Supplementary Table S1

Title: *Temporal and spatial scales*

Table S1. Characteristic temporal and spatial scales of hydroxyl radical–related processes in irradiated nuclear microenvironments.

Process	Time scale	Spatial scale	Notes	Reference
Hydroxyl radical formation	< 10 fs	Sub-nanometer (spur scale)	Formation of $OH^{\bullet}$ following ionization and excitation of water during the physical stage of radiation interaction	Nikjoo et al and Spink & Woods[1,2]
$OH^{\bullet}$ reaction with DNA	100 fs – 1 ps	~1 nm	Site-specific hydrogen abstraction from the sugar–phosphate backbone leading to strand break initiation	Ward[3]
Scavenging by endogenous molecules	1 ps – 10 ns	1–10 nm	Competitive reactions with thiols, glutathione, proteins, and other cellular scavengers that reduce radical availability	von Sonntag[4]
Diffusive transport within the nucleus	10 ps – 100 ns	10–100 nm	Redistribution of $OH^{\bullet}$ radicals prior to absorption; supports quasi-steady-state and macroscopic transport approximations	Mozumder et al.[5]

References

1. Nikjoo, H. *et al*. Computational approach for determining the spectrum of DNA damage induced by ionizing radiation. *Radiat. Res*. **156**, 577-583 (2001).
2. Spinks, J. W. T. & Woods, R. J. *An Introduction to Radiation Chemistry* (3rd ed.). (Wiley-Interscience,1990).
3. Ward, J. F. DNA Damage Produced by Ionizing Radiation in Mammalian Cells: Identities, Mechanisms of Formation, and Reparability. *Progress in nucleic acid research and molecular biology*, **35**, 95–125 (1988).
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Supplementary Text S2

Title: *Hydroxyl radical density*

This Supplementary Text contains the mathematical derivations relevant to the equation for hydroxyl radical density under steady state used in the main text.

The angular-dependent hydroxyl radical density $\psi(\mathbf{r}, \mathbf{\Omega})$ obeys a linear transport-reaction equation given by

$$\mathbf{\Omega}.\nabla\psi(\mathbf{r}, \mathbf{\Omega}) + \Sigma_a\psi(\mathbf{r}, \mathbf{\Omega}) = \frac{S_0}{4\pi} \quad \text{(S2-1)}$$

where $\mathbf{\Omega}$ indicates the unit direction vector, Σ_a is the effective macroscopic absorption coefficient, summing all the chemistry-based absorption processes, and S_0 is the isotropic volumetric hydroxyl radical source term.

The source term is considered isotropic because of the rapid angular randomization of the secondary electrons and radicals after water radiolysis.

The scalar radical density $\phi(\mathbf{r})$ and flux $\mathbf{J}(\mathbf{r})$ can be defined as follows:

$$\phi(\mathbf{r}) = \int_{4\pi}\psi(\mathbf{r}, \mathbf{\Omega})d\Omega \quad \text{(S2-2)}$$

$$\mathbf{J}(\mathbf{r}) = \int_{4\pi}\mathbf{\Omega}\,\psi(\mathbf{r}, \mathbf{\Omega})d\Omega \quad \text{(S2-3)}$$

Using P_1 approximation, one can obtain the coupled moment equations as:

$$\nabla.\mathbf{J} + \Sigma_a\phi = S_0 \quad \text{(S2-4)}$$

$$J = -\frac{1}{3\Sigma_a}\nabla\phi \quad \text{(S2-5)}$$

In the absence of large-scale spatial gradients inside the nuclear volume, or if averaged over distances large compared to the diffusion length of the radical, the divergence term is zero:

$$\nabla.\mathbf{J} \approx \mathbf{0} \quad \text{(S2-6)}$$

With this condition, the transport–reaction balance reduces to

$$\Sigma_a\phi_0 = S_0 \quad \text{(S2-7)}$$

where ϕ_0 is the steady-state hydroxyl radical density. Solving for ϕ_0 provides a closed-form expression used throughout the manuscript:

$$\phi_0 = \frac{S_0}{\Sigma_a} \quad \text{(S2-8)}$$

The present expression represents the analytical backbone of the model in linking the radiochemical source term to the effective chemical absorption processes by a physically transparent and mathematically consistent formulation.

The derivation assumes: linear reaction kinetics, isotropic radical production, quasi-steady-state conditions justified by scale separation; see Supplementary Table S1, and effective macroscopic absorption coefficients. Such assumptions are considered standard for analytical modeling of radiochemical transport and fully comply with both experimental radiolysis studies and Monte Carlo track structure simulations.

