Radiation Damage to DNA: From Initial Ionization Events to Final Damage Products

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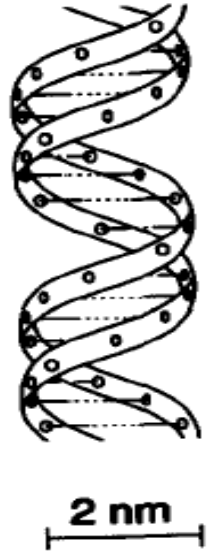
Clustered DNA Damage at Various LET (Goodhead, (1994), IJRB, Vol. 65 (1) pp. 13)



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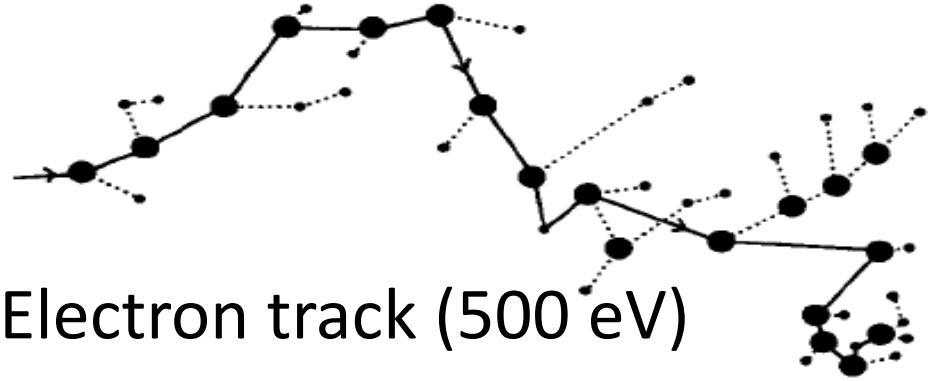
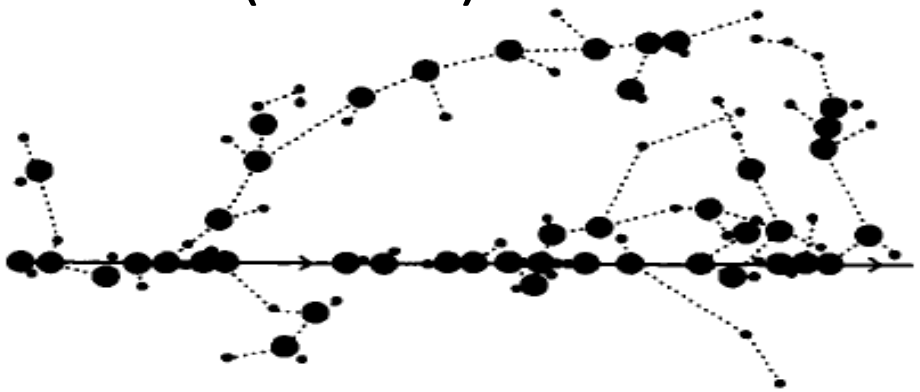


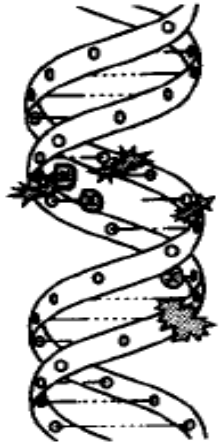
Electron track (500 eV)

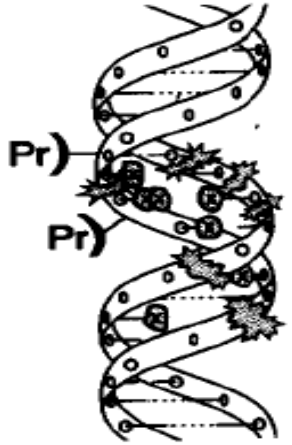
+

α-particle track (4 MeV)



