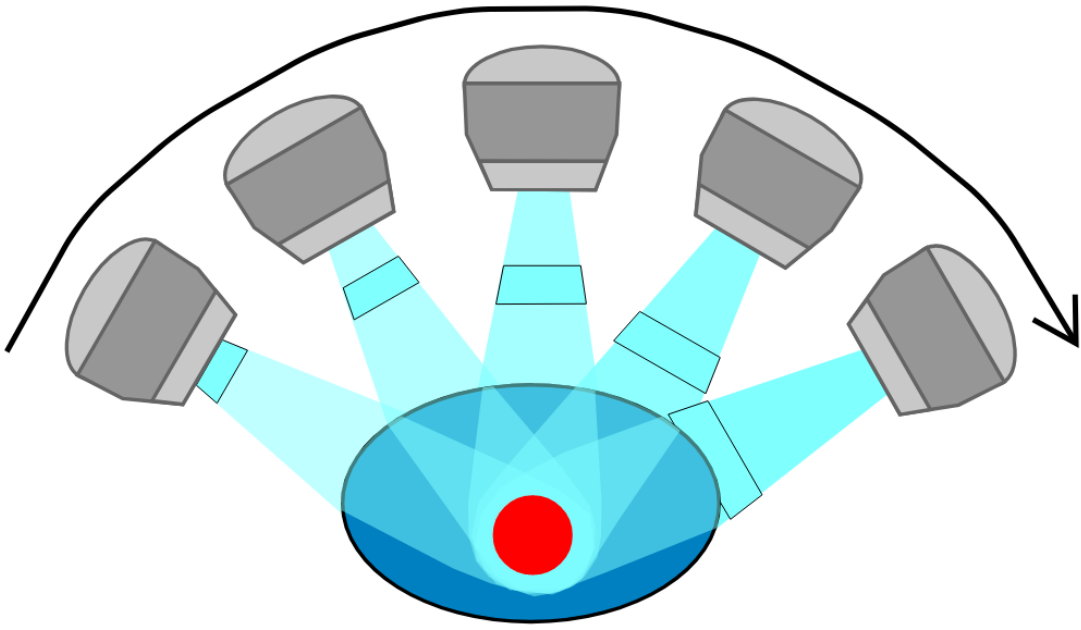
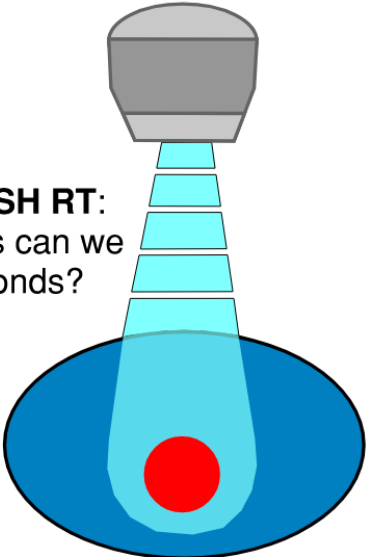


Stepping Towards Conformality

FLASH RT:
1 Beam ~20 Gy



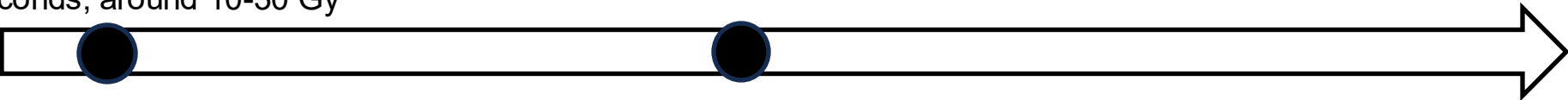
Split Beam FLASH RT:
How many beams can we deliver in 5 seconds?



