Radiolysis Simulations Used to Evaluate Radical Recombination Effects and Oxygen Limitations In Flash Radiotherapy

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INTRODUCTION

- As of 2014 Studies of ultra-high dose rate (UHDR) radiotherapy (RT) have shown a normal tissue sparing effect, terms the FLASH effect [1].
- The underlying radiochemical mechanisms remain poorly understood. Direct measurements rely upon longer lived water radiolysis species such as aqueous electrons (e^-_{aq}) and oxygen, to infer behaviours of toxic species leading to tissue damage.
- **This study uses kinetic modeling to identify which chemical pathways exhibit dose rate dependent behaviour and can be used to correlate to experimental data.**

METHODS

- A comprehensive physicochemical model of water radiolysis was developed
  - 16 molecular species
  - 56 coupled reaction rate equations,
  - with pulsed beam structures matched to published UHDR electron irradiation experiments.
  - range of oxygen tensions (0.1–10% O_2)
  - Dose rate conditions (0.3–300 Gy/s)
  - This code was developed in Matlab and runs using ode1 5 for robustness of stiff data,

Product	e^-_{aq}	•OH	H•	H_2O_2	H_2	OH-	H+	R•
Yield (μM/Gy)	0.27	0.28	0.06	0.07	0.05	0.01	0.28	0.06

Table 1: The concentration yields of radiation induced products of radiolysis from ~9 MeV electrons, with solutions pH of 7 .

