Challenges of Radiological Protection
in Research and Society
referring to Medical Field

October 3/2024
Milan, Italy
Sala Napoleonica/Via Sant'Antonio, 12
Università di Milano

Radiobiological basis of hypofractionation (*SBRT/Radiosurgery*) and impact on patient Radiation Protection

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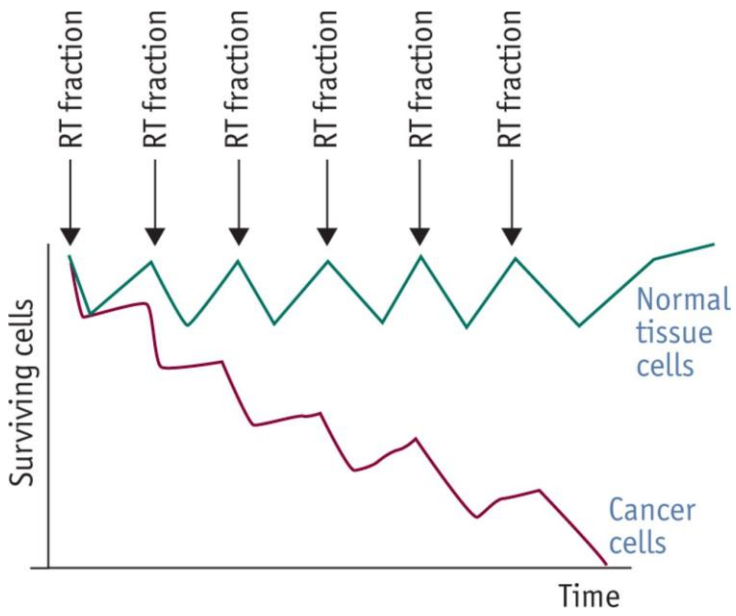
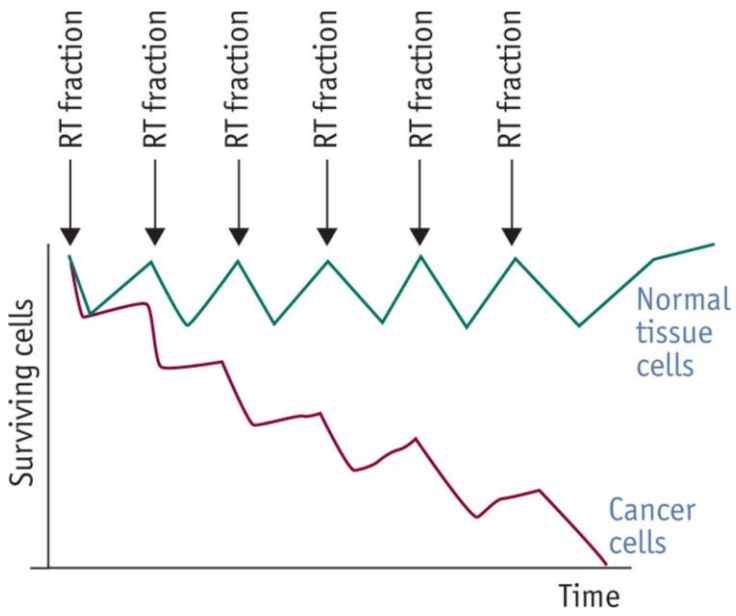
Universitv of Florence


RT fraction
RT fraction
RT fraction
RT fraction
RT fraction
RT fraction
Surviving cells
Normal tissue cells
Cancer cells
Time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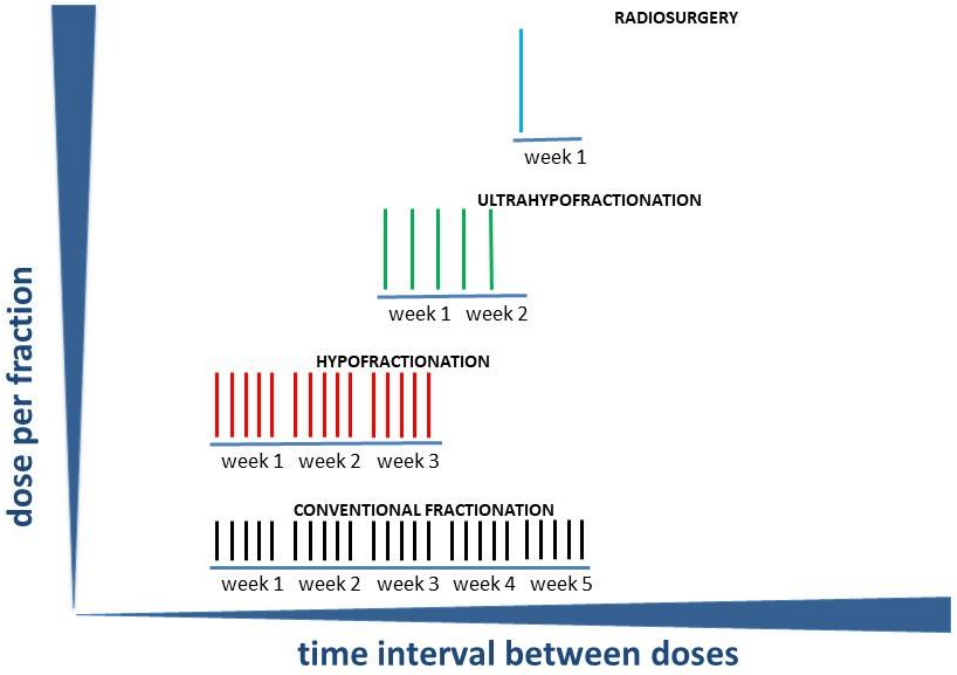