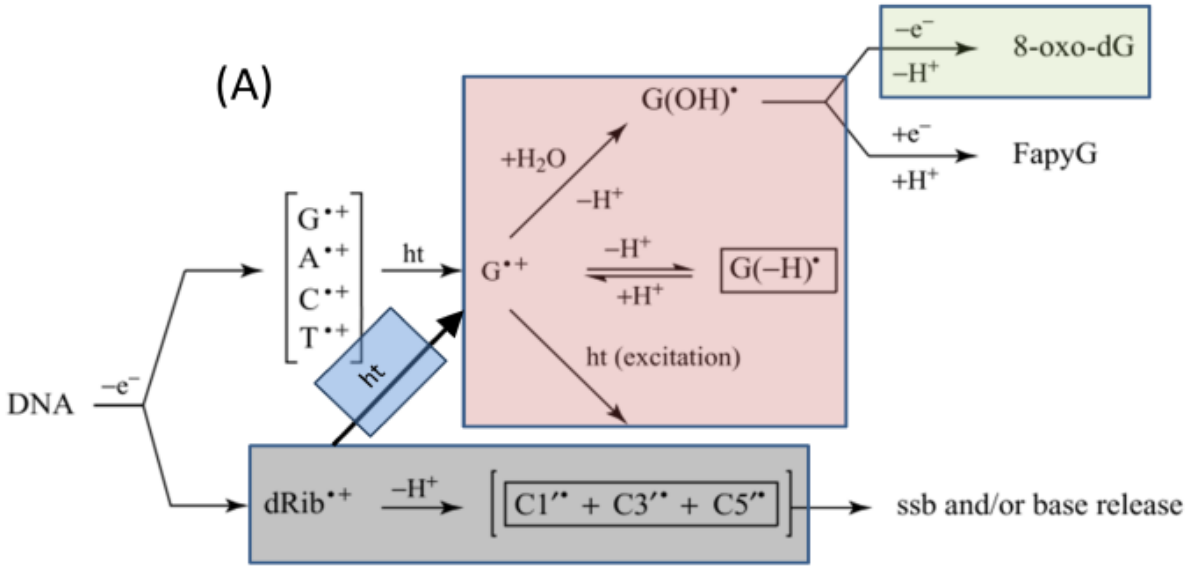
⇒

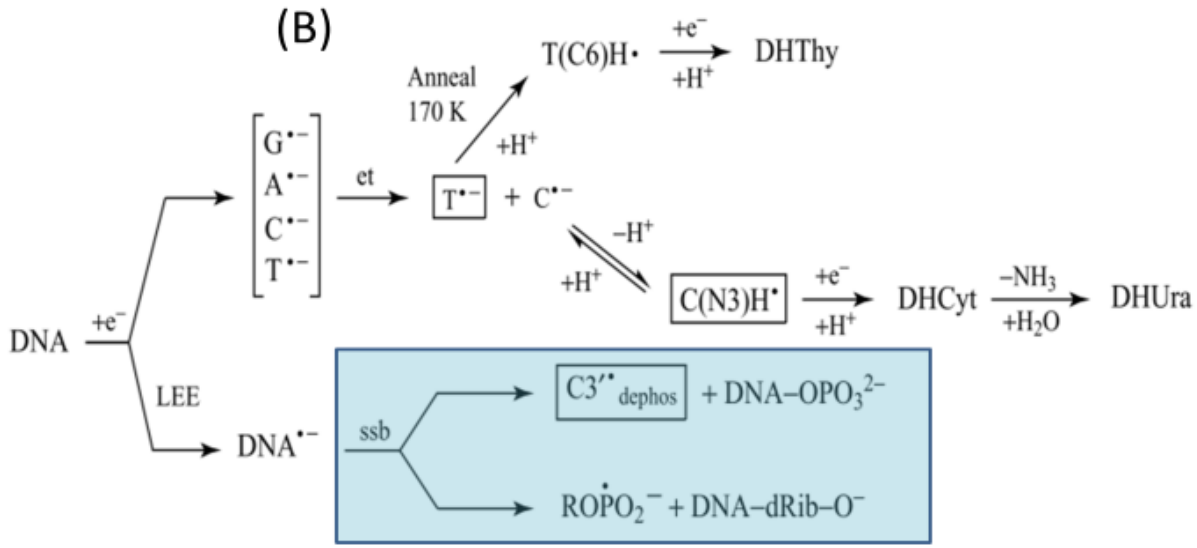




Radiation-Induced Ionization-Mediated DNA Radical Formation

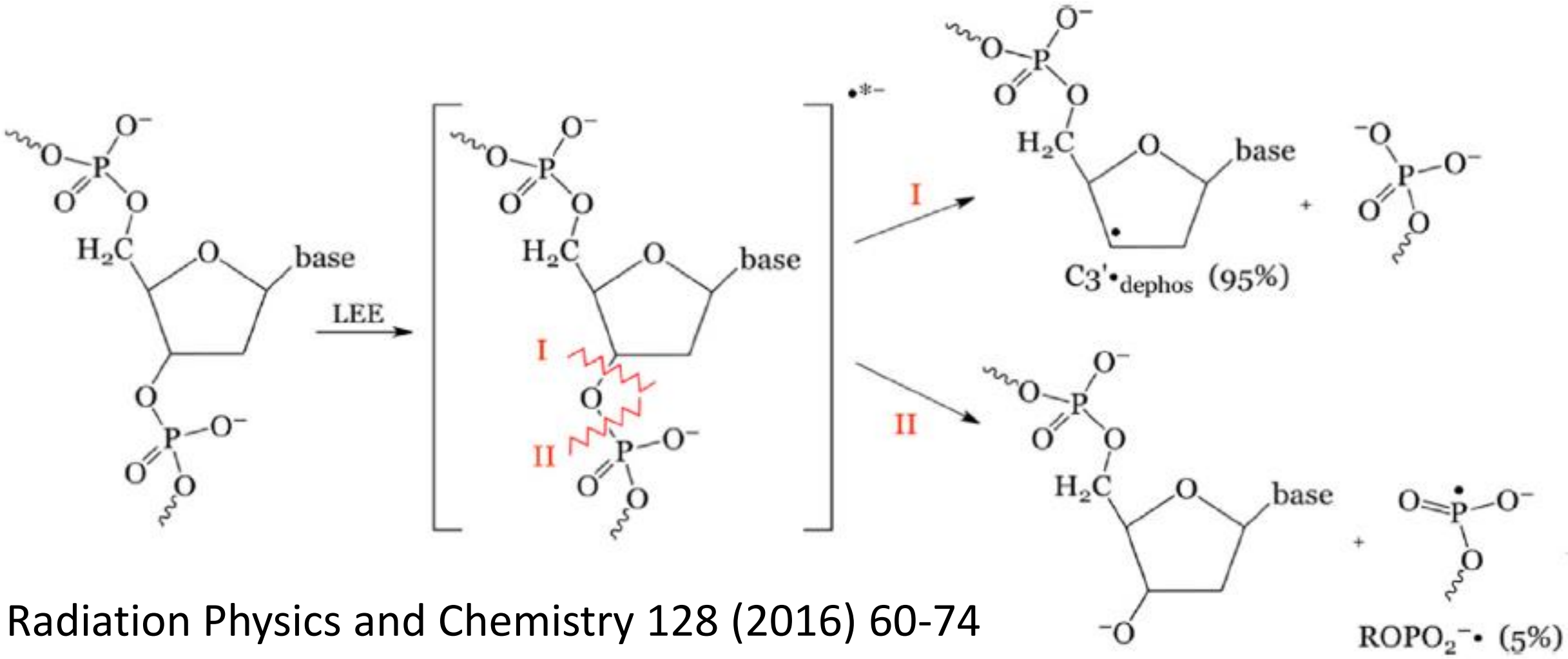
- Oxidative (A) and reductive (B) pathways to ionizing radiation-induced damage





- Before thermalization and localization, dissociative electron attachment of radiation-produced excess low energy electrons induce bond cleavage via an excited transient negative ion intermediate

LEE Leads to Strand Break as well as C3′• dephos and $ROPO_2^{-}$• Formation

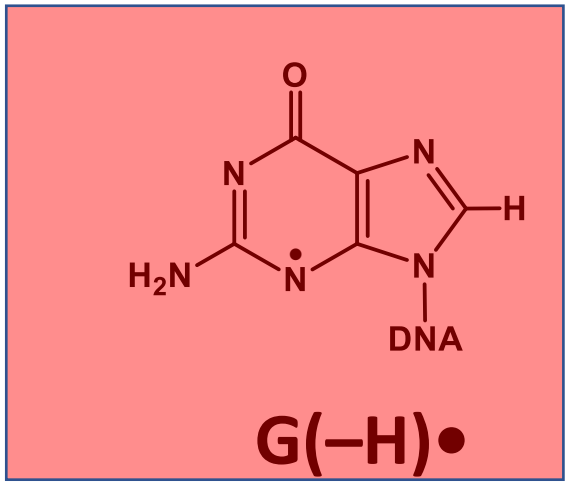


Radiation Physics and Chemistry 128 (2016) 60-74

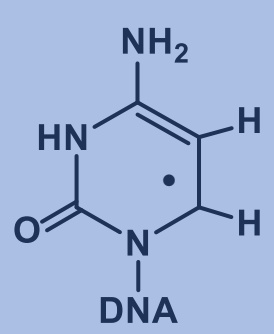
Radicals Trapped at 77 K in Irradiated Hydrated DNA

- Radicals found at 77 K in hydrated DNA and considered here:

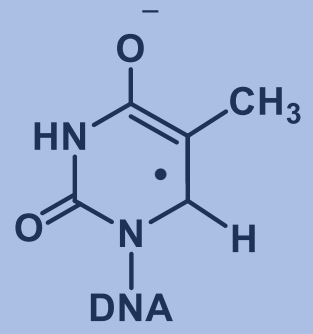
Oxidative



G(–H)•

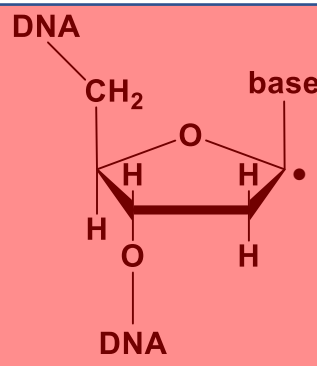


C(N3)H•

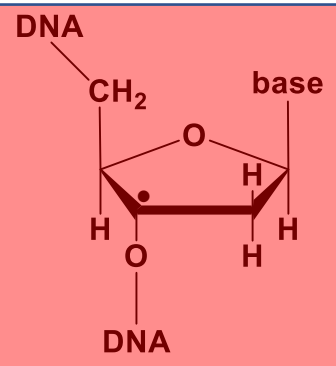


$T•^-$

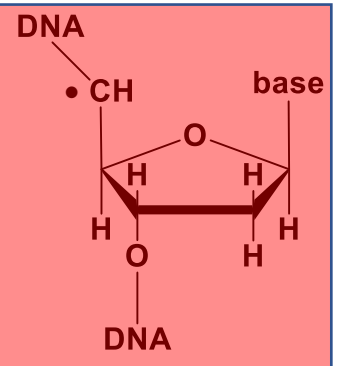
Reductive



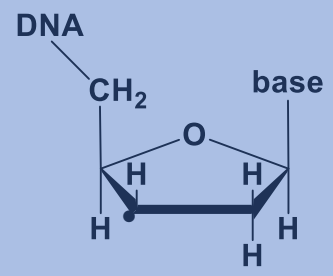
C1'•



C3′•



C5′•



$C3'•_{dephos}$

Ion-Beam (High LET) Irradiation of DNA

Experimental observations:

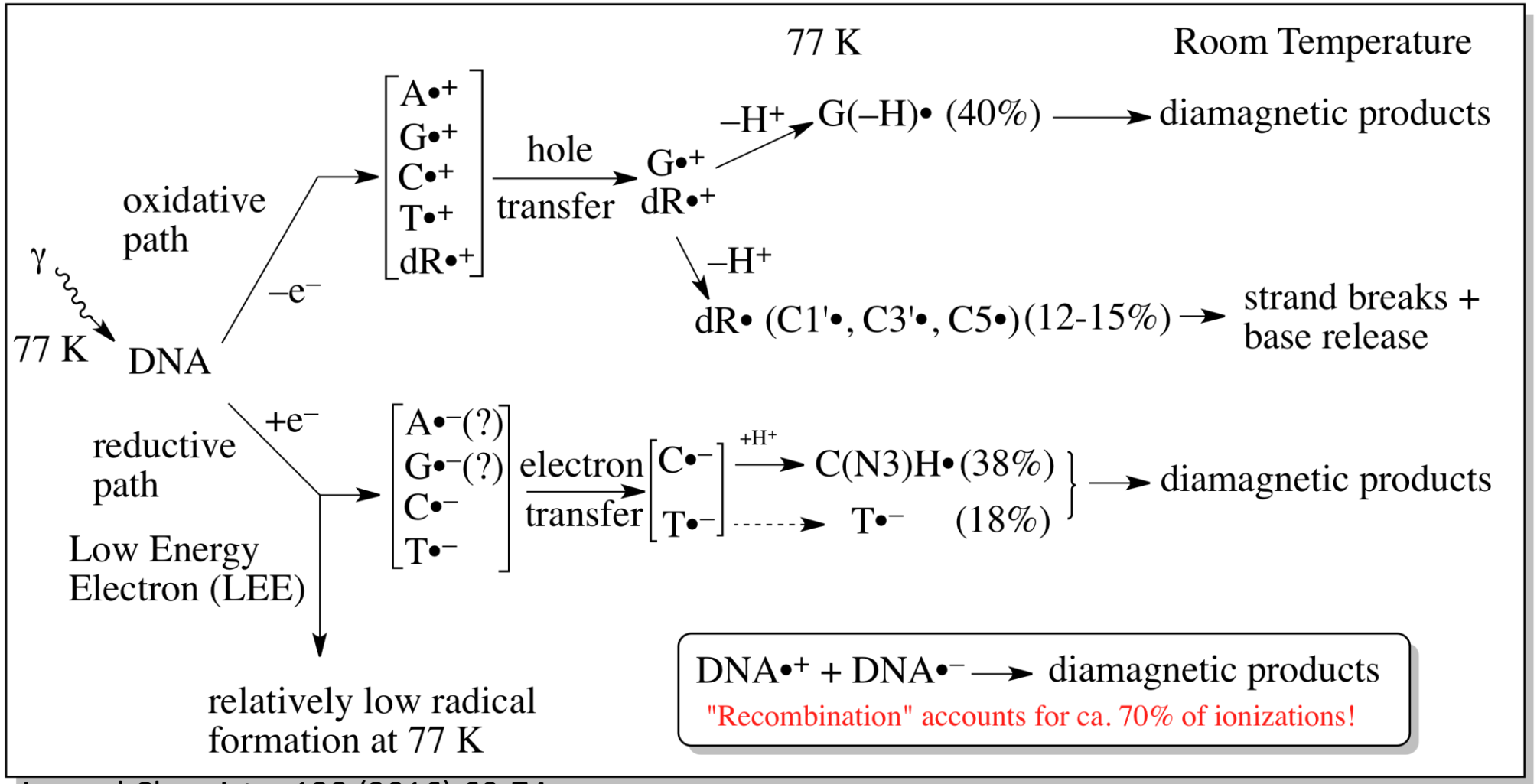
- Lower total yield of stabilized radicals at 77 K vs. low LET
- Higher relative amount of sugar radicals

Hypotheses:

Different spatial arrangement of energy deposition (track structure) leading to

- Excited state processes
- LEE processes

Penumbra Reactions and Radical Formation/Stabilization in Ion-Beam Irradiated DNA



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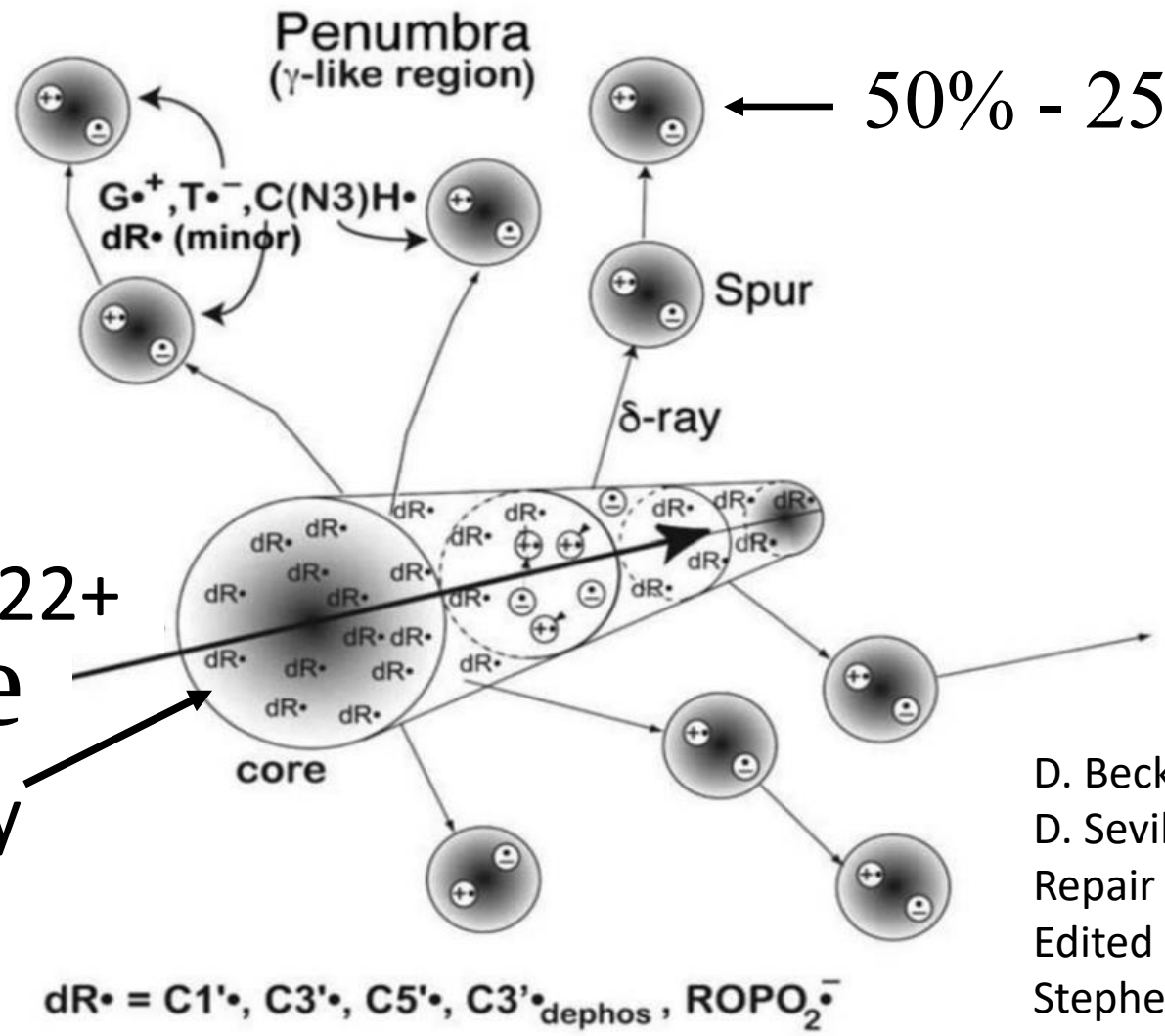
Sugar Radical Formation in Ion-Beam Core