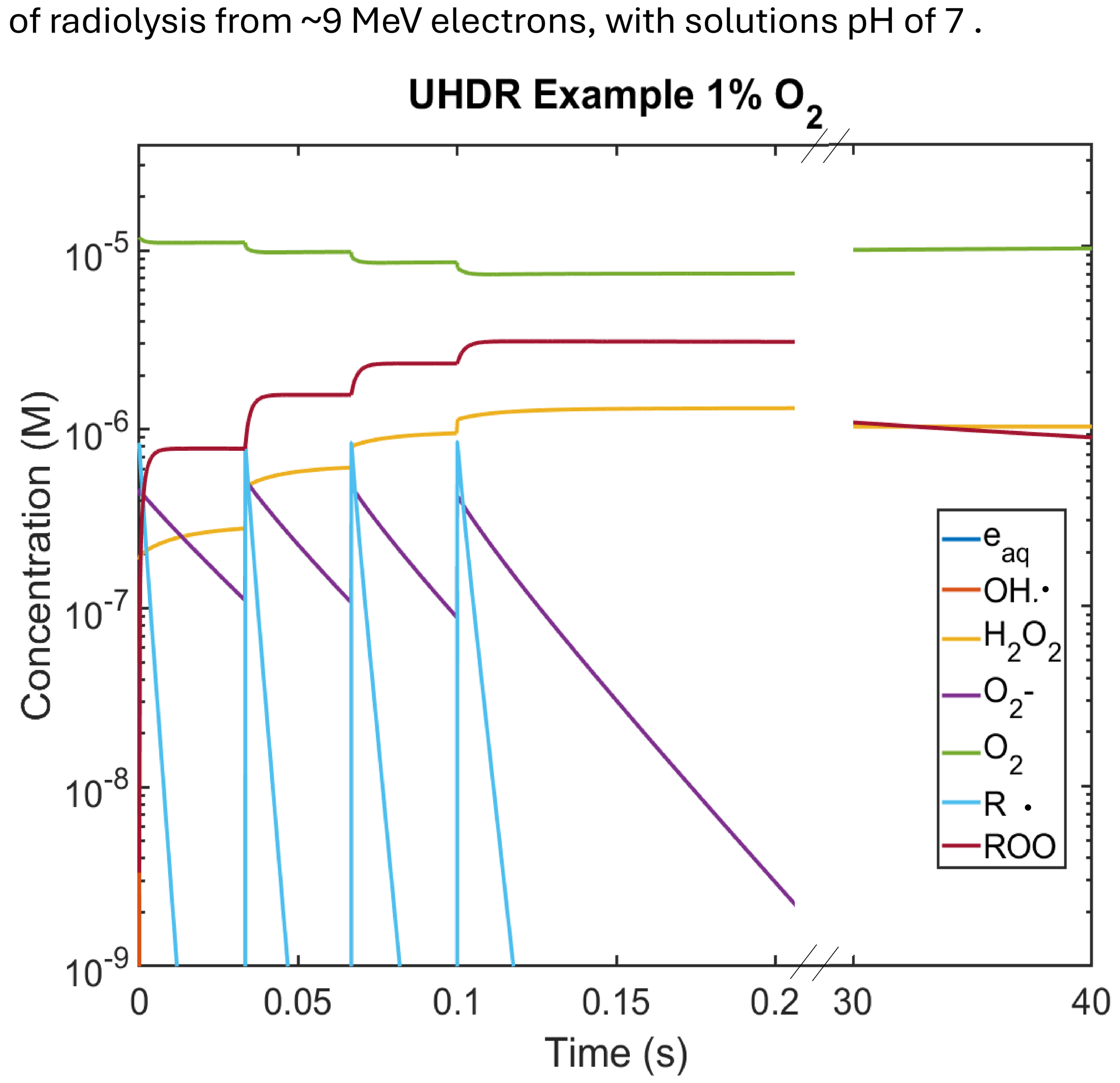

Figure 1. Example of a UHDR (75 Gy/s) with 2.5 Gy per pulse simulationswith several key radiolysis species plotted through to equivalent steady state. All simulations were carried out to 100s, to allow decay of long lifetime products such as peroxyl radicals.

RESULTS

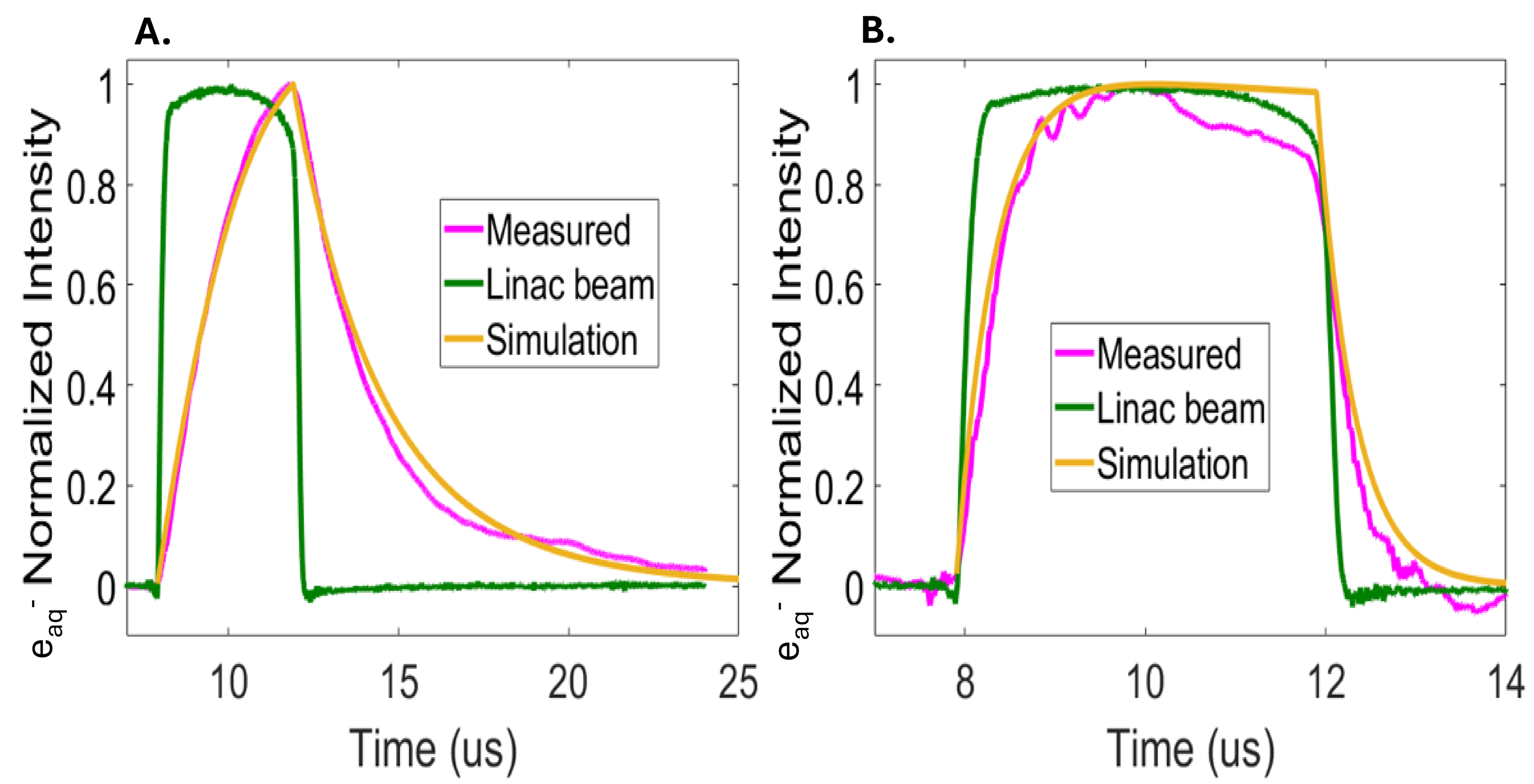

Figure 2. Measured experimental data and simulated rate equation data for transient aqueous electrons e^-_{aq} from a single 4 µs UHDR pulse at both low (~1%) oxygen (A) and high oxygen (B) (~10%). The measurements (pink) are overlaid with the simulations (yellow) and the pulse shape of the beam (green).

