INDIRECT ACTION OF RADIATION

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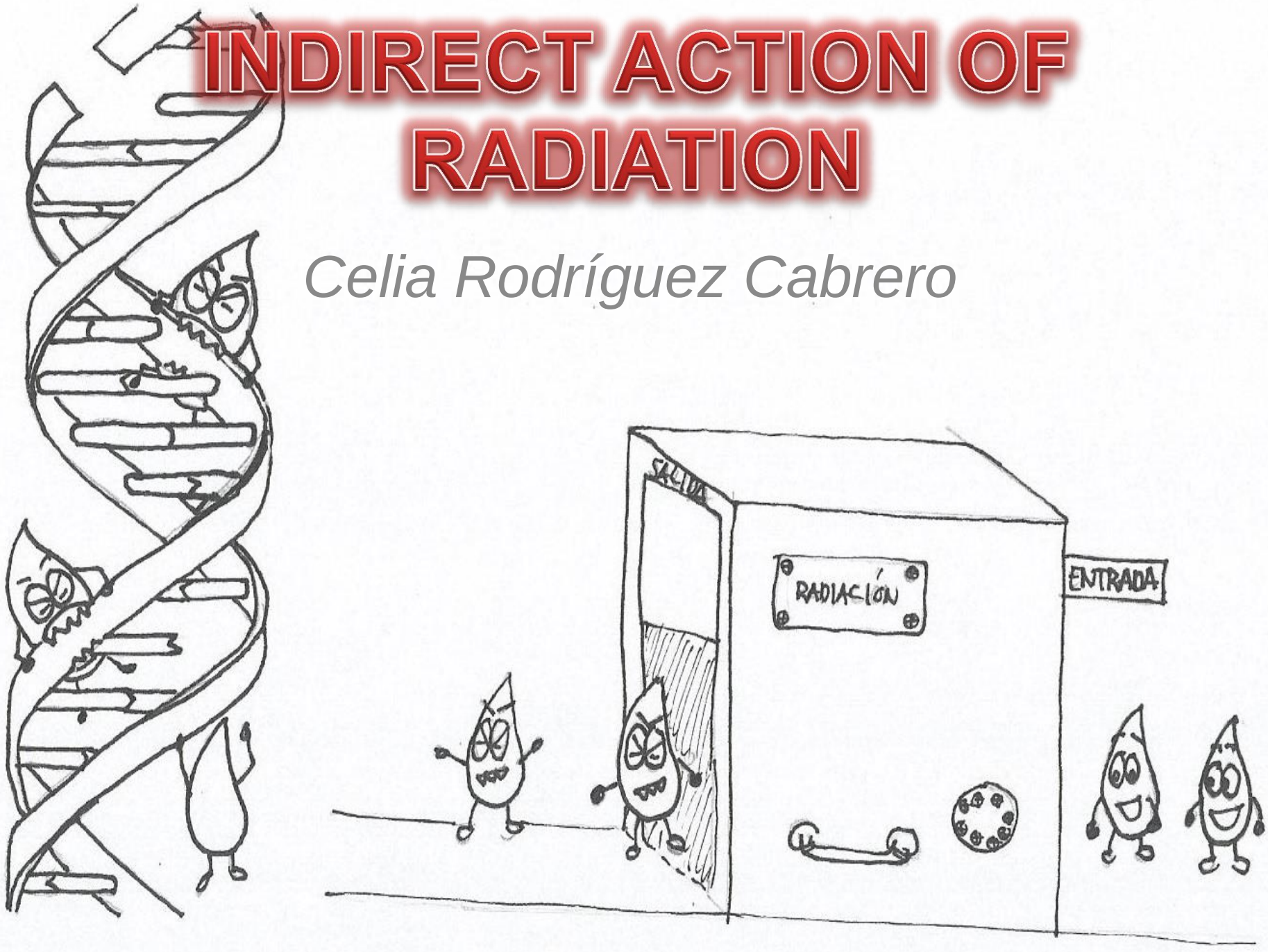