RADIOSURGERY
week 1
ULTRAHYPOFRACTIONATION
week 1 week 2
HYPOFRACTIONATION
week 1 week 2 week 3
CONVENTIONAL FRACTIONATION
week 1 week 2 week 3 week 4 week 5
dose per fraction
time interval between doses

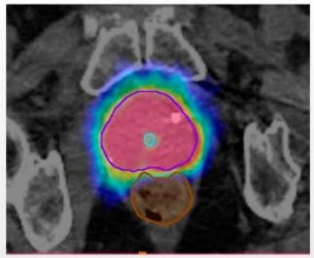
Stereotactic RT

- High dose per fraction
- Small volumes
- Single or very few fractions

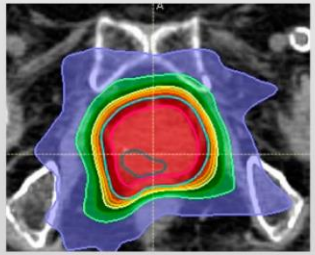
VS

Conventionnal RT

- Low dose per fraction
- Large volumes
- Multiple fractions

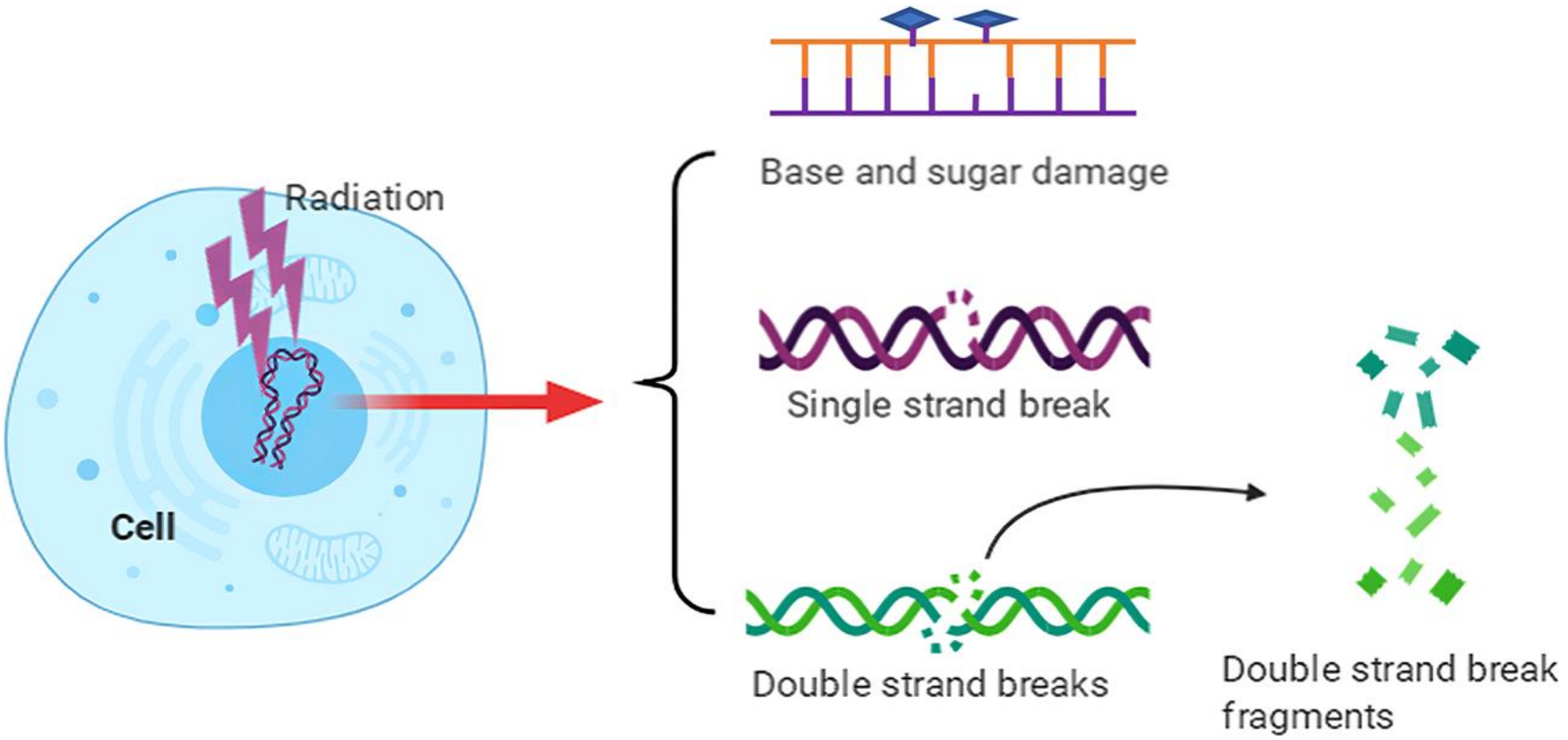


Prostate Cancer SBRT
36.25 Gy in 5 fractions
Tracking on fiducials : 3 mm margins