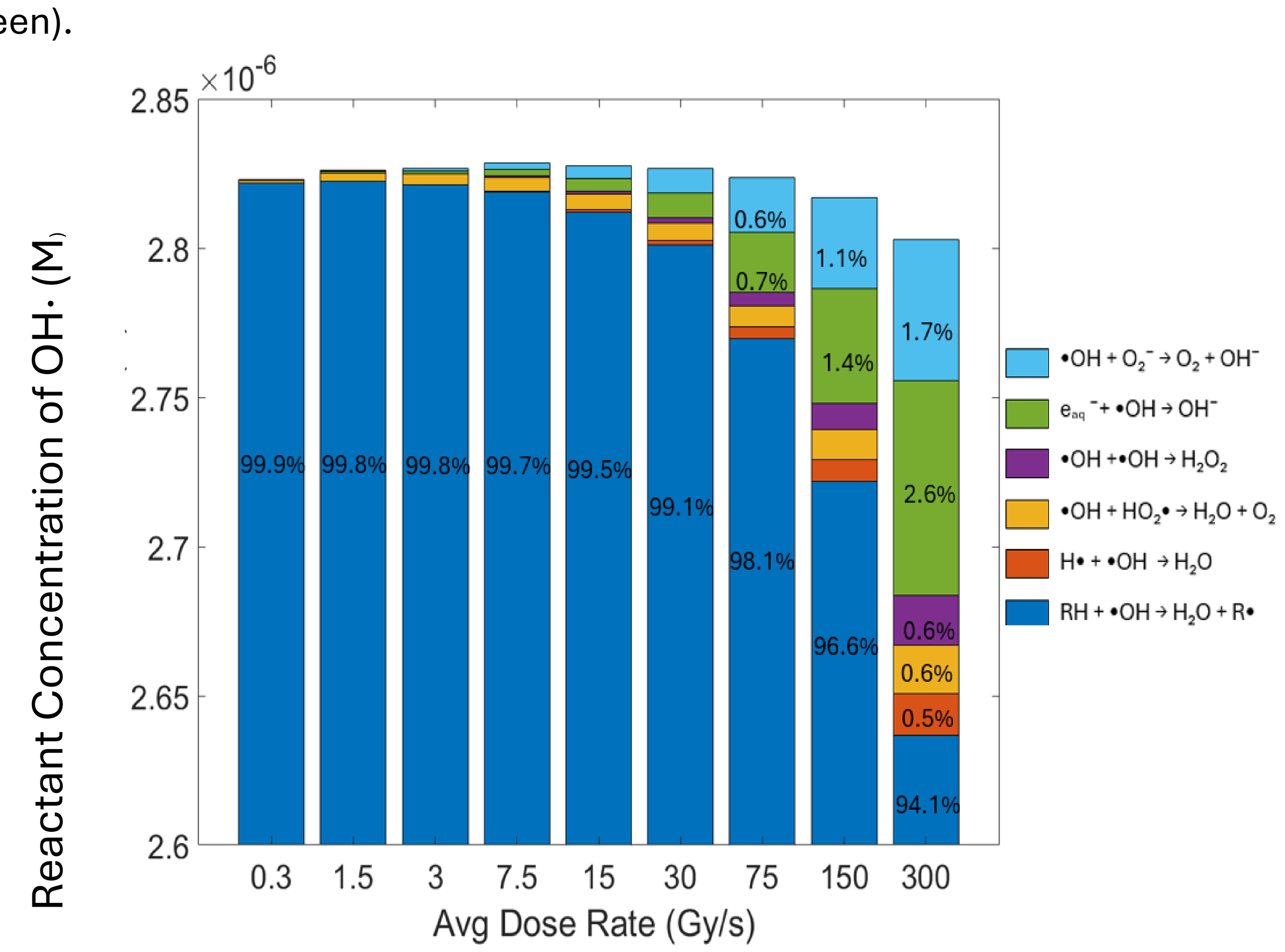

Figure 3. Hydroxyl radical scavenging reaction yields from simulated data using the following parameters: Initial O_2: 5%, Pulse Repetition Frequency: 30 Hz, Total Dose 10 Gy, pulse width: 4 us.