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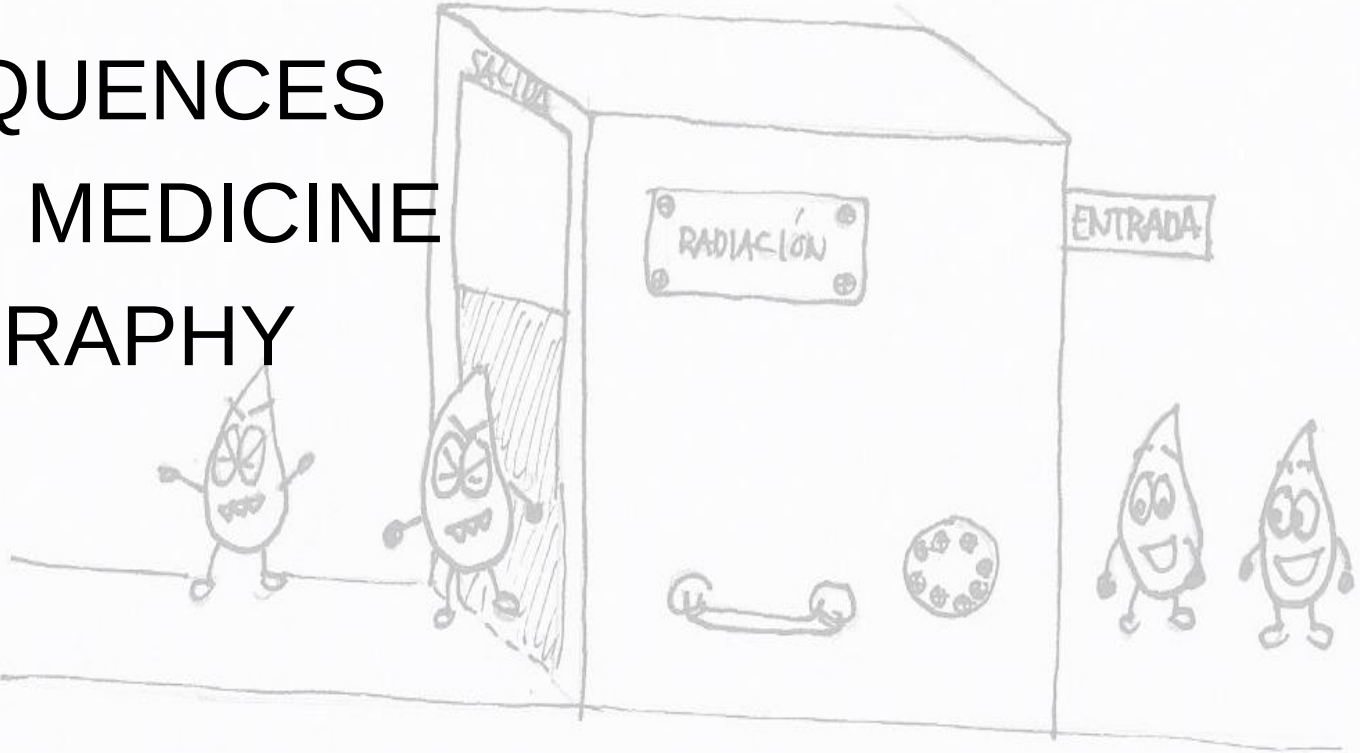


INTRODUCCIÓN

Ionizing Radiation is going to produce some reactions in cells to assimilate the energy that has been absorbed, direct or indirect.

“FREE RADICALS“ are the form of transfer of energy made by the indirect effect.

Water is the most frequent molecule in the human body, so it will be the most affected when it receives radiation, so it will form more radicals than other substances. This process is called **“WATER RADIOLYSIS”.** The result of this is DNA damage.

Imagen. Aspectos generales de la interacción de la radiación con el medio biológico. [Cited 2015 Mar 23]. Available from: http://www.elradon.com/web/wp-content/uploads/2012/04/biologicos.pdf

FREE RADICAL DEFINITION

- A free radical is a electrically neutral molecule, which has a unpaired electron, which means the electron isn't in its orbital position.
- They are very reactive and have a short life. Also, they act like intermediaries in chemical reactions and in many biological processes.
- Free radicals are the results of external or metabolic aggression and cause cellular and genetic damage.
- Normally, radicals recombine with each other for orbital neutralization. [1]

WATER RADIOLYSIS [2]

Radiation makes water form an ion H_2O^+ and an electron (e-) (called watery electron). This is known as ionization:

$$H_2O + \text{radiación} \rightarrow H_2O^+ + e^-$$

After this ionization, follows the process of dissociation, recombination, charge transfer and chemistry.