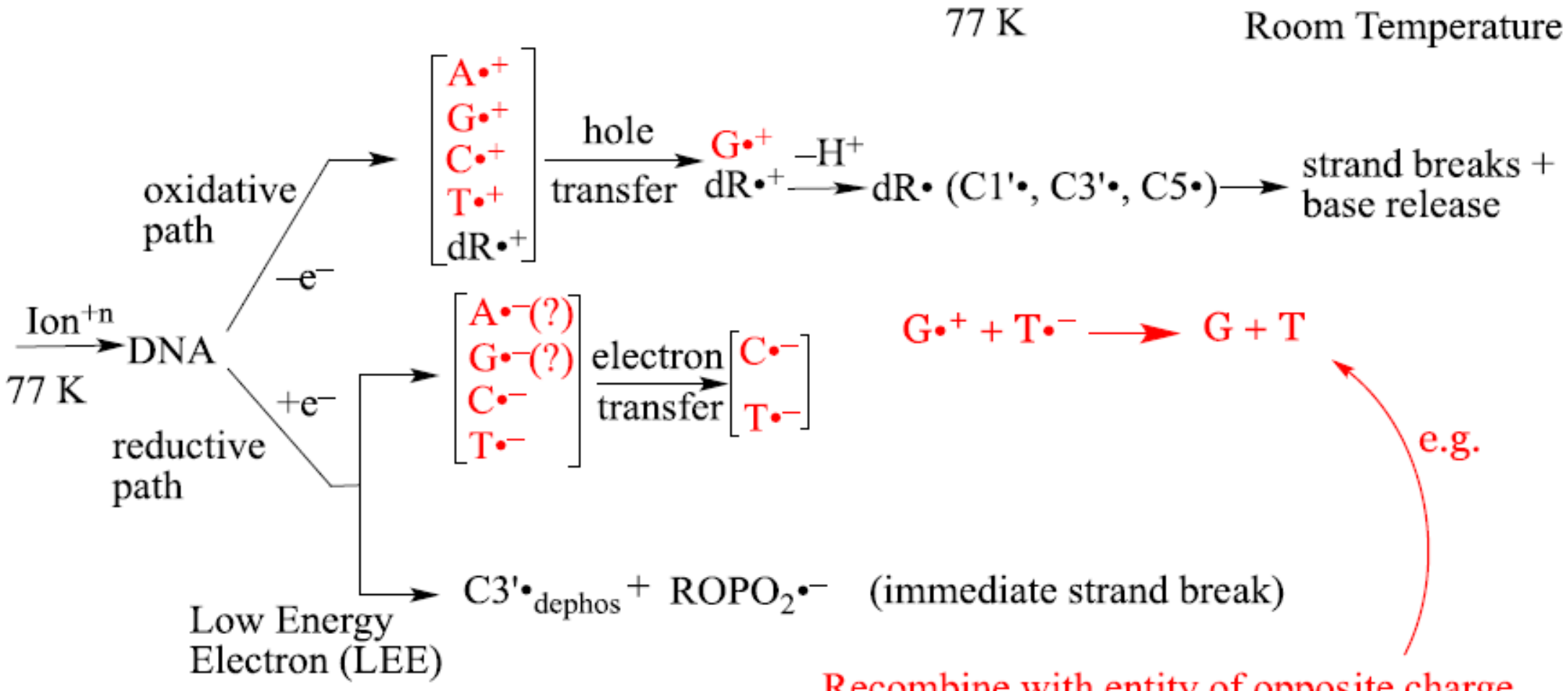
← 50% - 25% of energy

22+
Ne

50%-75% of energy

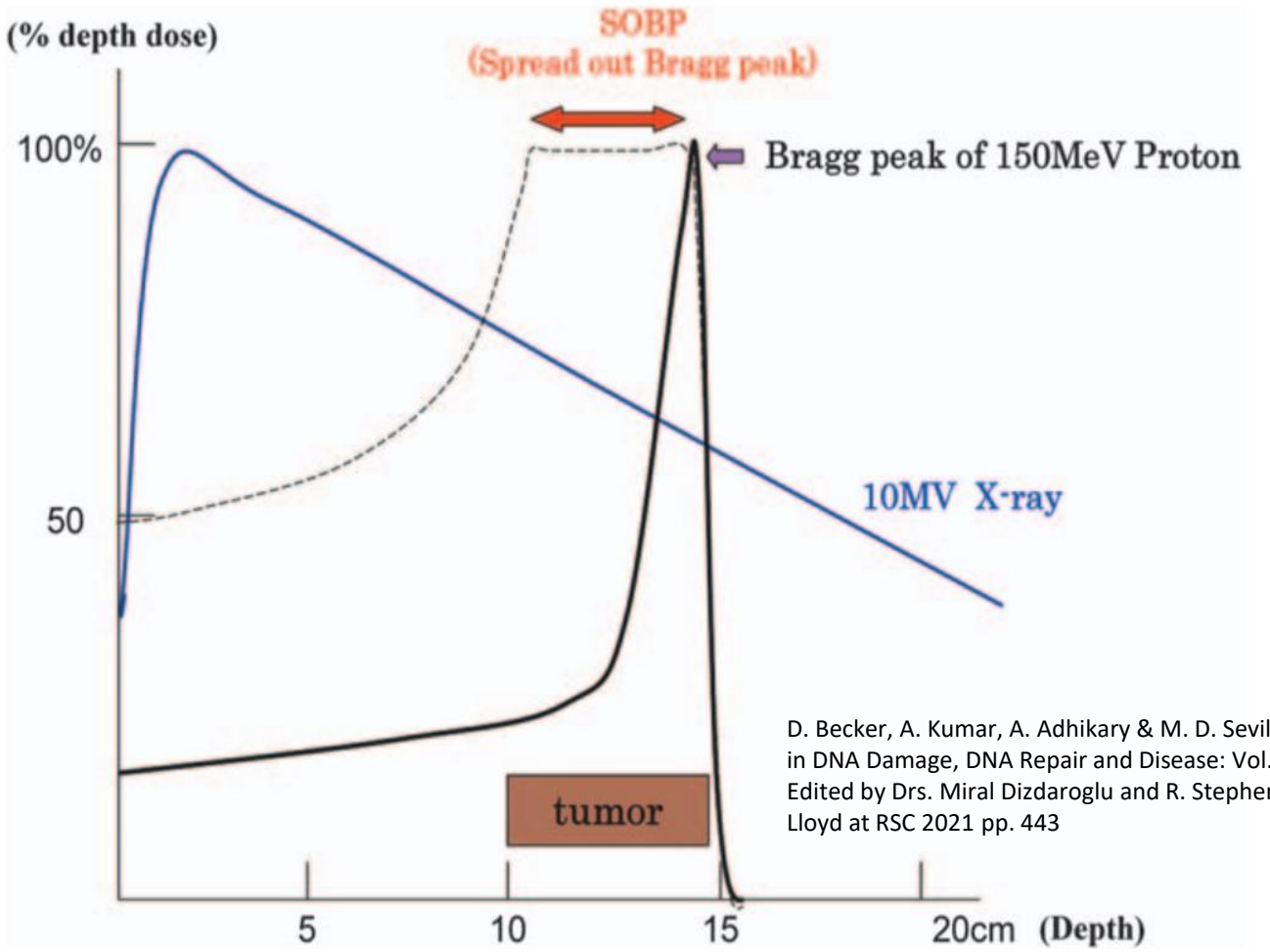
D. Becker, A. Kumar, A. Adhikary & M. D. Sevilla in DNA Damage, DNA Repair and Disease: Vol.2
Edited by Drs. Miral Dizdaroglu and R. Stephen Lloyd at RSC 2021 pp. 443

Core Reactions and Radical Formation/Stabilization in Ion-Beam Irradiated DNA



Radiation Physics and Chemistry 128 (2016) 60-74

Heavy Ion-Beam Bragg Peak



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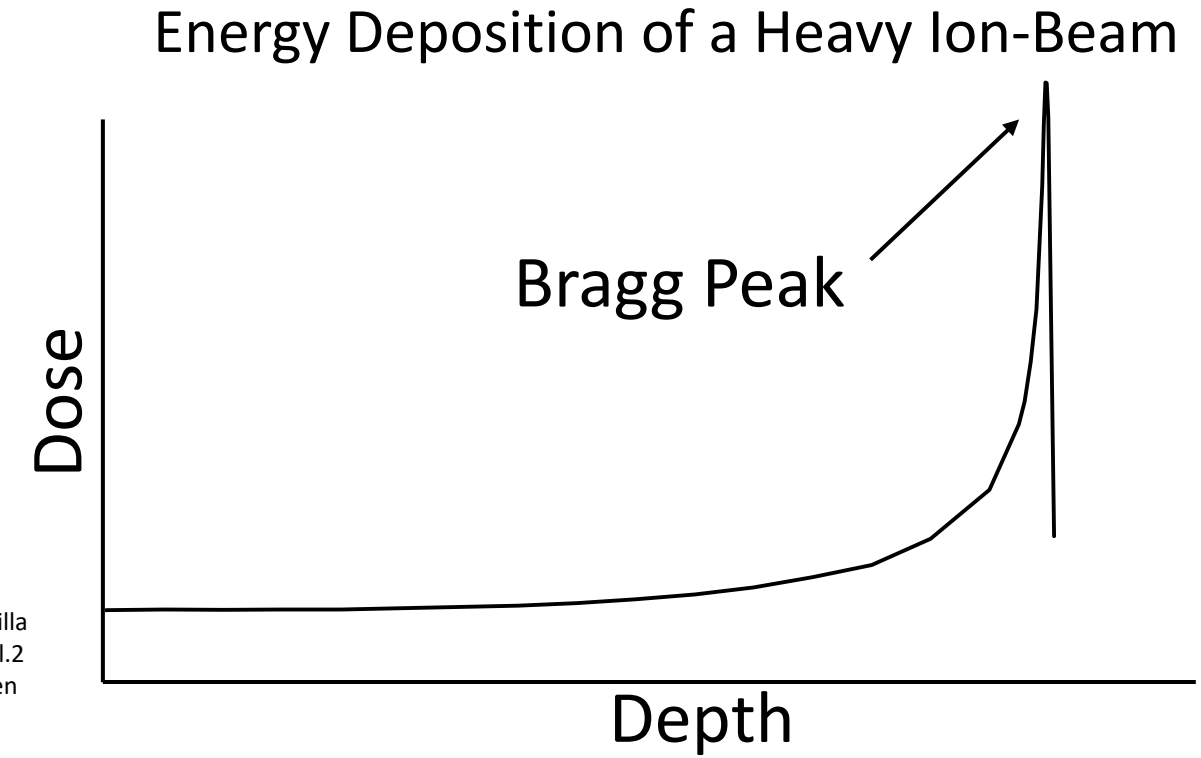
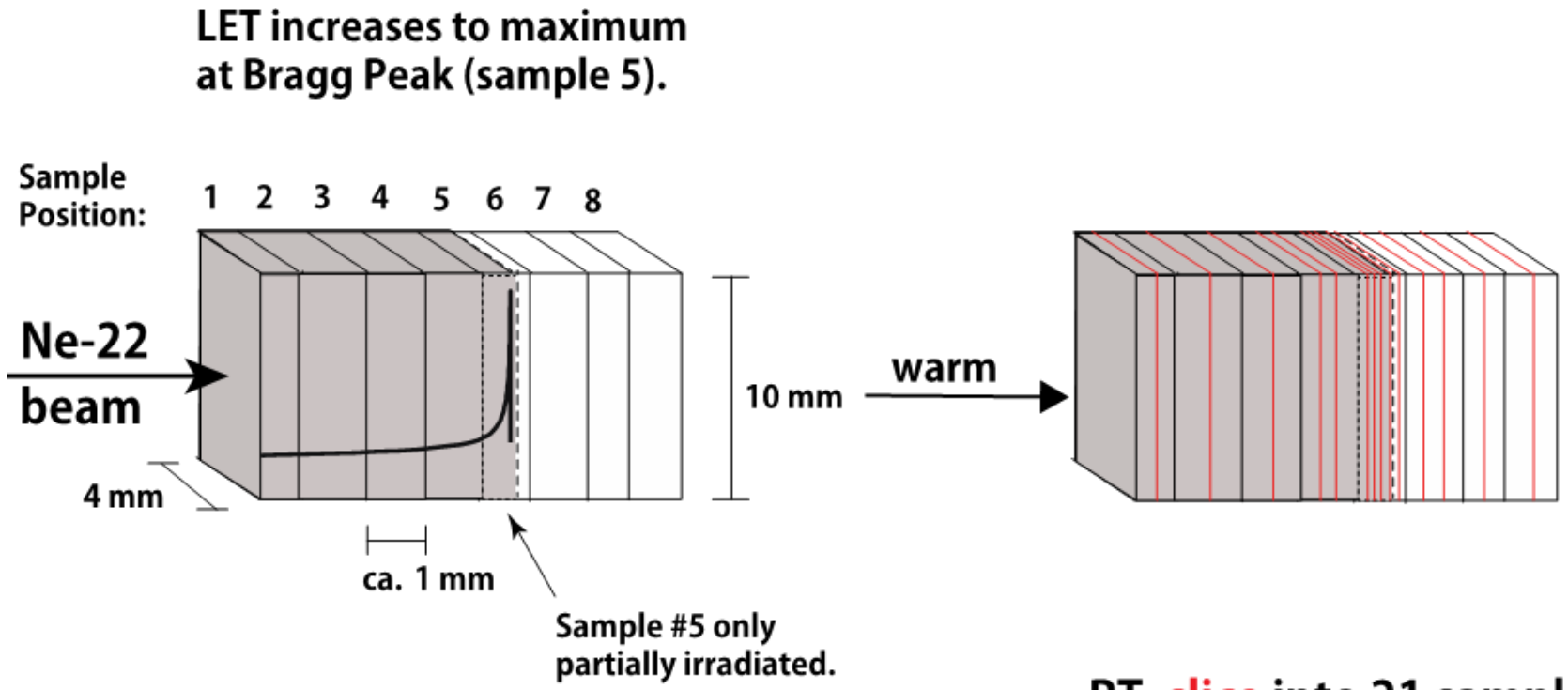