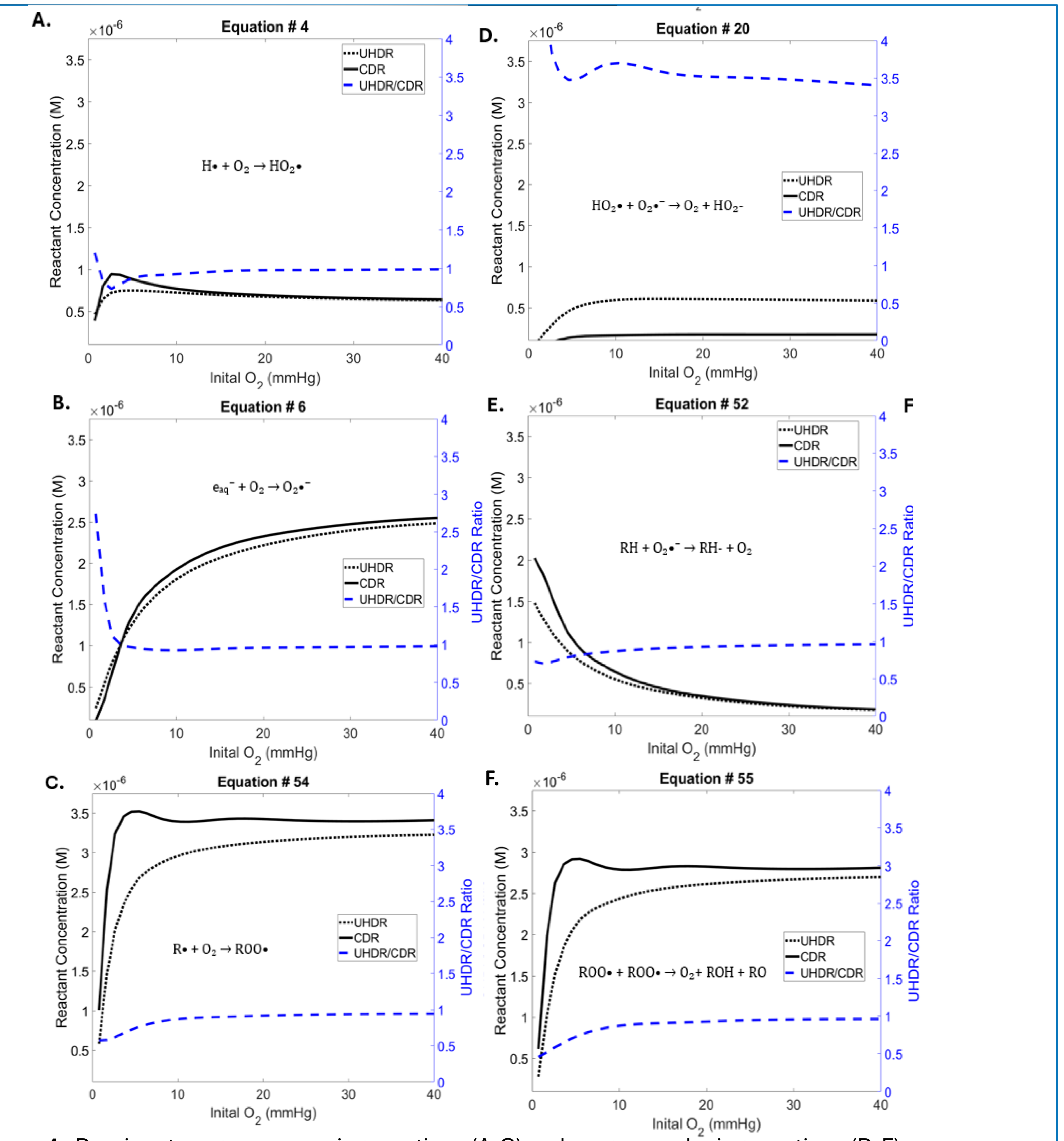

Figure 4. Dominant oxygen consuming reactions (A-C) and oxygen producing reactions (D-F) are shown as simulated for varying initial oxygen, with UHDR and CDR concentrations of each reactant (left axis) and UDHR/CDR ratio (right axis). Data was simulated using the following parameters: Pulse Repetition Frequency: 30 Hz, Total Dose 10 Gy, pulse width: 4 us. UHDR (Dotted line) corresponds to 150 Gy/s, 5 Gy per pulse delivery, and CDR (Solid Line) corresponds to 0.3 Gy/s delivery.

CONCLUSIONS

- This work identifies specific radiochemical pathways that exhibit true dose rate sensitivity and clarifies which proposed FLASH mechanisms are unsupported by homogeneous phase radical kinetics.
- Radical–radical recombination contributes too little (<5%) to account for known FLASH sparing at UHDR.
- Peroxyl radical and $HO_2•/O_2•^-$ chemistry shows dose rate dependent behavior within physiologic oxygen tensions associated with FLASH.
- A range of oxygen level between 1-3% oxygen shows a significant change in peroxyl radical generation.
- Although constrained by simplified aqueous conditions lacking scavengers and tissue heterogeneity, the model provides mechanistic insight into the radiochemical regimes dominating the homogeneous phase chemistry.

REFERENCES

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