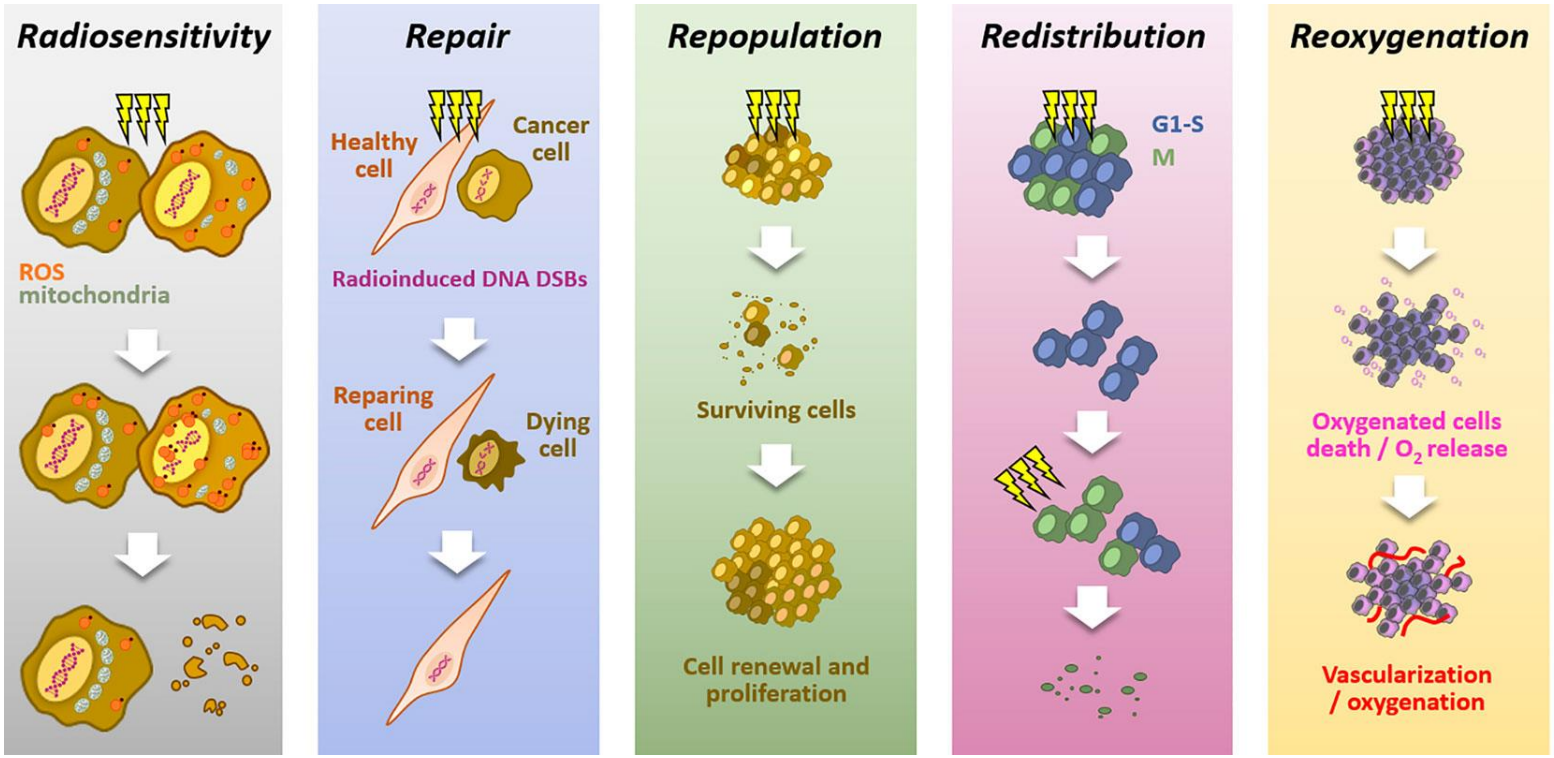


Prostate Cancer Conv-RT
78 Gy in 38 fractions
No tracking : 5 mm margins

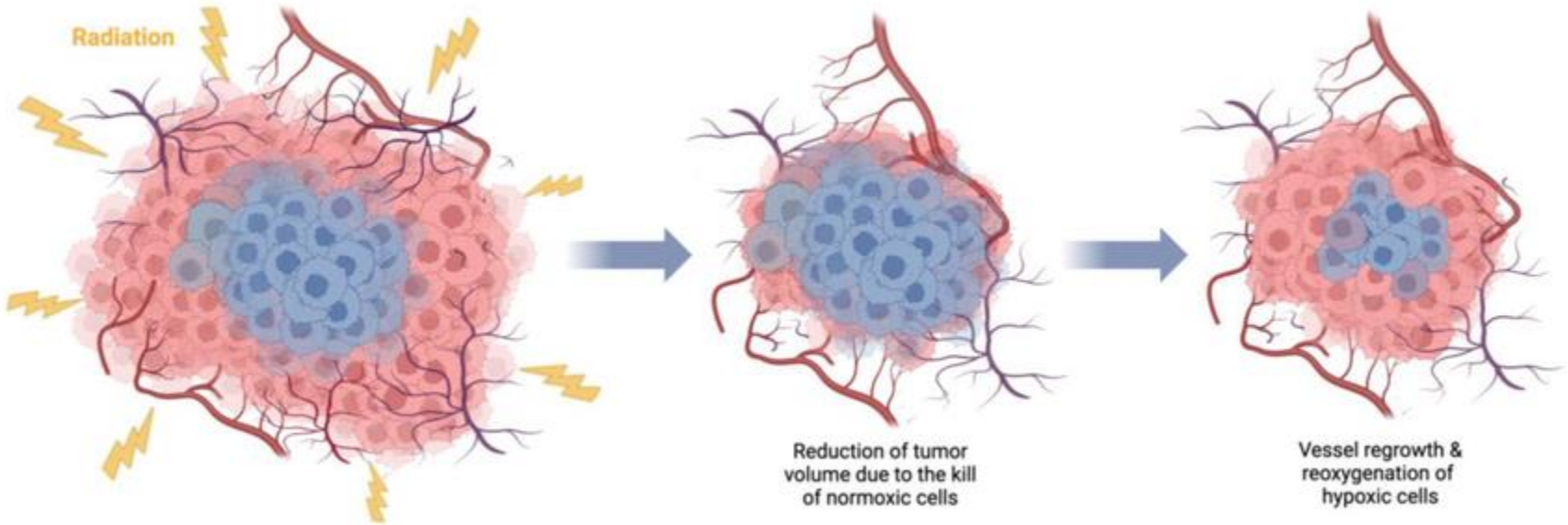
Kinj, R.; Bourhis, J. How Stereotactic Radiotherapy Changed the