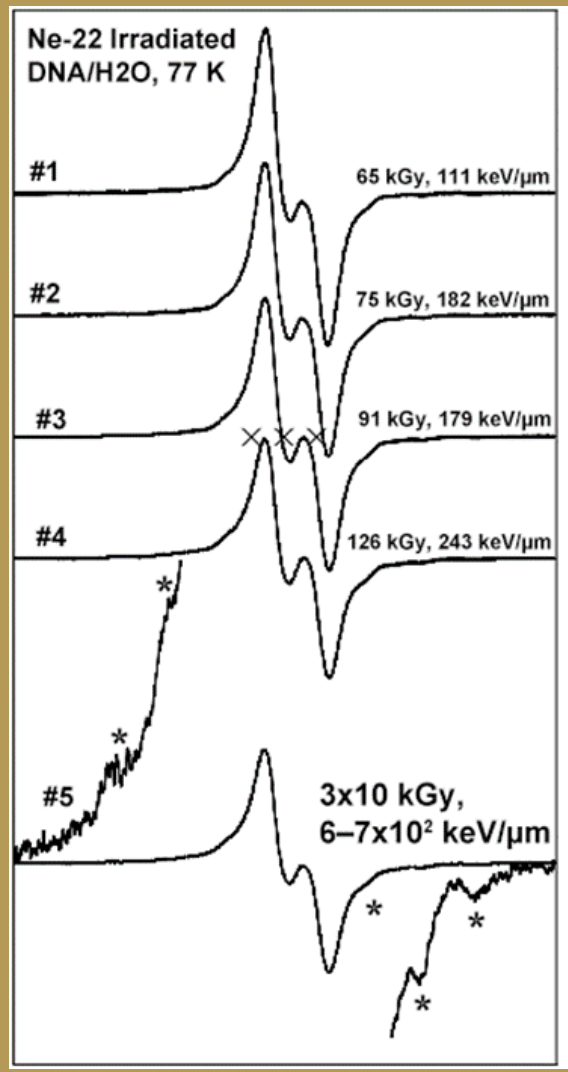
Sample Preparation for Ion-Beam Irradiation

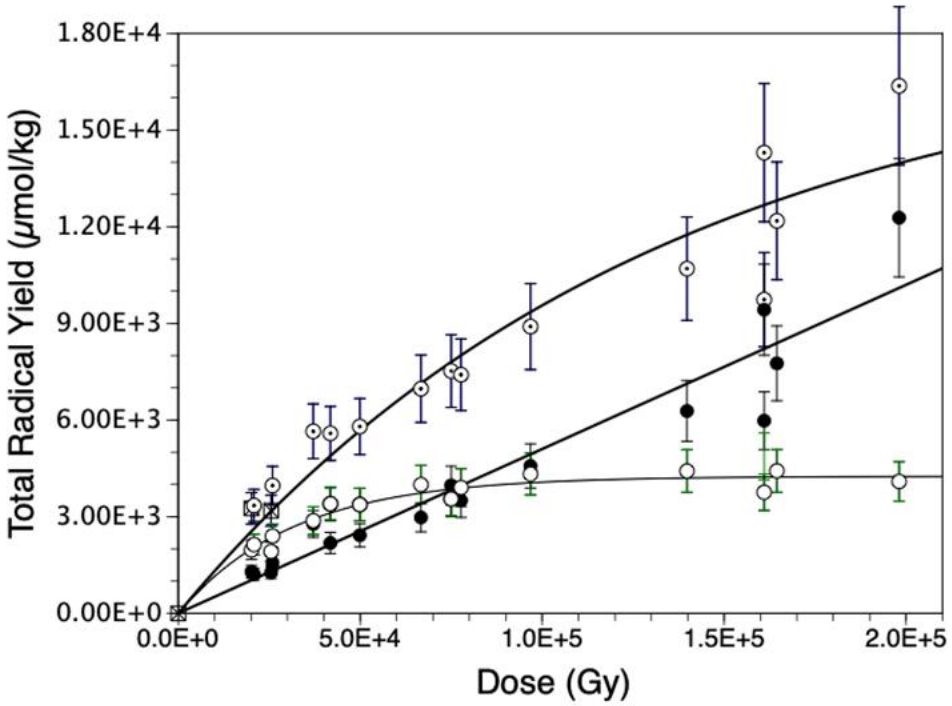
- Isolated direct-type effect with hydrated ($\Gamma = 12 \pm 2$ H_2O/nucleotide) DNA in anaerobic conditions