Conformal FLASH RT

FLASH RT studies typically use one beam of pulses, delivered in milliseconds, around 10-30 Gy

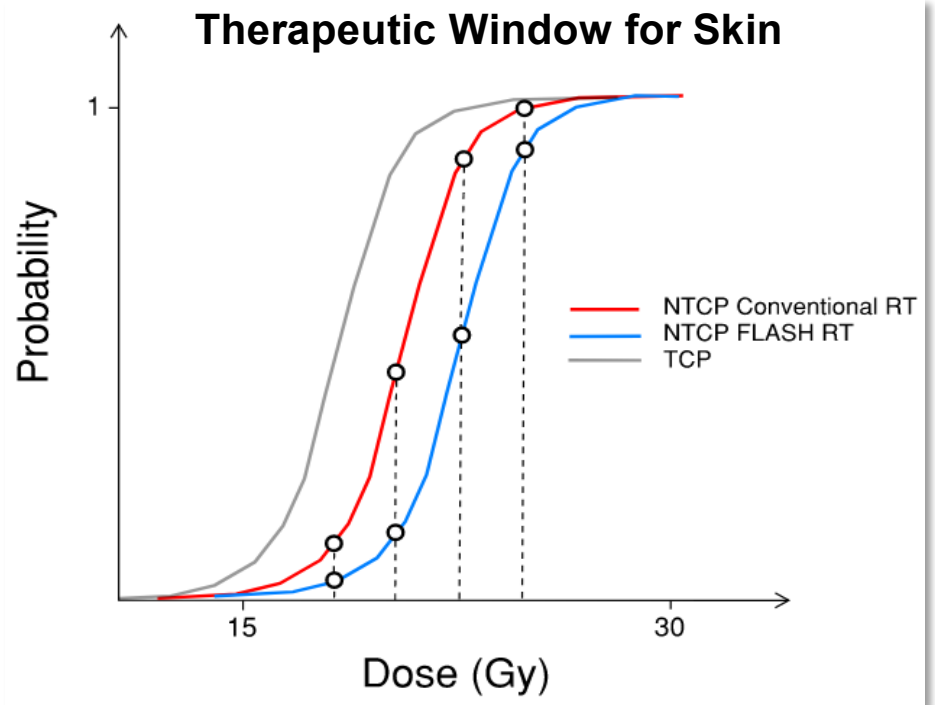
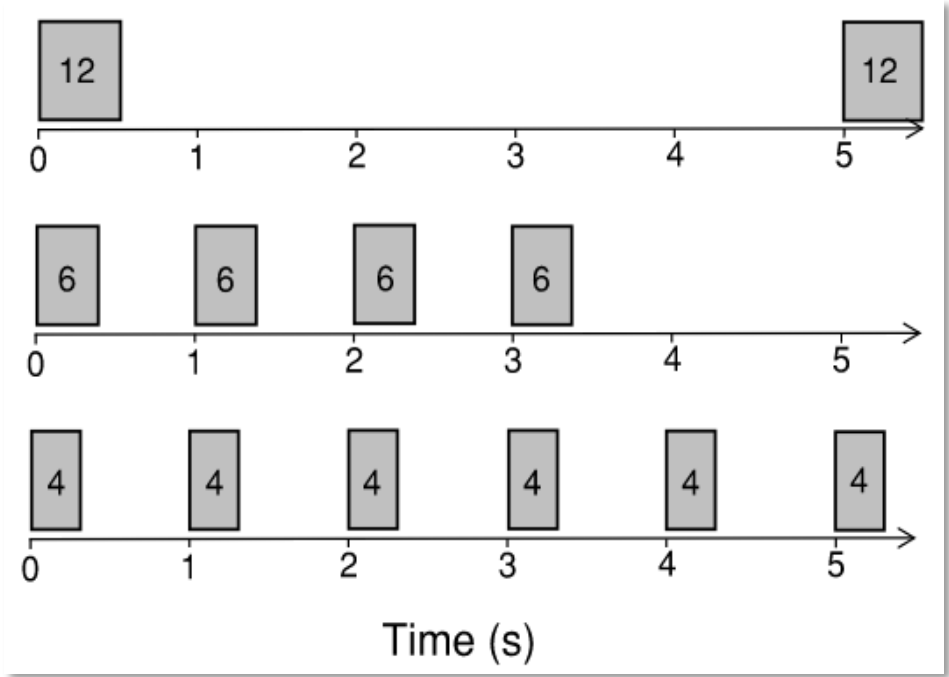
Current Research



Largely unsuitable for clinical application

Multiple Beam Study Design

Divide 24 pulses (~1 Gy per pulse) into 2, 4, and 6 beams, delivered within five seconds.