Landscape in Cancer Care. *Cancers* **2023**, *15*, 1734.


Radiation
Cell
Base and sugar damage
Single strand break
Double strand breaks
Double strand break fragments

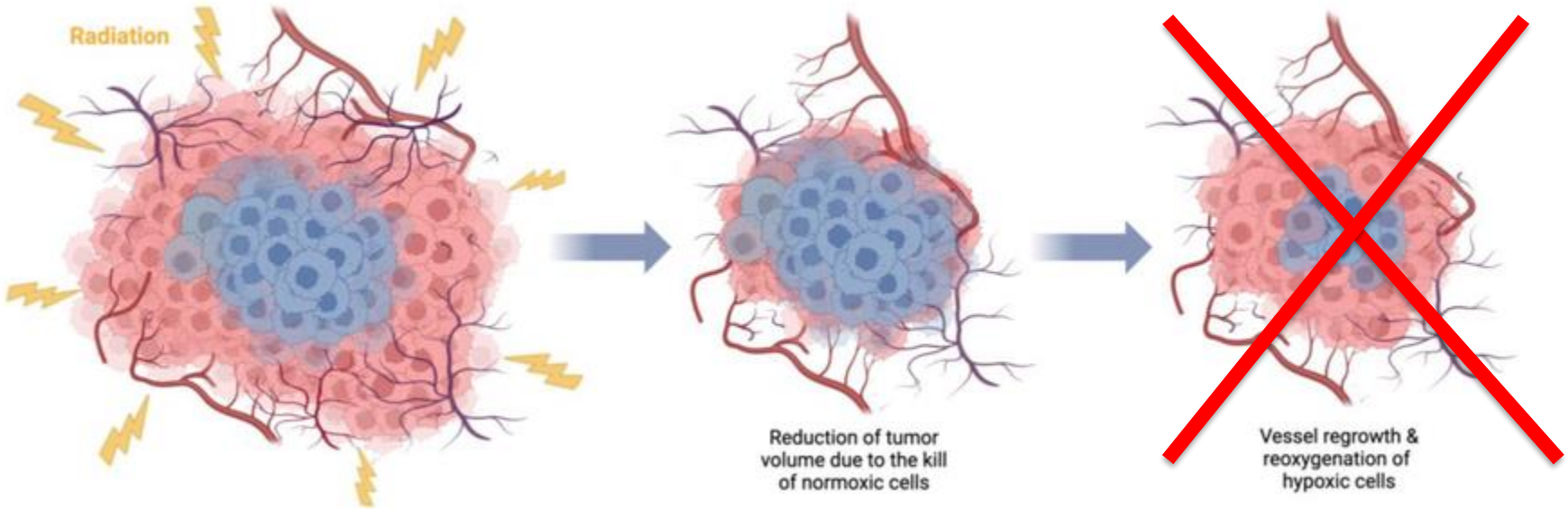
The «Rs»