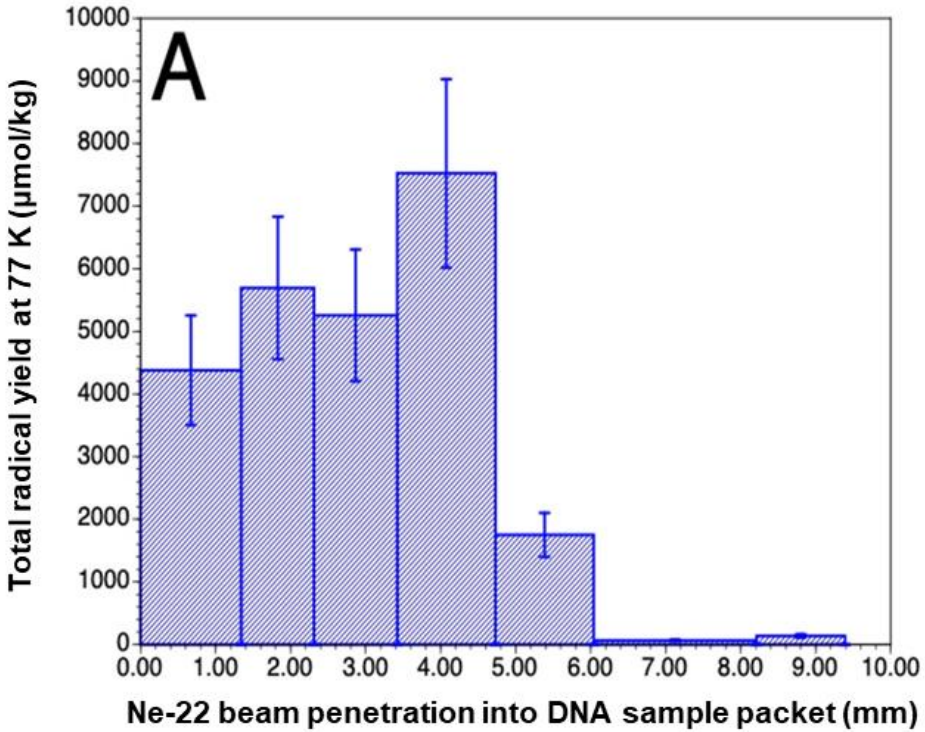


ACS Omega, 2021, 6, 16600-16611

Radicals Trapped at 77 K in Hydrated DNA







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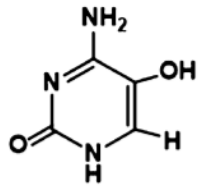
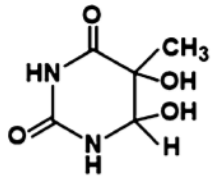
Room Temperature Damage Products

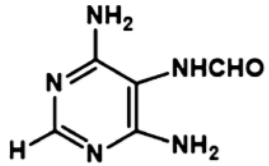
- Final Damage Products Considered



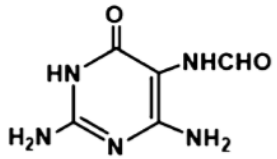
5-hydroxycytosine



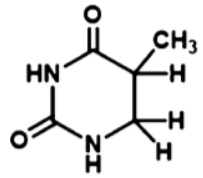
thymine glycol



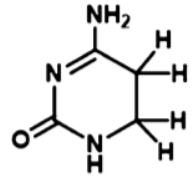
4,6-diamino-5-formamidopyrimidine



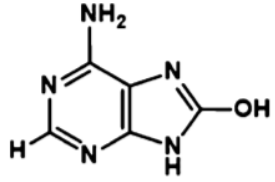
2,6-diamino-4-hydroxy-5-formamidopyrimidine