Validate the FLASH NTCP curve:

Target doses \approx 22-26 Gy

Skin Score Damage Assay

- 50 albino male b6 mice per dose target
- Daily monitoring for thirty days post irradiation
- Animals sacrificed and skin samples collected for histological analysis

Skin scoring guide:

- 0.5 - Minimal damage. Very slight abnormality or no change from normal.
- 1 - Low damage. Definite reddening and/or white scales and/or puffiness.
- 1.5 - Medium damage. Moist desquamation in a single small area.
- 2 - High damage. Moist desquamation in multiple areas.
- 2.5 - Very high damage. Breakdown of large/most areas of skin with definite moist exudate.
- 3 - Extreme damage. Complete moist breakdown of limb, often stuck to body.



Grade 0.5, minimal damage

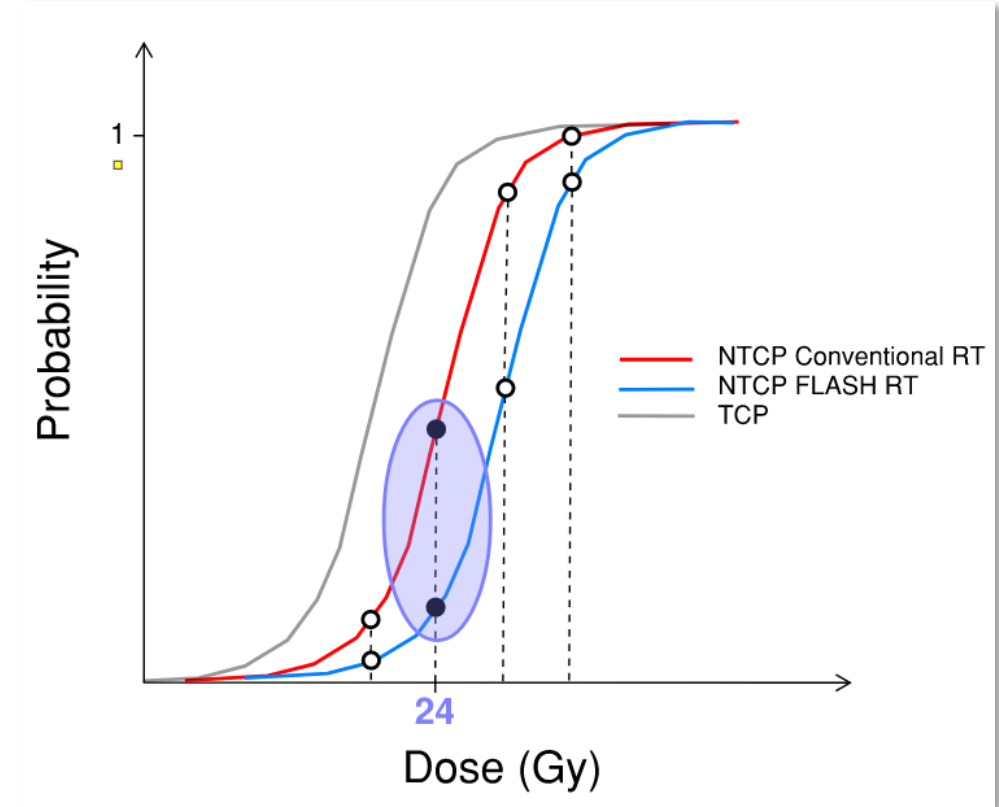
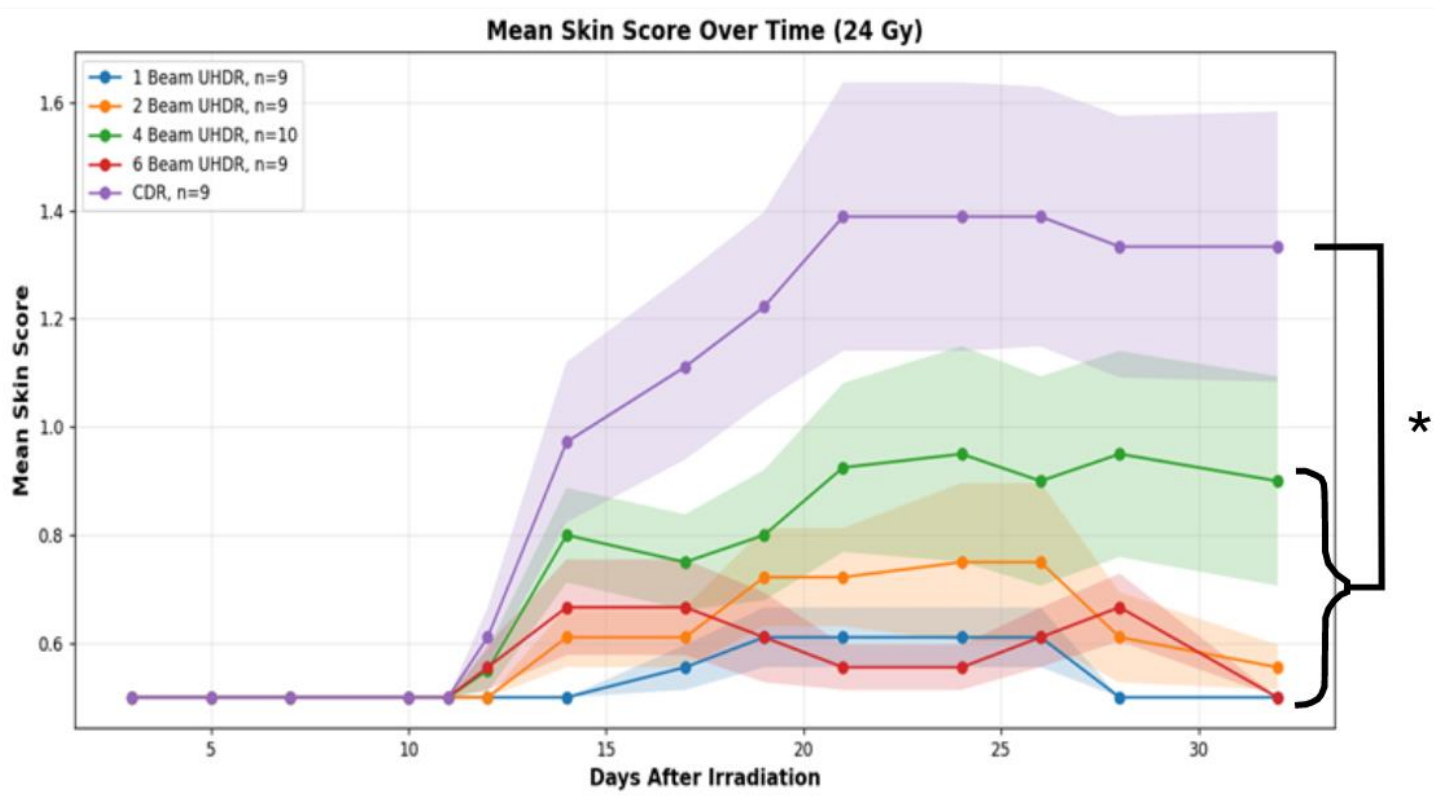


