Evaluation Of The Effect Of Oxygen In FLASH Irradiation Through GEANT4-DNA

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Overview

- Introduction
  - FLASH-RT
  - Oxygen effect
  - Oxygen depletion
- Geant4-DNA Simulation
  - Geometry &Methodology
  - OER-weighted dose
- Conclusion

FLASH Radiotherapy (FLASH-RT)

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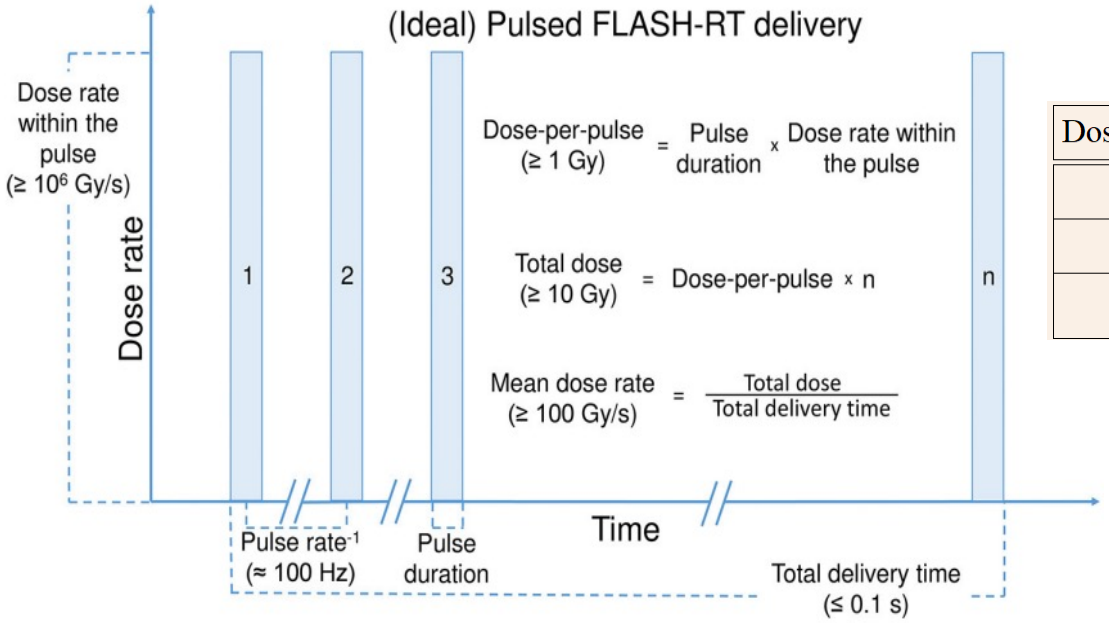
Pulsed FLASH-RT delivery parameters

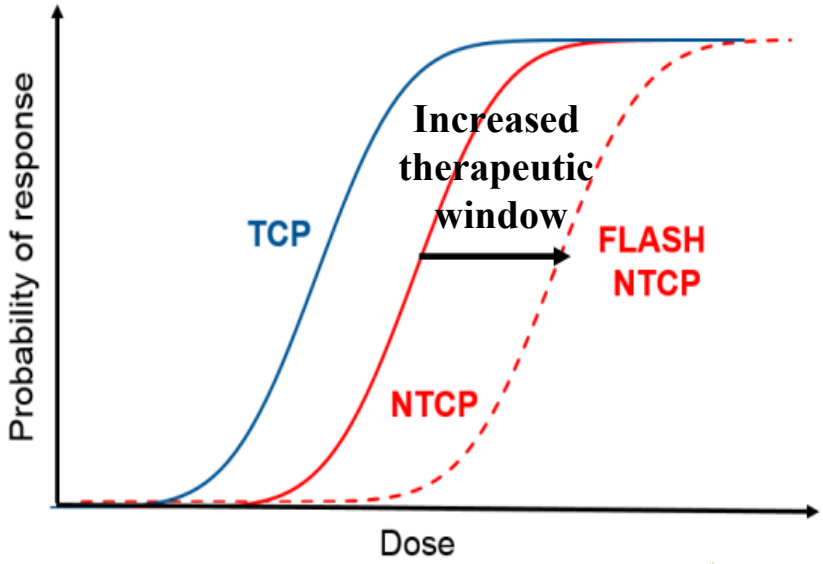


Dose per pulse (pulse duration $*$ Dose rate within the pulse)	$\geq 1 Gy$
Total dose (Dose per palse$*$number of puls)	$\geq 10 Gy$
Total delivery time	$\leq 0.1 s$
Mean dose rate($\frac{Total\ dose}{Total\ delivery\ time}$)	$\geq 100 \frac{Gy}{s}$