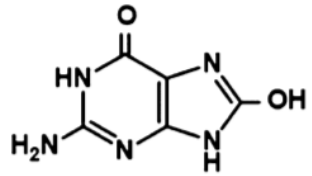
5,6-dihydrothymine



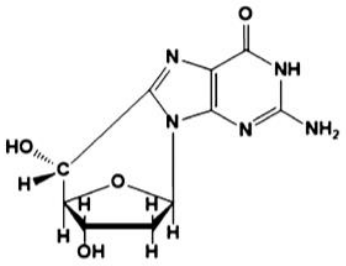
5,6-dihydrocytosine



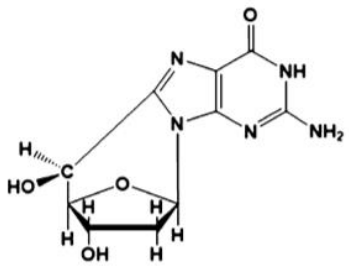
8-hydroxyadenine



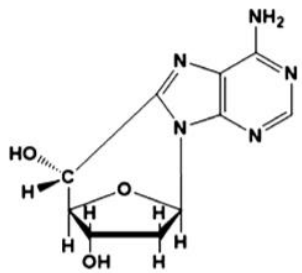
8-hydroxyguanine



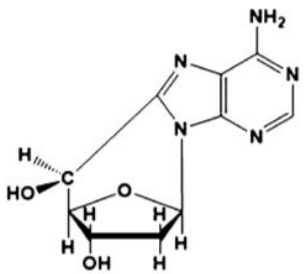
(5'*R*)-8,5'-cyclo-2'-deoxyguanosine



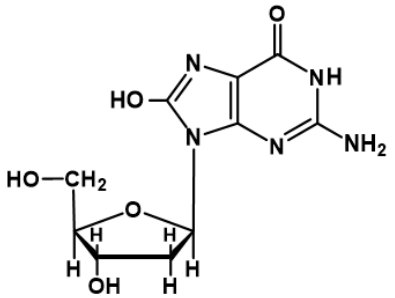
(5'*S*)-8,5'-cyclo-2'-deoxyguanosine



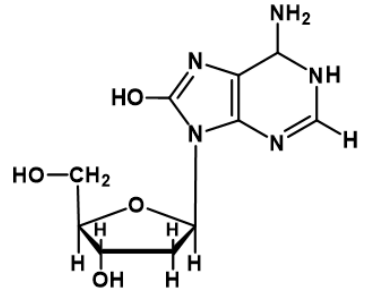
(5'*R*)-8,5'-cyclo-2'-deoxyadenosine



(5'*S*)-8,5'-cyclo-2'-deoxyadenosine



8-hydroxy-2'-deoxyguanosine



8-hydroxy-2'-deoxyadenosine

ACS Omega, 2021, 6, 16600-16611

Conclusion: Location of the Bragg Peak is Not the Location of Maximum Damage

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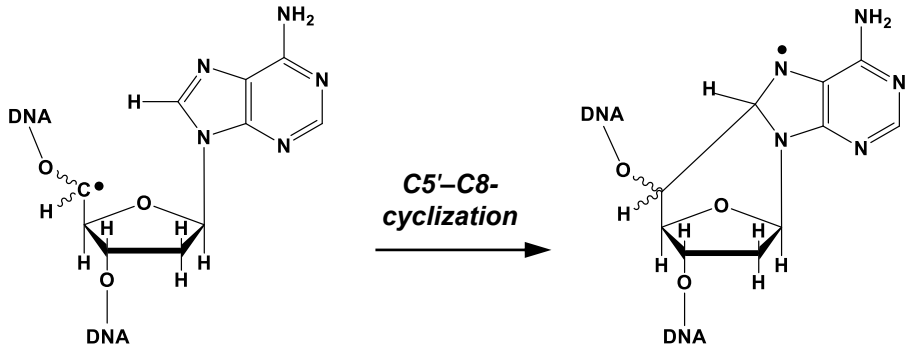
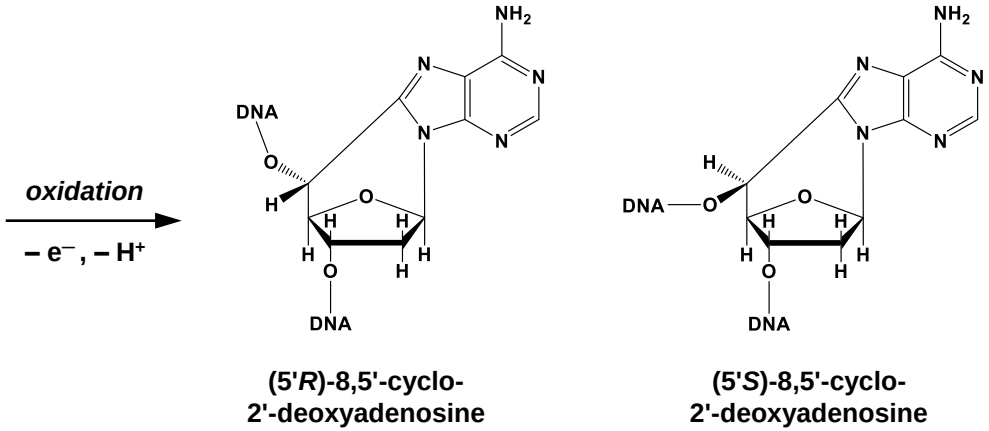
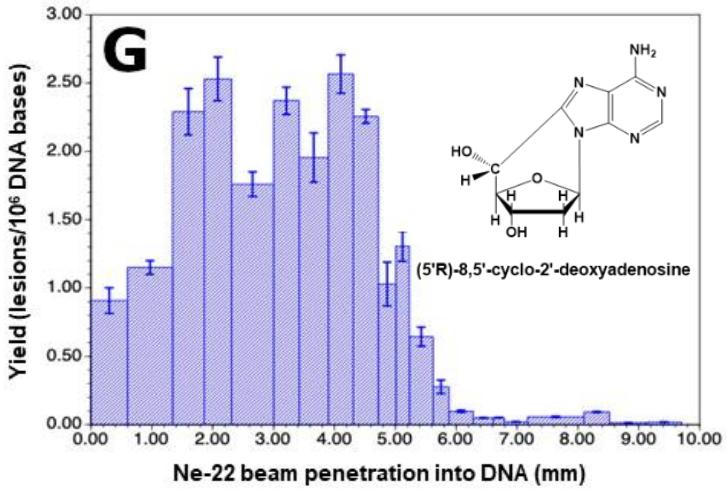
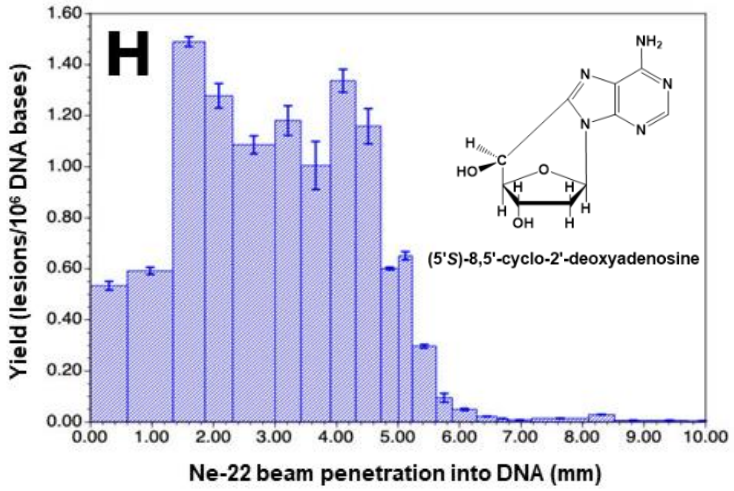
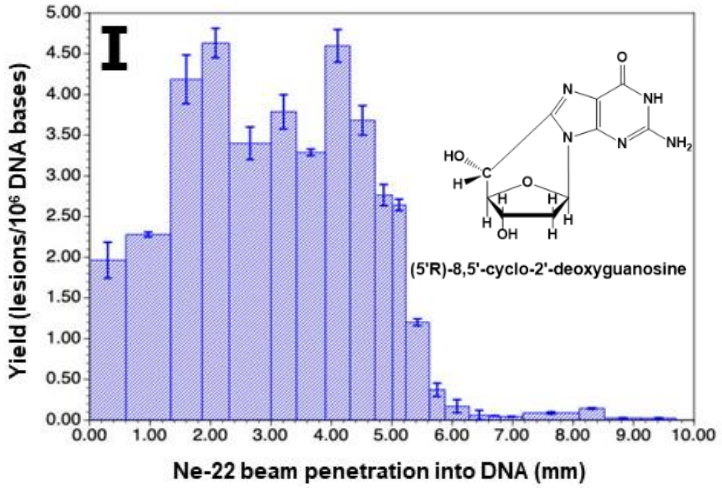
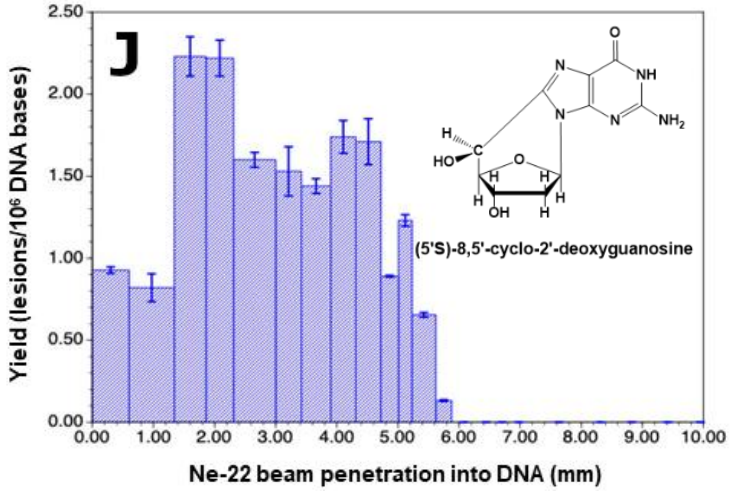






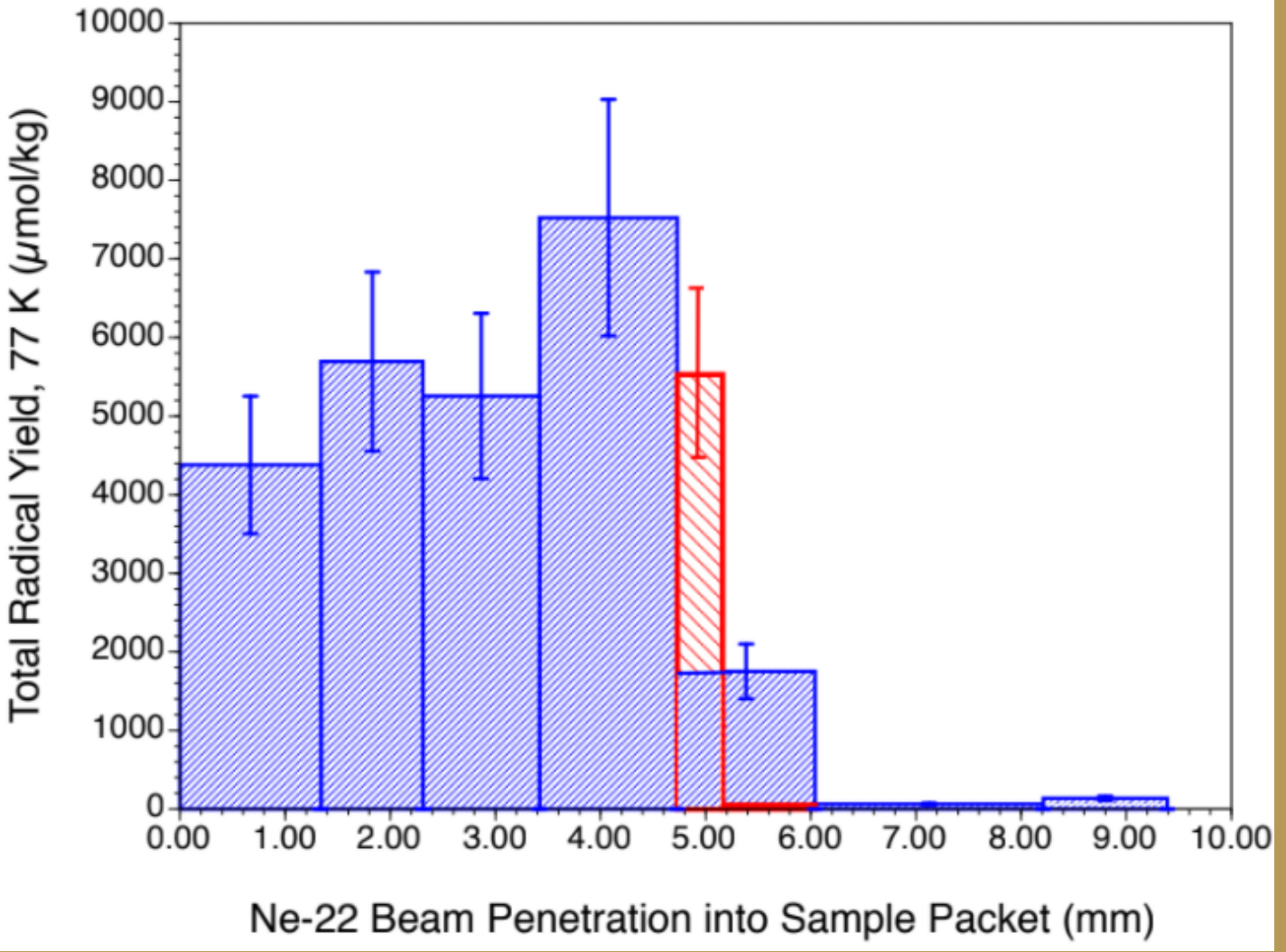






Conclusion: Location of the Bragg Peak is Not the Location of Maximum Damage

- Bragg peak determined to be *ca.* 5.2 mm
- Maximum amount of damage was found to occur just before the Bragg peak



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Collaborators and Support

- Thanks to Profs. Amitava Adhikary, David Becker, and Michael D. Sevilla
- Special thanks to Drs. Kant, Jaruga, Coskun, and Dizdaroglu (NIST) for their collaboration, help, and support
- OU Chemistry Department
- NIH NCI R01CA045424
- CBR,OU
- Thomas Baumann NSCL, MSU for his support and collaboration and NSCL, MSU for giving us ion-beam time