Grade 2, high damage



Grade 3, extreme damage

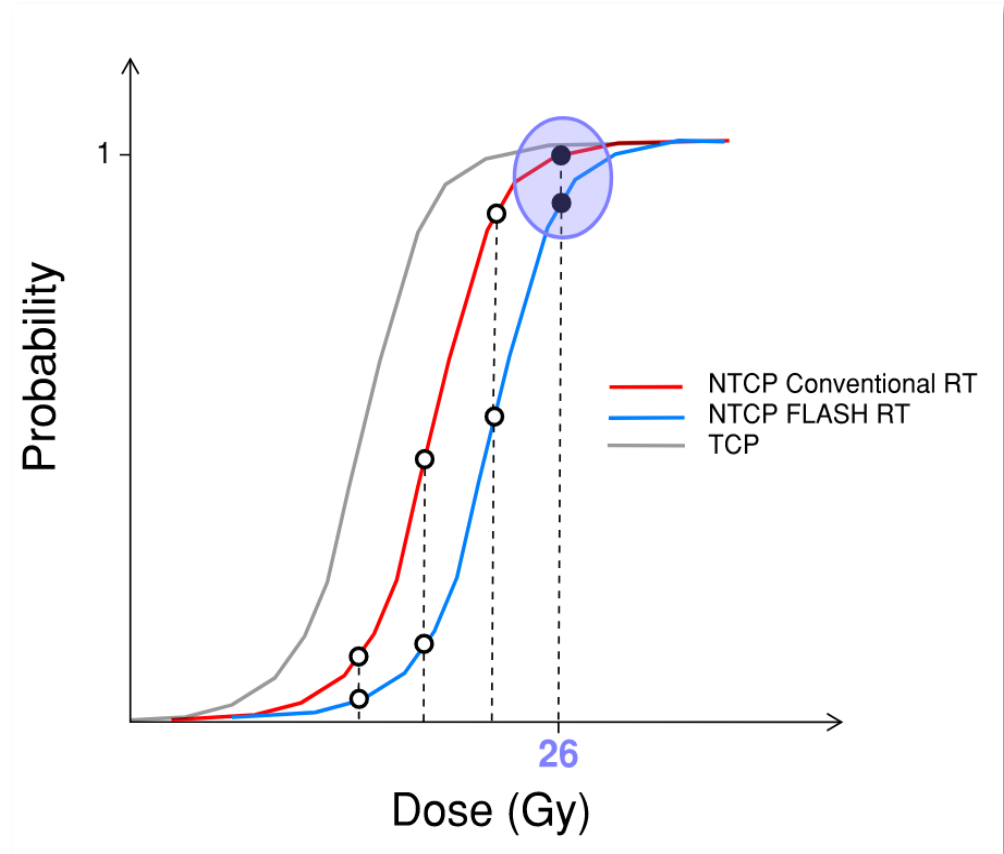
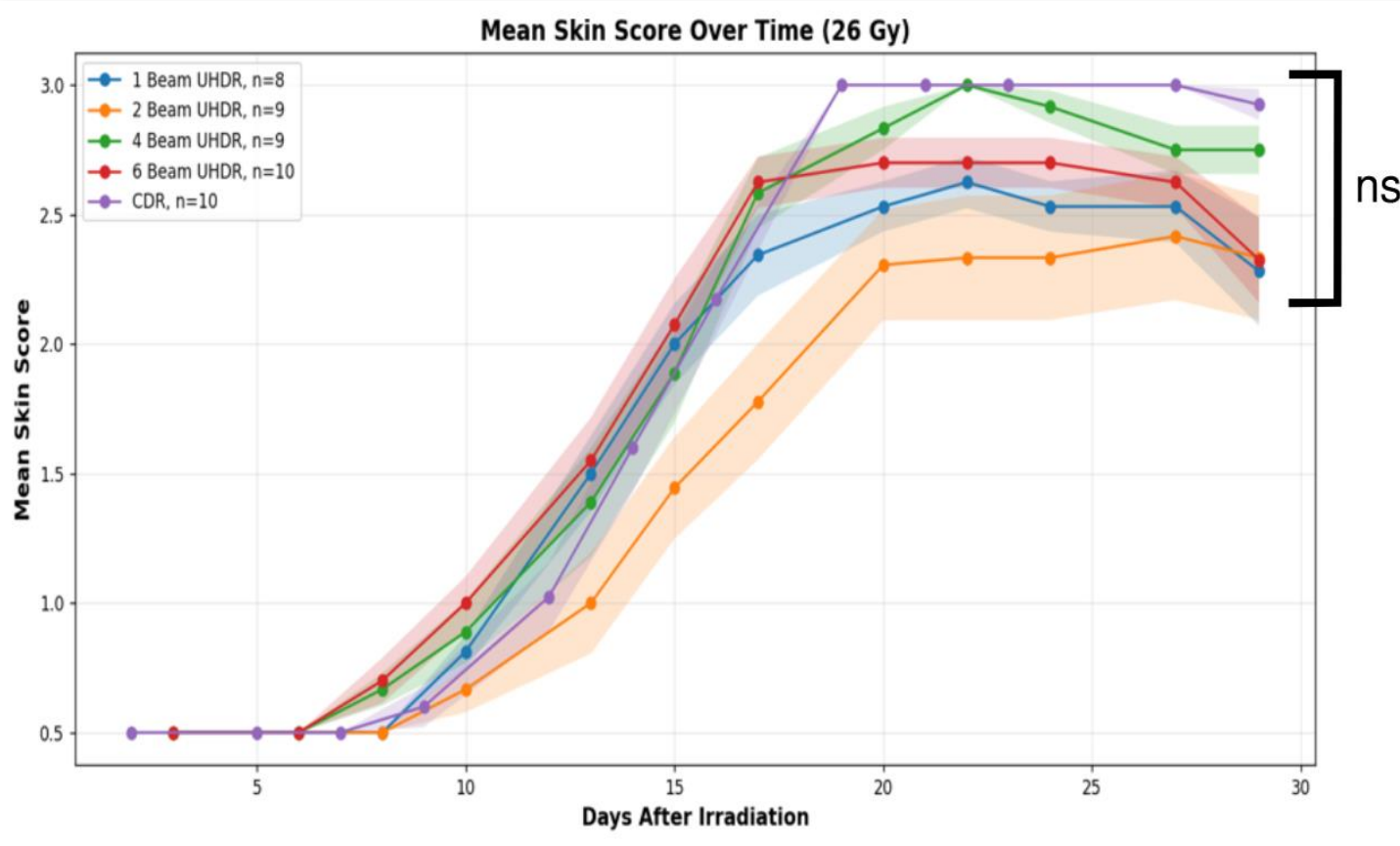
24 Gy: FLASH Sparing Preserved