- Ion H_2O^+ is unstable and it will quick form H^+ and radical OH•.

$$H_2O^+ \rightarrow H^+ + OH^\bullet$$

- The unpaired electron can interact with organic molecules or other water molecules. The products will be radical H• and ion OH^-.

$$e^- + H_2O \rightarrow H_2O^- \rightarrow H^\bullet + OH^-$$

WATER RADIOLYSIS

There is another way to form free radicals, it consists of the excitation of the water molecule when ionizing radiation has an impact on water. The process which are produce when water is excited are not well known but it is believed that it's possible that the radicals H• y OH• can be dissociated.

$$H_2O + \text{radiación} \rightarrow H_2O^* \rightarrow H^\bullet + OH^\bullet$$

There are secondary processes post-excitation: fluorescence, radical dissociation, ion dissociation, chemistry, etc.

WATER RADIOLYSIS

- OH- y H+ are particles with opposites charges, they tend to attract for neutralization and form water. These don't produce significant damage in general.

$$H^+ + OH^- \rightarrow H_2O$$

- OH• y H• are radicals with neutral charge that have a unpaired electron they have a strong reactivity, that's why they create chemical bond between atoms of other molecules (for example functional organic like proteins or nucleotides).

WATER RADIOLYSIS

Not all free radicals are going to reach DNA, their distribution is diverse and most of them will neutralize creating water, the creation of other molecules like hydrogen peroxide (most known in Spanish as Agua Oxigenada) and H_2. The next picture shows reactions:

$$H^{\bullet} + H^{\bullet} \rightarrow H_2$$

$$OH^{\bullet} + OH^{\bullet} \rightarrow H_2O_2$$

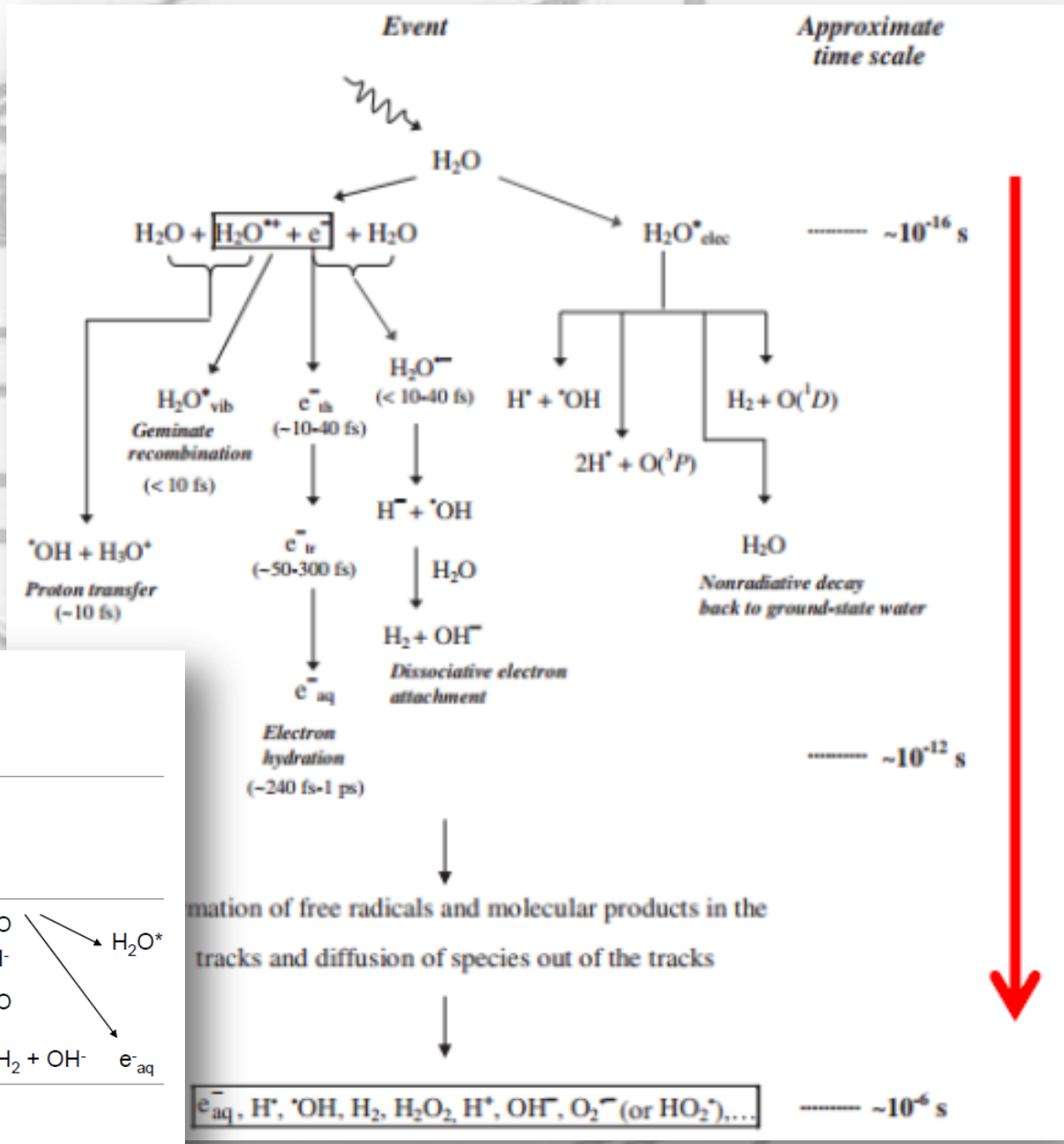
$$H^{\bullet} + OH^{\bullet} \rightarrow H_2O$$