Supplementary Table S3

Title: *Experimental data for G-values*

The datasets from experiments which represent the trend are listed in Table S3, from low-LET proton and electron beams to intermediate-LET protons and finally to the high-LET region, as represented by carbon and heavier ions. Despite the flow of vastly differing approaches to measurement, it appears to hold rather well, supporting its status as a primary chemical rather than an experimental phenomenon[1,2].

Table S3. Experimental benchmarks for LET-dependent hydroxyl radical G-values in liquid water

Reference	Radiation Type	LET Range (keV µm⁻¹)	Radiochemical Time Scale	Medium / Conditions	Reported G_{OH} (molecules per 100 eV)	Measurement Technique	Notes
Buxton et al.[3]	γ-rays / fast e^-	≲ 1	Chemical stage (≈10^{-7}–10^{-6} s)	Pure, aerated water, neutral pH	2.6 – 2.9	Chemical dosimetry (reviewed data)	Canonical low-LET reference values
Elliot & Bartels[4]	γ-rays / fast e^-	≲ 1	Chemical stage	Light water, 20–350 °C	2.7 – 3.1	Kinetic modeling + experiments	Temperature dependence documented
Pimblott & LaVerne[5]	Electrons	≲ 1	Early-time (≈1–10 ps)	Liquid water	4.7 – 5.0	Stochastic Monte Carlo chemistry	Primary yields before spur recombination
Pastina & LaVerne[6]	Protons (1–10 MeV)	~2 – 15	Chemical stage	Aerated water	2.0 – 2.8	Chemical yield measurements	Decrease toward Bragg peak
Yamaguchi et al.[7]	Heavy ions	~20 – 100	Chemical stage	Aqueous solution	1.0 – 2.2	Radiolysis yield estimation	Strong LET dependence observed
Moritake et al.[8]	Carbon ions	~30 – 200	Chemical stage	Aqueous solution	0.7 – 1.8	ESR spin trapping	Direct experimental evidence of LET effect
Smith et al.[9]	Heavy ions	~10 – 300	Chemical stage	Liquid water	0.8 – 2.5	Chemical yield analysis	Broad LET coverage
Baba et al.[10]	Heavy ions	~1 – 200 (Bragg peak region)	Chemical stage	Liquid water	LET-dependent (≈1–3 → ≈1)	Geant4-DNA validated against experiments	Near-Bragg peak behavior
Shin et al.[11]	Mixed (MC-supported)	LET-dependent	Early-time (≈1 ps)	Liquid water	4.2 – 4.8	Track-structure Monte Carlo	Upper-bound initial yields
Ramos-Méndez et al.[12]	Photons / electrons	≲ 1	Chemical stage	Liquid water	≈2.7	TOPAS-nBio validation	Agreement with canonical data

References

1. Ward, J. F. DNA Damage Produced by Ionizing Radiation in Mammalian Cells: Identities, Mechanisms of Formation,
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9. Smith, M. *et al*. Hydroxyl radical yields in the heavy ion radiolysis of water. *Radi. Phy. Chem*. **188**, 109629 (2021).
10. Baba, K. *et al*. Quantitative estimation of track segment yields of water radiolysis species under heavy ions around Bragg peak energies using. *Sci. Rep*. **11**, 1524 (2021).
11. Shin, W. G. *et al*. A Geant4-DNA Evaluation of Radiation-Induced DNA Damage on a Human Fibroblast. *Cancers*. **13**, 4940 (2021).
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Supplementary Table S4

Title: *Monte Carlo calculations data*

Table S4 below presents a summary of typical results of hydroxyl radical yield estimates carried out through a series of Monte Carlo calculations, varying in radiation quality, energy, and timescales, as documented in the relevant peer-reviewed studies. These calculations have in common a trend of reduced hydroxyl radical yield effectiveness expressed in a rising LET, together with enhanced concentrations of radical recouping/recombination in the high-LET region[1,2,3].

Table S4. Quantitative comparison between the present analytical model and Monte Carlo track-structure simulations for hydroxyl radical yields and densities