Radiosensitivity
ROS
mitochondria
Repair
Healthy cell
Cancer cell
Radioinduced DNA DSBs
Reparing cell
Dying cell
Repopulation
Surviving cells
Cell renewal and proliferation
Redistribution
G1-S
M
Reoxygenation
Oxygenated cells death / O_2 release
Vascularization / oxygenation

Re-oxygenation

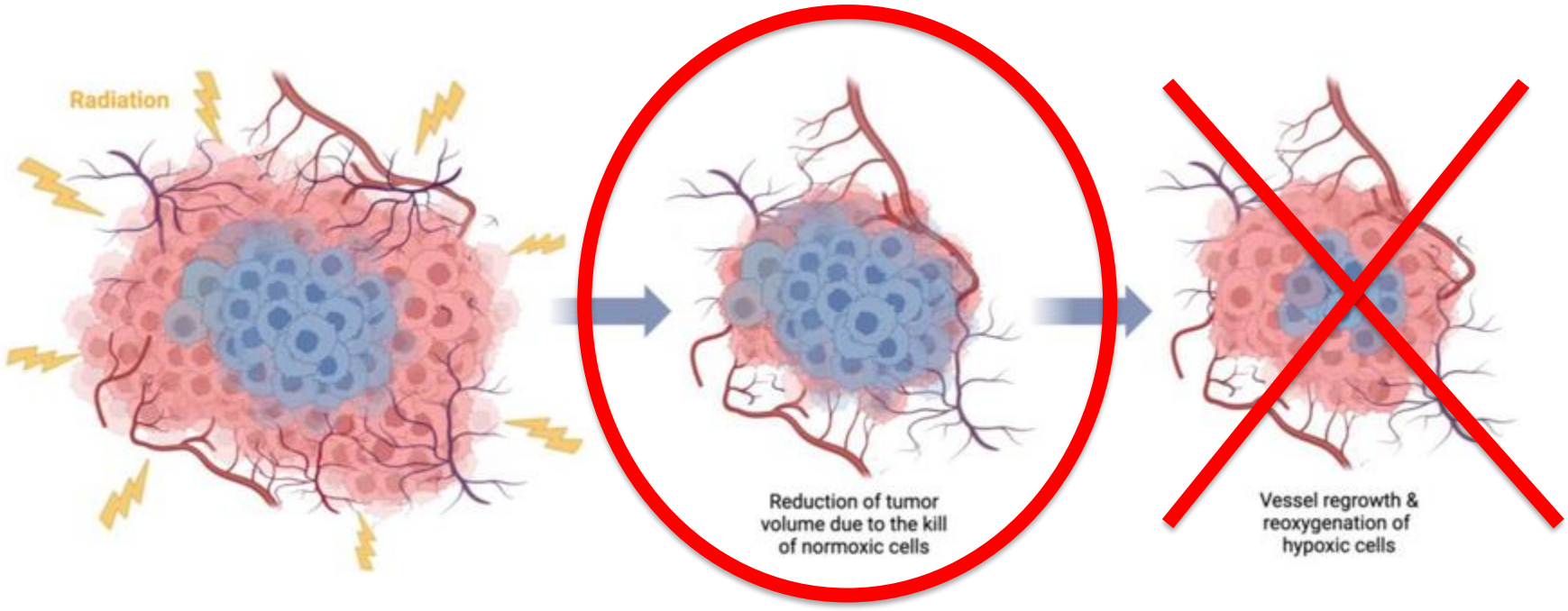


Re-oxygenation



radiosurgery

Re-oxygenation

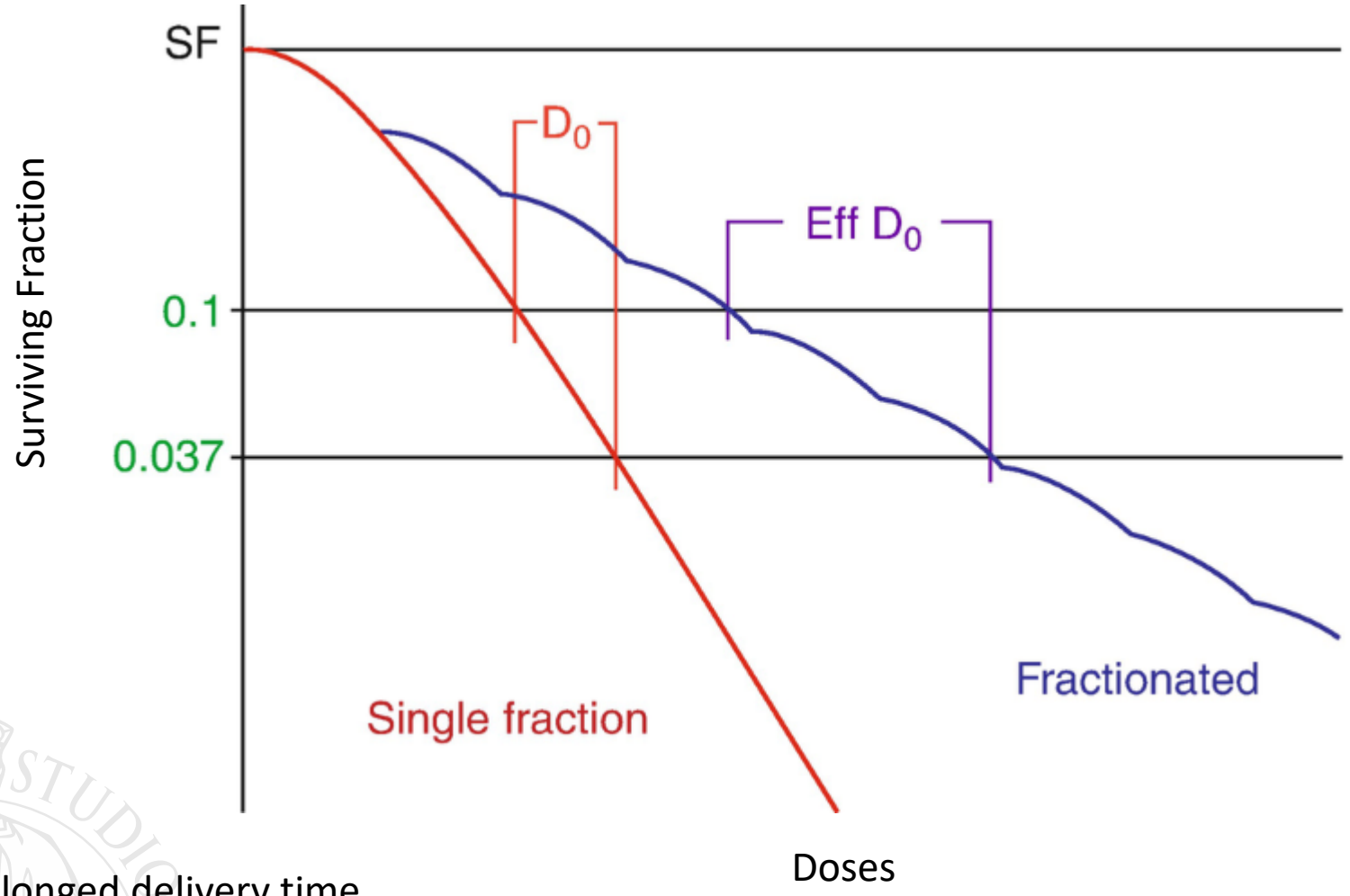


moderate hypofractionation