One-Way ANOVA p-value: 10^{-5}

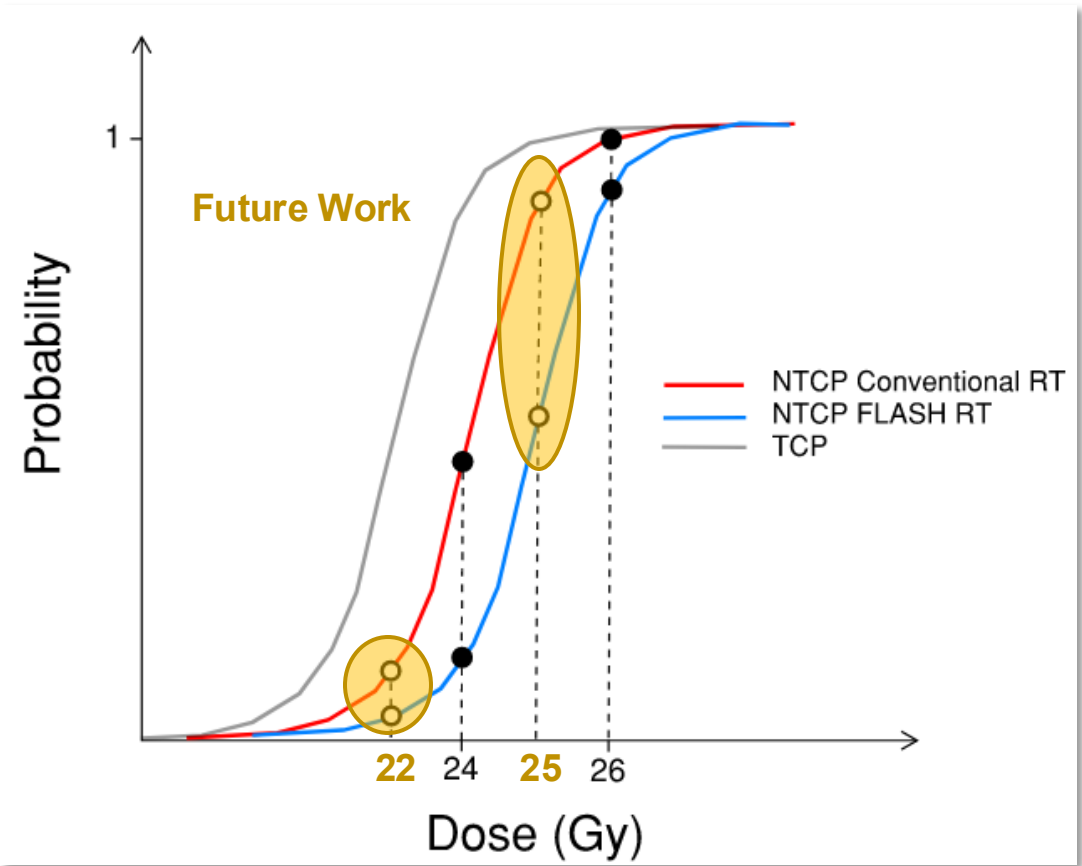
ANOVA Contrast between CDR and UHDR p-value: 10^{-15}

26 Gy: No FLASH Sparing



One-Way ANOVA p-value: 0.76

Conclusions



Initial Conclusions

- The FLASH sparing effect is **preserved** when splitting delivery into multiple beams

Looking Forward

- Conformal FLASH RT is highly clinical relevant
- Electrons are not feasible for CRT, we need to investigate other modalities



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