Wilson J D. et al, 2020

TCP: Tumor Control Probability

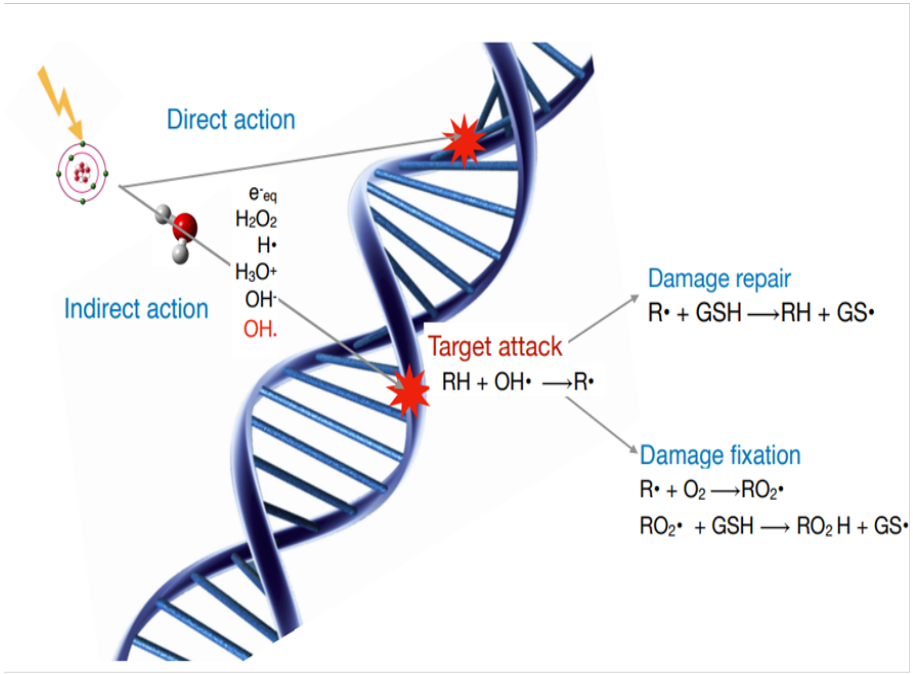
NTCP: Normal Tissue Complication Probability



Oxygen Effects

On the nanoscopic level the oxygen effect is described as a combination of two main phenomena:

1) the oxygen fixation hypothesis



2) Toxic reactive oxygen species (ROS)