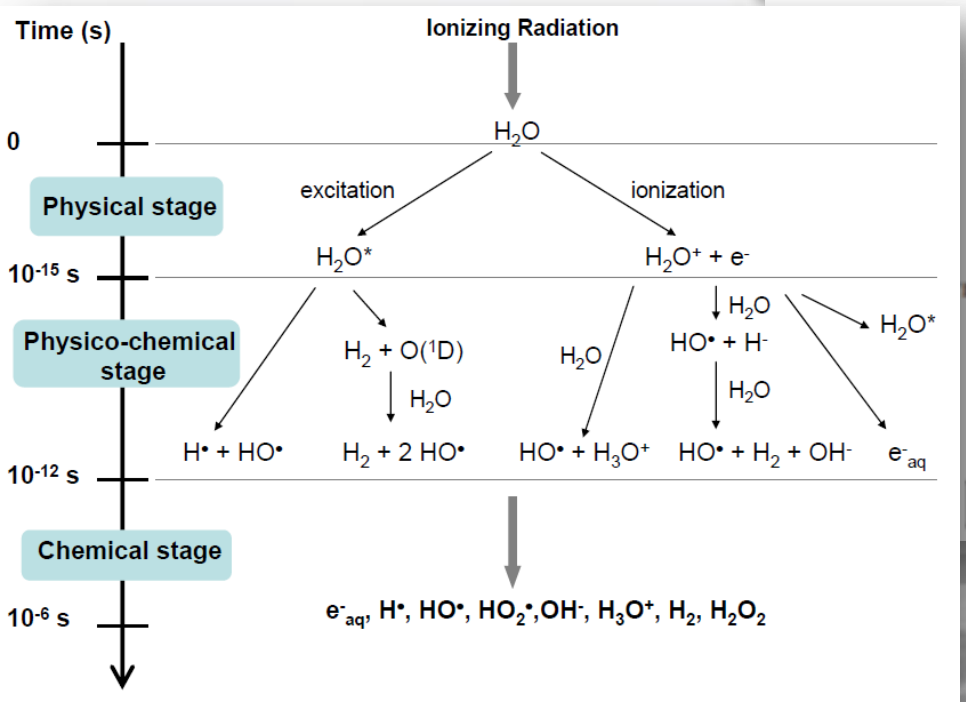
Radicals can generate another in the cell nucleus, which attacks the DNA's structure, like we can observe in the next case:

$$H_2O + H^{\bullet} \rightarrow H_2 + OH^{\bullet}$$

E.I: Azzam et al. / Cancer Letters 327 (2012) 48-60

Sophie Le Caër. Water Radiolysis: Influence of Oxide Surfaces on H2 Production under Ionizing Radiation. Water 2011, 3, 235-253; doi:10.3390/w3010235