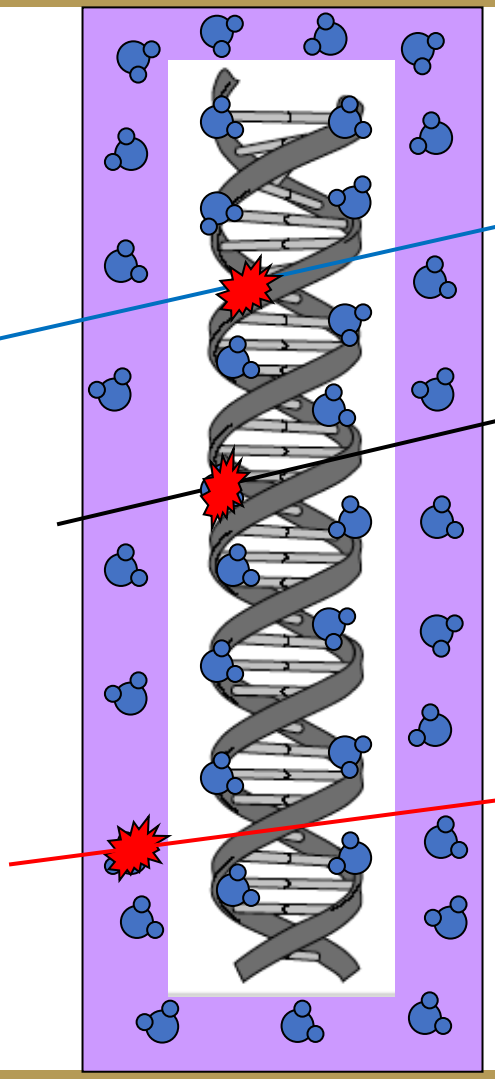
Thank you for your attention!

See poster no. 12

Direct-Type vs. Indirect Effect of Radiation

Direct-type effect
=

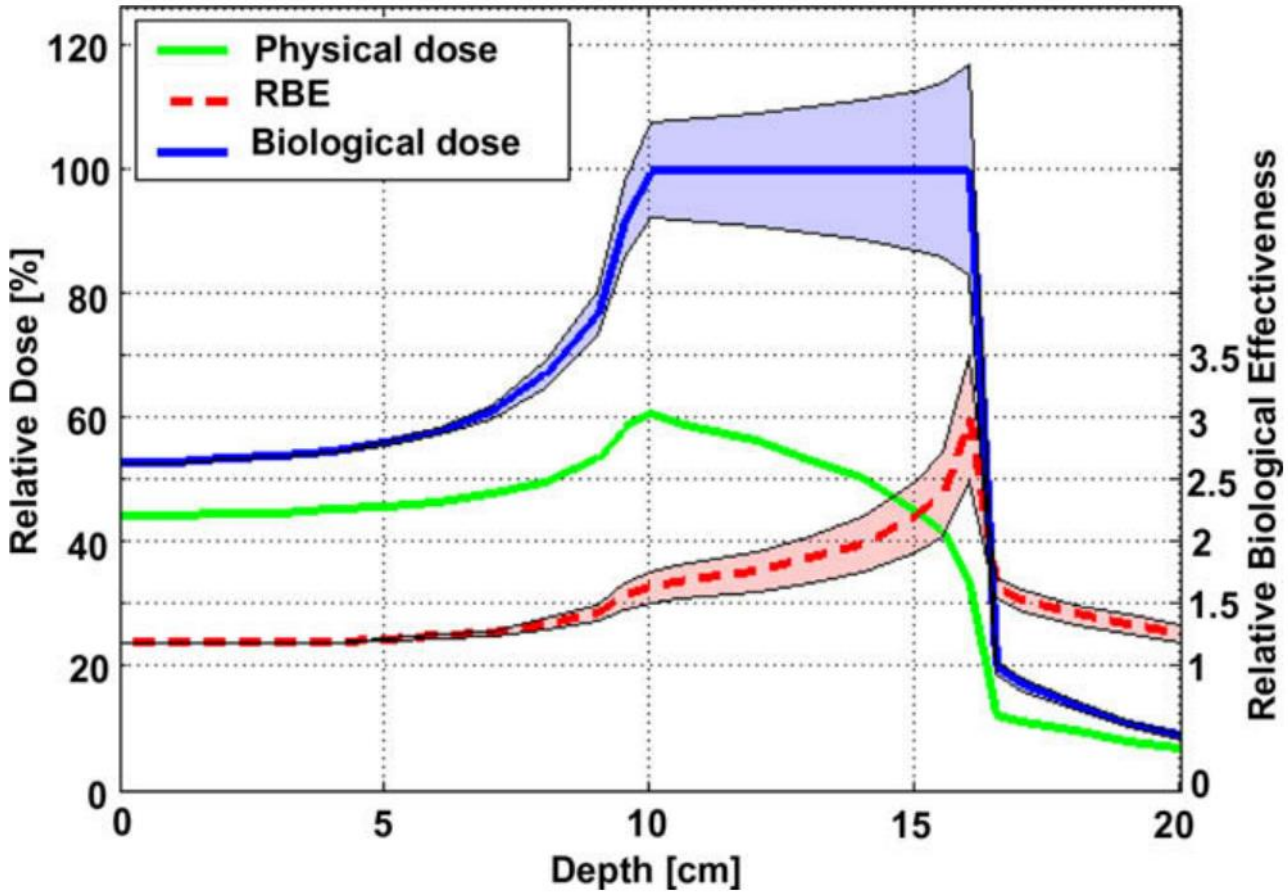
Direct effect
+
Quasi-direct effect

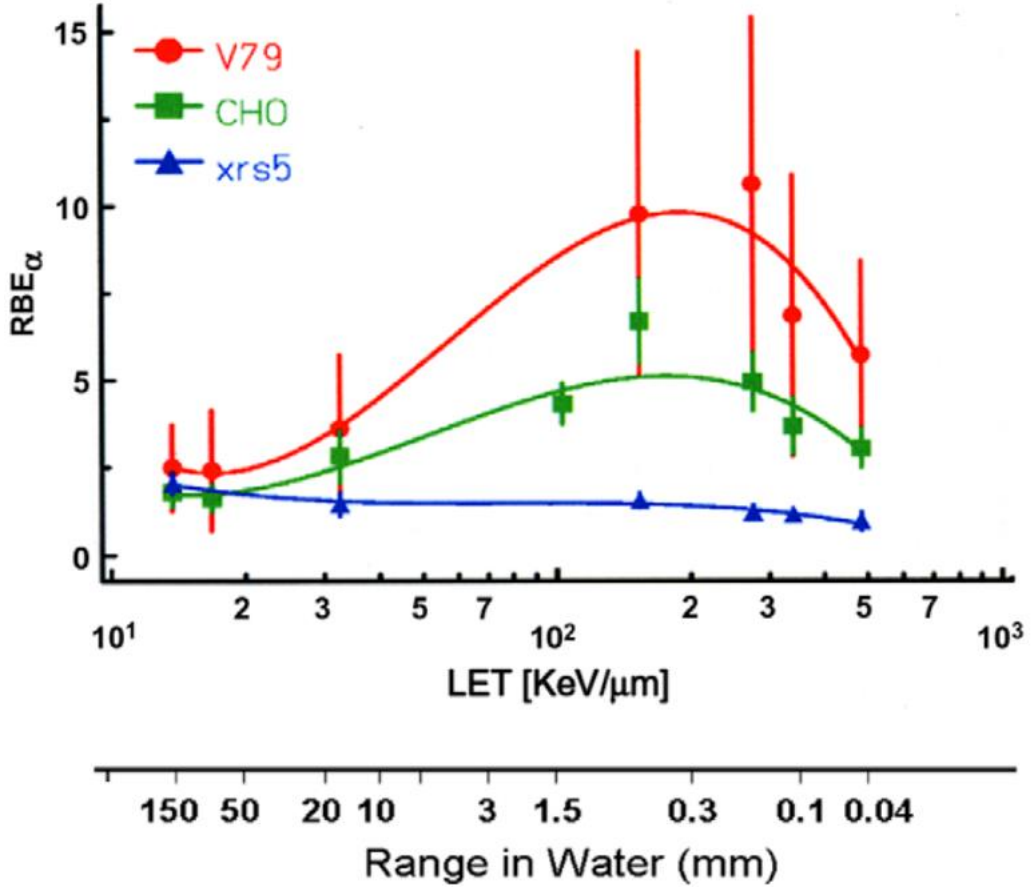


- Direct ionization of bases, sugar-phosphate (Direct effect)
- Ionization of adjacent solvation water: fast hole/electron transfer. (Quasi-direct effect)

- **Ionization of bulk water: diffusion of reactive species (•OH, e_{aq}^- + others) to DNA. (Indirect effect)**

SOBP in Tumor Radiotherapy





Radiotherapy and Oncology, 2010, 95, 3-22