$$e^-_{aq} + O_2 \longrightarrow O_2^{\bullet -}$$

$$H^\bullet + O_2 \longrightarrow HO_2^\bullet.$$

$$OER(pO_2) = \frac{D_{pO_2}}{D_{\text{normoxic}}}\Big|_{\text{same effect}}$$

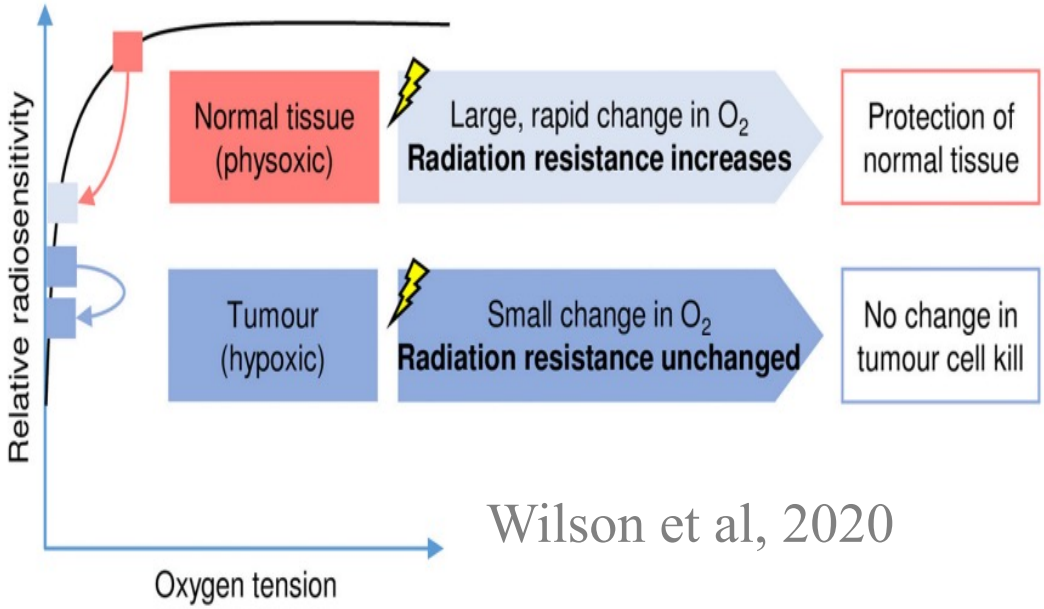
Oxygen Enhancement Ratio

Oxygen Depletion

Radiation consumes locally O2 by the **radiolysis induced reaction:**

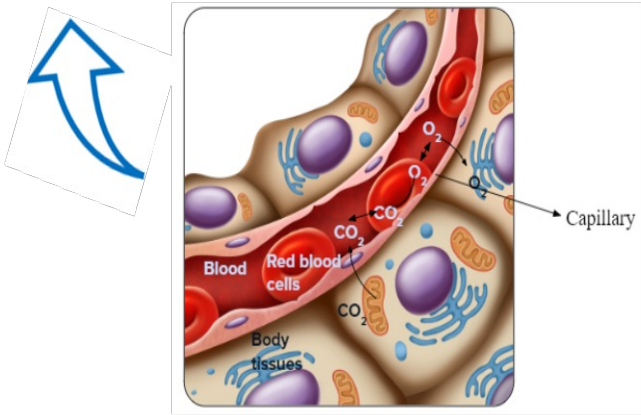
$$e^-_{aq} + O_2 \longrightarrow O_2^{\bullet -}$$

$$H^{\bullet} + O_2 \longrightarrow HO_2^{\bullet}$$



Wilson et al, 2020

Reoxygenation from nearby capillary ~ Millisecond time scale (**ms**)



1. The depletion of oxygen induce radiobiological **radioresistance** through **OER (pO2)**

2. This may explain differential effect between normal tissue and tumore based on $\Delta OER_{NT} > \Delta OER_{T}$

RADIATION RESEARCH 76, 522–532 (1978)

Oxygen Diffusion into Mammalian Cells following Ultrahigh Dose Rate Irradiation and Lifetime Estimates of Oxygen-Sensitive Species

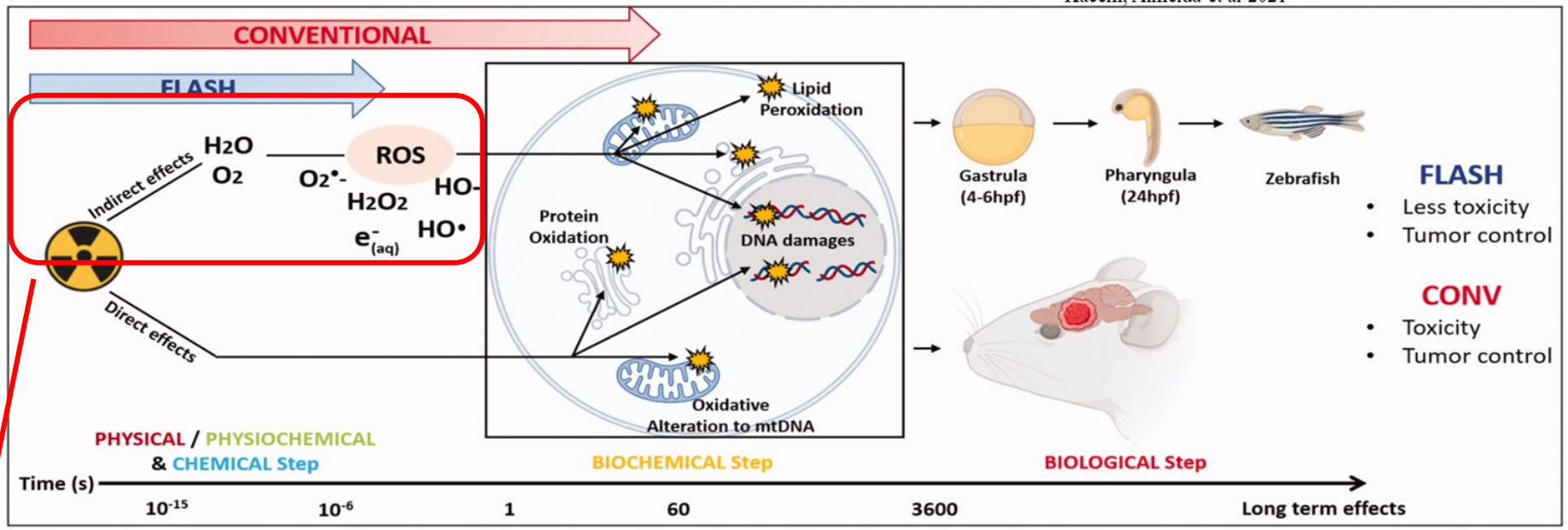
C. CLIFTON LING, HOWARD B. MICHAELS, EDWARD R. EPP, AND ELEANOR C. PETERSON

Division of Radiation Biophysics, Department of Radiation Medicine, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts 02114

LING, C. C., MICHAELS, H. B., EPP, E. R., AND PETERSON, E. C. Oxygen diffusion into mammalian cells following ultrahigh dose rate irradiation and lifetime estimates of oxygen-sensitive species. *Radiat. Res.* 76, 522–532 (1978).