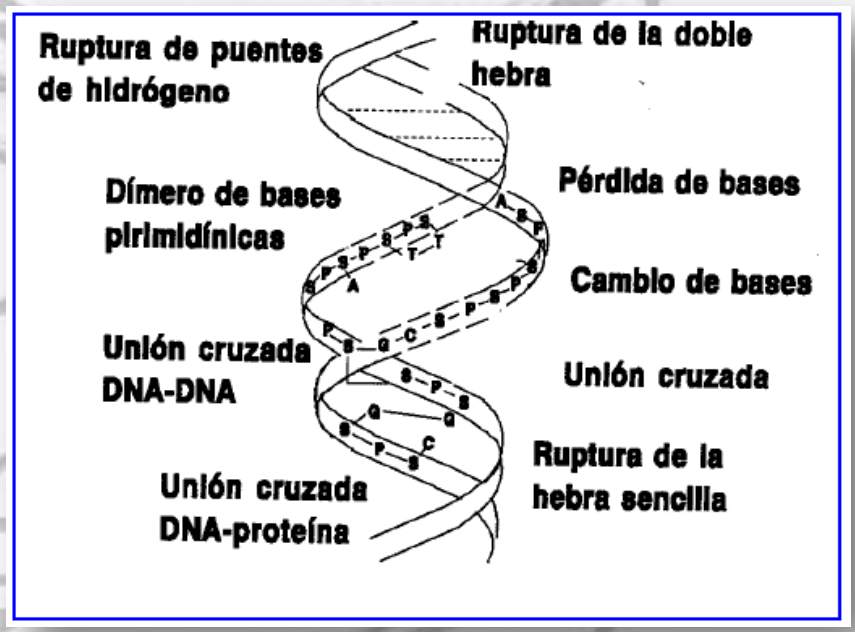




CONSEQUENCES

The main problem of the free radicals' action is much more important. The damage cause in the affected molecule can be of different types: free radicals don't cause damage if they join to non essential molecules like lipids, carbohydrates or proteins but when they interact with DNA there is damage. Their action can produce:

- Damage in nitrogenous bases
- Simple break chain
- Double break chain
- Multiple localized damage [3]



Picture. Bibliography number [1]

USES IN MEDICINE

Oxygen make tumors more sensitive to radiation. There are more free radicals when radiation impacts on the tumor, if there is oxygen, they mix (and free radicals can’t be neutralized) and there is biological damage because of the creation of toxic products for tumoral cells.

Conclusion: radiosensitivity of the tumor can be used for treatment.

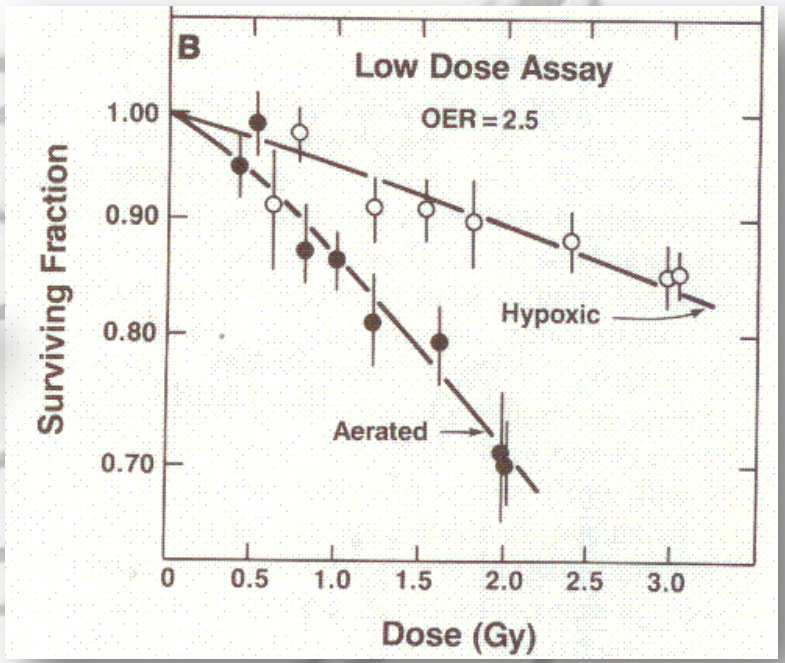
$$O_2 + R\bullet \rightarrow RO_2\bullet \rightarrow ROOH$$

USES IN MEDICINE

- Oxygen Enhacement Ratio (OER) is used to calculate the dose of radiation that a tumor needs.
- OER lets know the dose of radiation that a tumor would need in two situations, the presence and the lack of oxygen. The purpose is getting the same biological effect. The formula to calculate it is:

$$OER = \frac{Dose\ need\ to\ kill\ cells\ without\ oxygen}{Dose\ need\ to\ kill\ cells\ with\ oxygen}$$

- The more oxygen a tumor has, the smaller the fraction of survival for the same dose. You can see in this chart.



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2. *Wikipedia. Radiobiología. Etapa química. No hay fecha [cited 2015 May 14]. Available from: http://es.wikipedia.org/wiki/Radiobiolog%C3%ADa*
3. *Radiology notes.*

Note: The pictures in the background has been painted by Celia Rodríguez Cabrero, author of this work.