radiosurgery

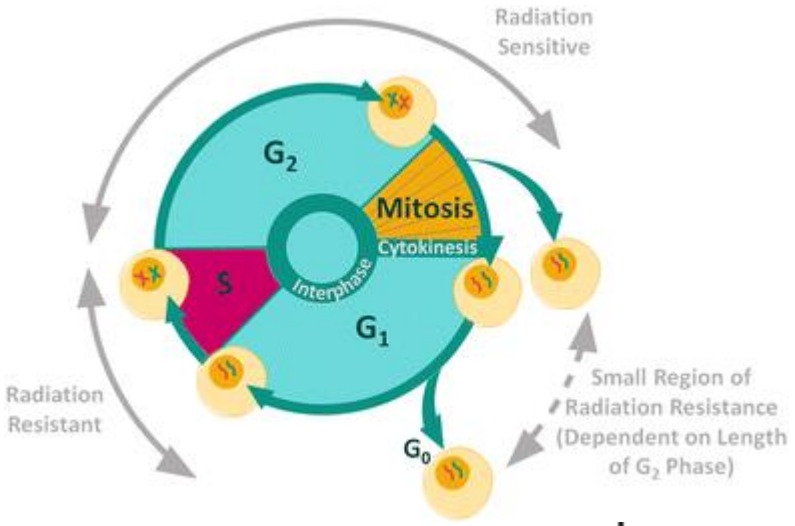
Repair

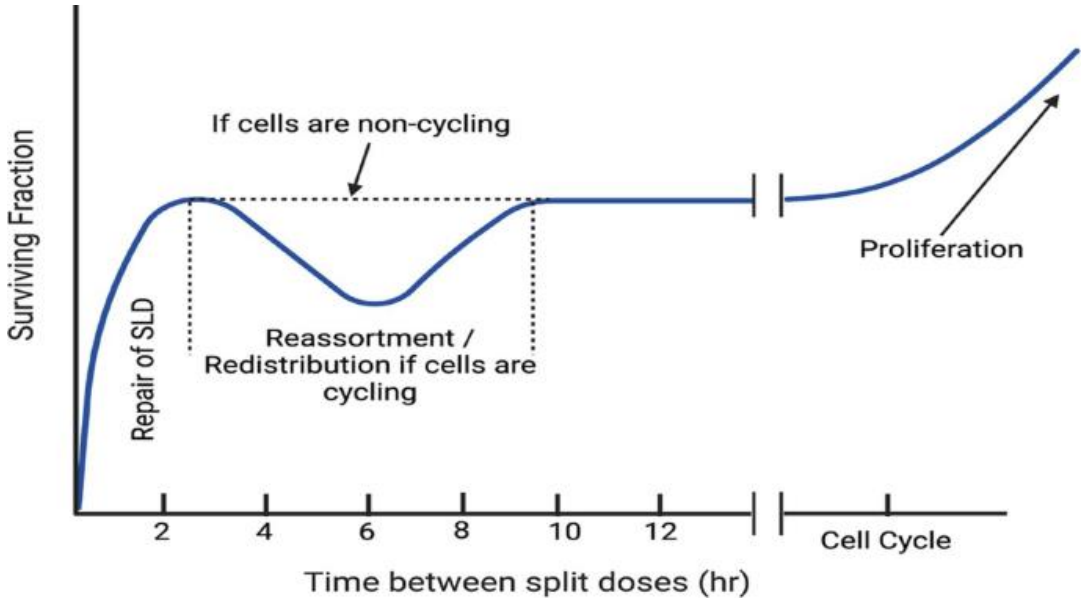
REPAIR OF SUBLETHAL DAMAGE



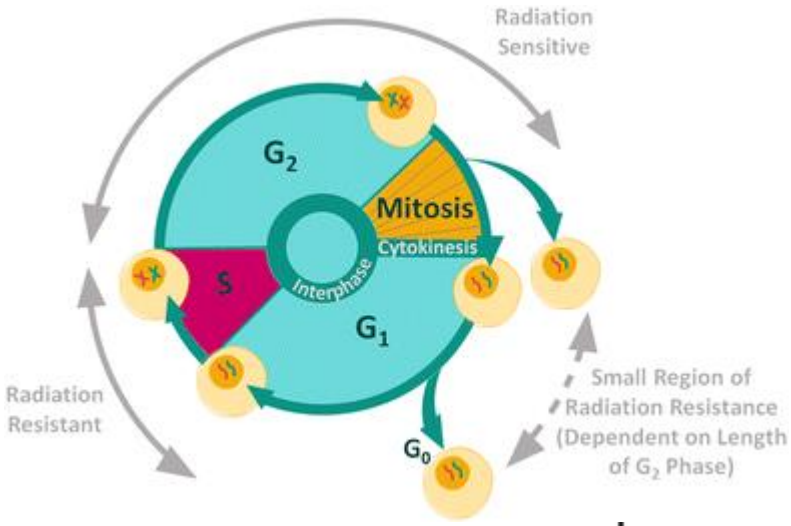
Prolonged delivery time

Redistribution