FLASH-RT & Geant4-DNA

Kacem, Almeida et al 2021



Geant4-DNA simulation (pre-chemical and chemical stages):

1. interaction of water radicals induced by particle irradiation
2. radiolytic production of reactive oxygen species (ROS)
3. **G-values** of different chemical species.

$$G = \frac{\text{Number of species}}{100\text{eV of deposited energy}}$$

&

Post processing:

1. **Calculation of Oxygen consumption**
2. **OER-weighted dose** calculation under dynamic oxygenation

To **evaluate the effect of oxygen** in FLASH irradiation, the result of **Geant4-DNA** simulation compared with the **TRAX-CHEM code**

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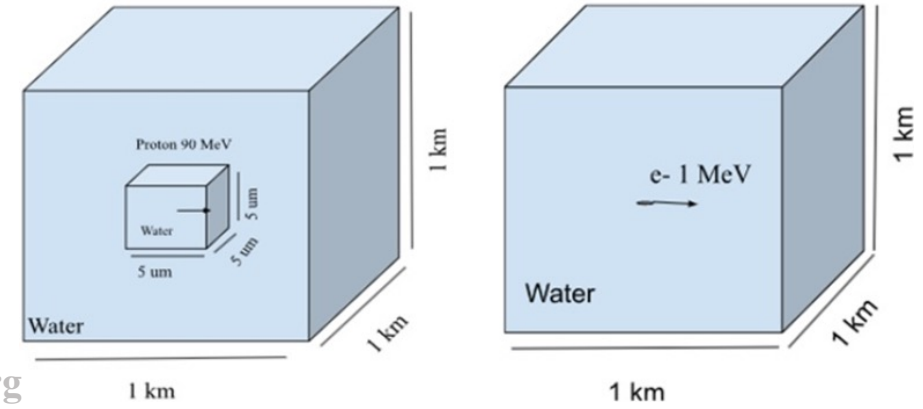
Geometry & Methodology

Geant4-DNA-SCAVENGER example

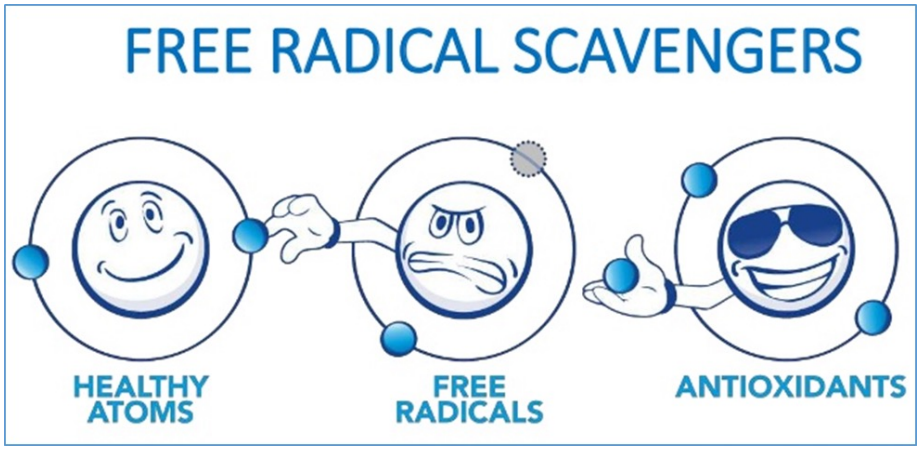
Geant4 11.1/source/examples/extended/medical/dna/Scavenger

- **Monoenergetic point source** beams of **electron** (1 MeV), **proton** (90 MeV)



Geant4-DNA collaboration web site; http://geant4-dna.org

- Calculating of **G-value** of radiochemical species at different oxygen concentrations (1ps-1µs) through **SCAVENGER example**.