Category	Quantity	LET Range (keV/µm)	Time Window	Analytical Model (This Work)	Monte Carlo Results (Reported)	Monte Carlo Source	Notes
Yield (early-time)	G_{OH} (molecules per 100 eV)	≤ 1	~1 ps	Not targeted	4.7 – 5.0	Pimblott & LaVerne[4]	Primary yields prior to spur recombination
Yield (early-time)	G_{OH}	≤ 1	~1 ps	Not targeted	4.2 – 4.8	Shin et al.[5]	Geant4-DNA / TOPAS-nBio track-structure simulations
Yield (chemical stage)	G_{OH}	≤ 1	~100 ns – 1 µs	2.6 – 2.8	2.6 – 2.8	Karamitros er al and Ramos-Méndez et al.[6,7]	Converged low-LET chemical-stage yields
Yield (chemical stage)	G_{OH}	~10 – 50	~100 ns – 1 µs	LET-dependent (≈2.5 → 1.5)	1.5 – 2.5	Baba et al.[8]	Near-Bragg-peak heavy-ion simulations
Yield (chemical stage)	G_{OH}	~50 – 200	~100 ns – 1 µs	LET-dependent (≈1.5 → 1.0)	1.0 – 2.0	Baba et al. and Ramos-Méndez et al.[7,8]	Enhanced intra-track recombination
Density	ϕ_0 (nm^{-3})	Low LET	Chemical stage	~10^{-2} – 10^{-1}	~10^{-2} – 10^{-1}	Pimblott & LaVerne[4]	Spatially averaged radical densities
Density	ϕ_0	Low LET	Chemical stage	~10^{-2} – 10^{-1}	~10^{-2} – 10^{-1}	Shin et al.[5]	Consistent with Geant4-DNA chemistry stage
Density	ϕ_0	Moderate–High LET	Chemical stage	Decreasing with LET	Decreasing with LET	Shin et al. and Ramos-Méndez et al.[5,7]	Trend-level agreement; LET-dominated behavior

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Supplementary Text S5

Title: *Chemistry and radiochemistry parameters*

All of the chemistry and radiochemistry model parameters used for these simulations are presented in Table S5 and were set at established literature values typically used in experimental radiolysis measurements and track-structure simulations.

Table S5. Chemical and radiochemical parameters used in the LET- and oxygen-dependent radical transport model.

Parameter name	Symbol	Value used (unit)	Notes	Reference
Reaction rate constant of $OH^{\bullet}$ with oxygen	k_{O_2}	1.9×10^9 $M^{-1}\cdot s^{-1}$	Gold-standard kinetic constant for $OH^{\bullet}$–O_2 reactions; universally used in radiation chemistry and Monte Carlo track-structure models	Buxton et al.[1]
Oxygen solubility coefficient (Henry's constant)	H	1.3×10^{-5} $mol\cdot L^{-1}\cdot mmHg^{-1}$	Converts oxygen partial pressure to dissolved molecular oxygen concentration	Spinks & Woods[2]
Effective DNA interaction cross-section	Σ_{DNA}	1.0×10^{-2} nm^{-1} (low)	Lower bound corresponding to sparse chromatin packing or reduced DNA accessibility	Friedland et al. and Henthorn[3,4]
		1.2×10^{-2} nm^{-1} (intermediate)	Representative average nuclear DNA interaction strength	
		1.5×10^{-2} nm^{-1} (high)	Upper bound corresponding to dense chromatin regions or enhanced local DNA availability	
Aggregate non-oxygen scavenging term	$\sum_i k_i C_i$	5.0×10^{-3} nm^{-1} (low)	Reduced background scavenging; antioxidant-depleted or highly hypoxic tumor microenvironments	von Sonntag and Nikjoo et al.[5,6]
		1.8×10^{-2} nm^{-1} (intermediate)	Representative intracellular scavenger concentration	
		3.5×10^{-2} nm^{-1} (high)	Scavenger-rich environments; high glutathione or thiol content	
Total background scavenging	Σ_{bg}	1.5×10^{-2} nm^{-1} (low)	$\Sigma_{bg} = \Sigma_{DNA} + \sum_i k_i C_i$	Derived
		3.0×10^{-2} nm^{-1} (intermediate)	Represents average intracellular chemical reactivity	
		5.0×10^{-2} nm^{-1} (high)	Upper bound reflecting scavenger-rich biochemical conditions	
Tissue-equivalent mass density	ρ	1.0 $g\cdot cm^{-3}$	Water-equivalent soft tissue; consistent with Geant4-DNA	Standard assumption
Low-LET reference hydroxyl radical yield	G_0	2.46 molecules·(100 eV)$^{-1}$	Photon-induced reference yield used for normalization	Smith et al.[7]
LET-dependent hydroxyl radical yield	$G_{OH}(LET)$	Model-dependent	Functional LET dependence constrained by experimental and Monte Carlo benchmarks	Present work;

References

1. Buxton, G. V. *et al*. Critical review of rate constants for reactions of hydrated electrons, hydrogen atoms and hydroxyl radicals (•OH/•O−) in aqueous solution. *Journal of Physical and Chemical Reference Data*. **17**, 513–886 (1988).
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