ASTRO ANNUAL MEETING
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Does the UHDR Skin Sparing Effect Maintain Efficacy in the Awake Murine Model? Investigation of Competing Irradiation Conditions

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INTRODUCTION

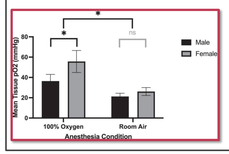
FLASH radiotherapy delivers large, single-fraction treatments at ultra-high dose rates (UHDR, >40 Gy/s) that **reduce normal-tissue toxicity while preserving tumor control,** unlike conventional dose rate (CDR).

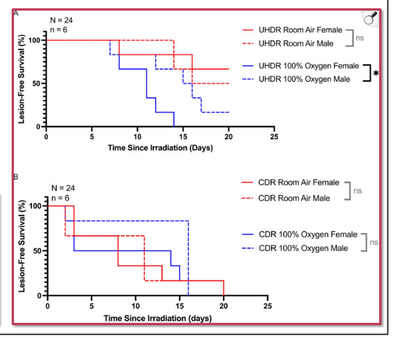
AIM

Compare skin toxicity between UHDR and CDR in **awake vs. isoflurane-anesthetized** mice.

PRIOR STUDY: UHDR SEX VARIATIONS

First observation of a sex difference in normal-tissue damage following UHDR irradiation [1]





Method

1. **Probe** — Oxyphor PtG4 via Retro-orbital Injection 60-min prior to beam on
2. **Pre-Irradiation** — Confirm dose using PTW flashDiamond, Anesthetize Iso Group
3. **Irradiation** — Deliver 25 Gy (surface) using IntraOp Mobetron 9 MeV Electrons
4. **Monitor** — Daily white-light imaging Follow-up for 30 days
5. **Score** — Independently score between 2 graders, average scores

	Male		Female	
	Awake	Isoflurane + 21% O_2	Awake	Isoflurane + 21% O_2
UHDR 375 Gy/s	N = 21	N = 20	N = 10	N = 10
CDR 0.17 Gy/s	N = 20	N = 20	N = 10	N = 10

Male — Awake Combined

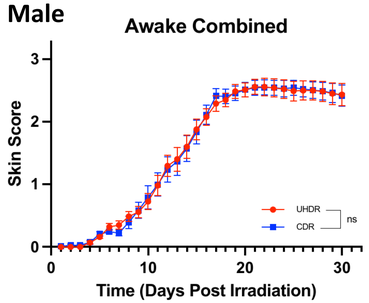


Fig 1. Male, awake — UHDR vs CDR: no sparing (n.s.).

Male — Iso + RA Combined

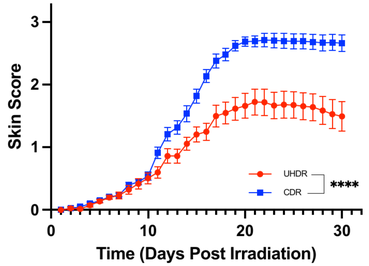


Fig 2. Male, isoflurane + room air — UHDR vs CDR: sparing ($p < 0.0001$).

Female — Awake Combined

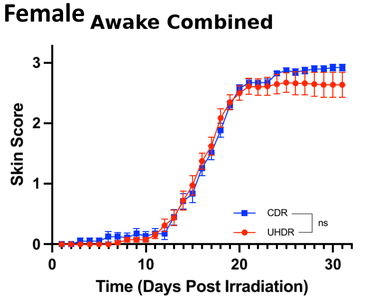


Fig 3. Female, awake — UHDR vs CDR: no sparing (n.s.).

Female — Iso + RA Combined

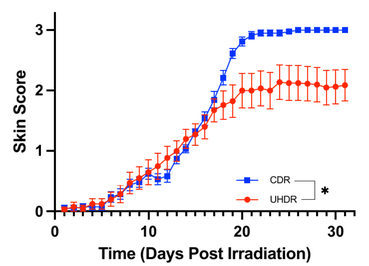


Fig 4. Female, isoflurane + room air — UHDR vs CDR: sparing ($p < 0.05$).

Results UHDR Sparing Appeared Only in Anesthetized Mice

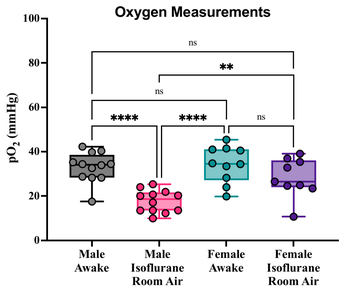


Fig 5. Irradiated tissue baseline pO_2, taken during irradiation **(Trace shown in Live: Tissue pO_2 Traces)**

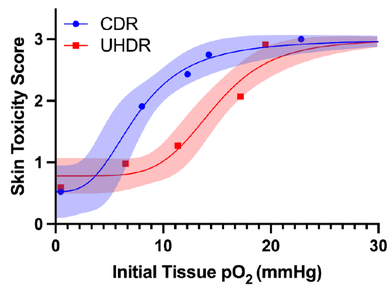
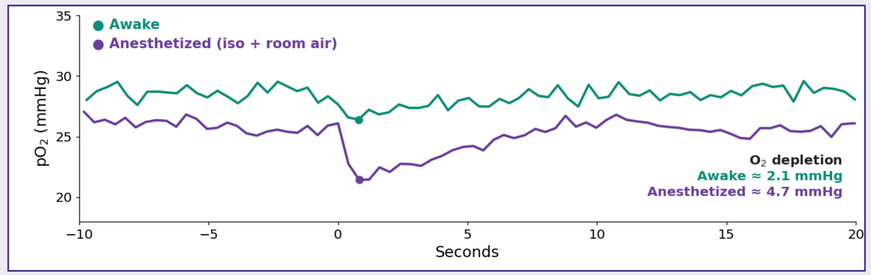
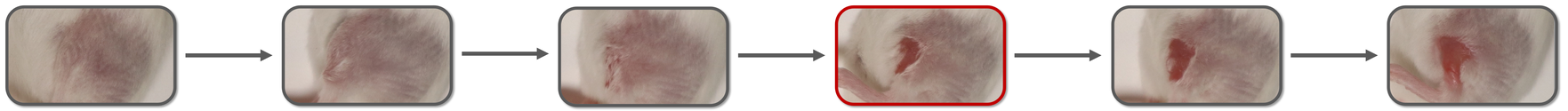


Fig 6. Prior work: **sparing peaks at pO_2 ≈ 7–16 mmHg** and vanishes at high pO_2 [2]

LIVE: TISSUE pO_2 TRACES CONSITENT WITH PRIOR LITERATURE [3]



SKIN TOXICITY SCORING SCALE



Score 0	Score 1	Score 1.5	Score 2	Score 2.5	Score 3
Normal skin	Erythema	Moist desquam.	Ulceration (endpoint)	Confluent desquam.	Severe breakdown

CONCLUSIONS

- At 25 Gy, **no UHDR skin sparing in awake mice, but significant sparing in anesthetized mice.**
- Loss of sparing in awake animals was driven by the UHDR oxygen effects.

REFERENCES

1. Tavakkoli AD, et al. Anesthetic oxygen use and sex are critical factors in the FLASH sparing effect. Adv Radiat Oncol 2024;9:101492.
2. Hunter DI, et al. Systematic tissue oxygen variation modulates murine skin radiation toxicity at UHDR. Phys Med Biol 2026;71:095023.
3. Cao X, et al. Quantification of oxygen depletion during FLASH irradiation. Int J Radiat Oncol Biol Phys 2021;111:240–8.

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