- A **scavenger** is a chemical substance added to a mixture in order to remove or deactivate impurities and unwanted reaction products.

$$e^-_{aq} + O_2 \longrightarrow O_2^{\bullet -}$$

$$H^\bullet + O_2 \longrightarrow HO_2^\bullet$$

- In this simulation, **dissolved molecular oxygen** is defined as a **scavenger.**

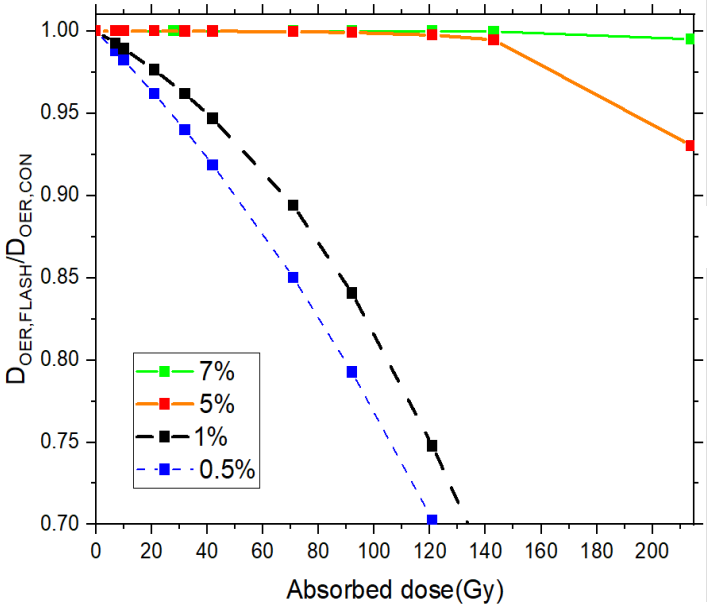
Ratio of OER-weighted dose of Flash vs. conventional dose rate

$$[O_2^{\bullet -} + HO_2^{\bullet}] = \int G_{O_2^{\cdot -} + HO_2^{\cdot}} ([O_2](D))\, dD$$

$$D_{OER,DYN} = \int OER([O_2](D))\, dD$$

$$D_{OER,CONV} = D \cdot OER([O_2]_{ini})$$

The ratio OER-weighted dose of Flash vs. conventional dose rate irradiation for different initial oxygenation as a function of dose (at 1 µs).



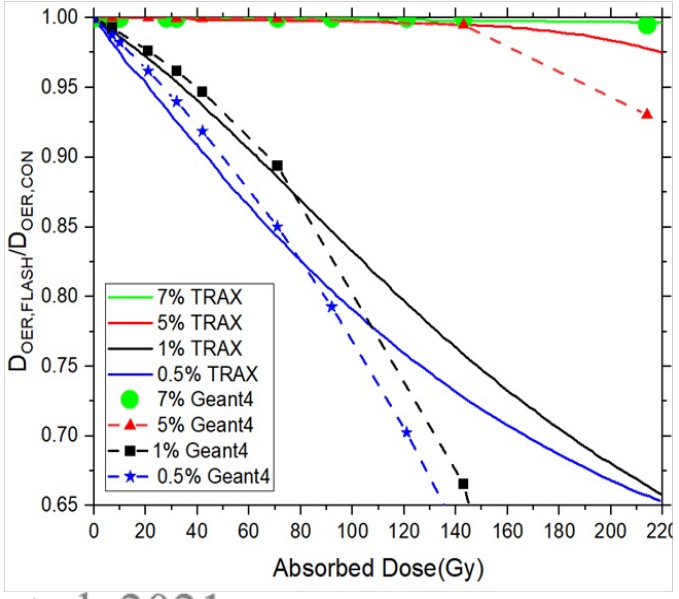
Parametrization of OER proposed by Grimes and Partridge:

$$OER(pO_2) = 1 + (\Phi_O/\Phi_D)(1 - \exp(-\varphi\, pO_2))$$

$$(\Phi_O/\Phi_D = 1.63,\ \varphi = 0.2567)$$

Grimes DR, Partridge M 2015

Comparison of the ratio OER-weighted dose of Flash vs. conventional dose rate irradiation between Geant4-DNA and TRAX-CHEM for different initial oxygenation as a function of dose at 1 µs.



Boscolo D et al, 2021

Conclusion

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1. Using **Geant4-DNA** and **OER factor**, specifically for low LET radiation, we have shown that **oxygen depletion is not observed in the range of clinical doses** and **complete depletion is not supported** by the calculation model implemented in this work.

2. The sparing effect of Flash irradiation is more important in tumor tissue than in normal tissue. (The results are consistent with the results obtained from TRAX-CHEM code.)

3. Although Geant4-DNA toolkit, as one of the Monte Carlo track structure codes, is suited for this class of simulation, further improvements are needed in the **physico-chemical and chemical stages.**

Thanks for your attention

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GEANT4
A SIMULATION TOOLKIT

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