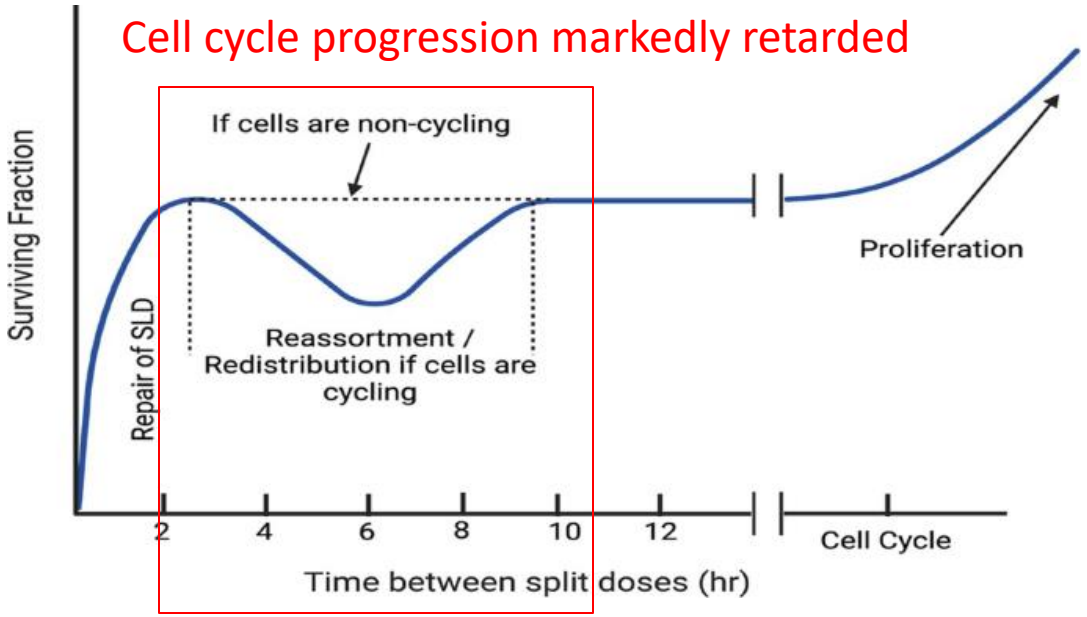




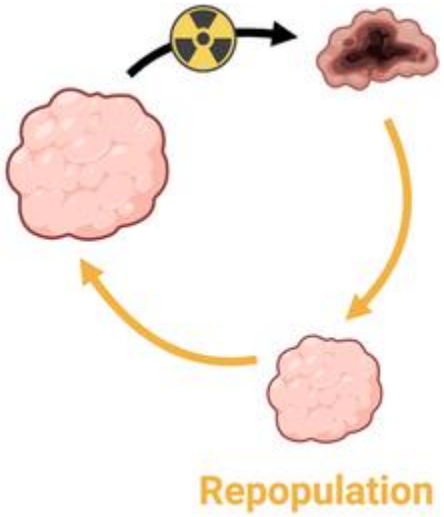
Redistribution

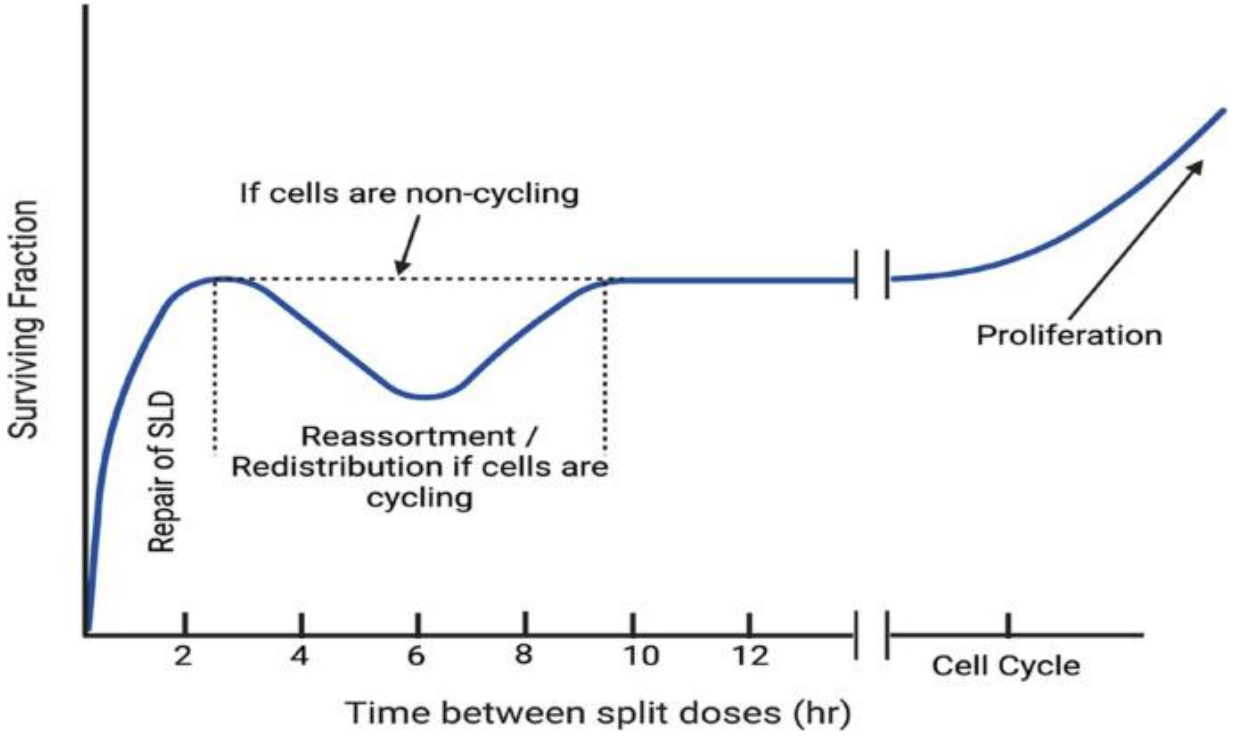


Cell cycle progression markedly retarded

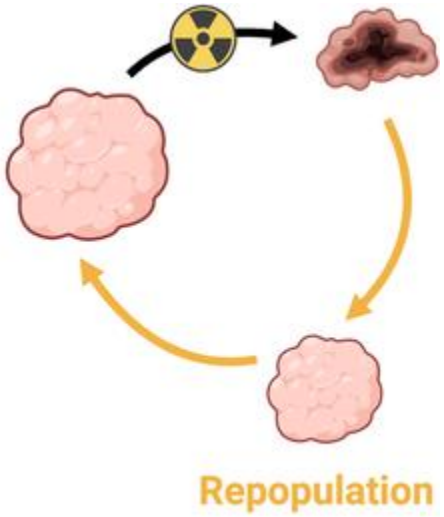


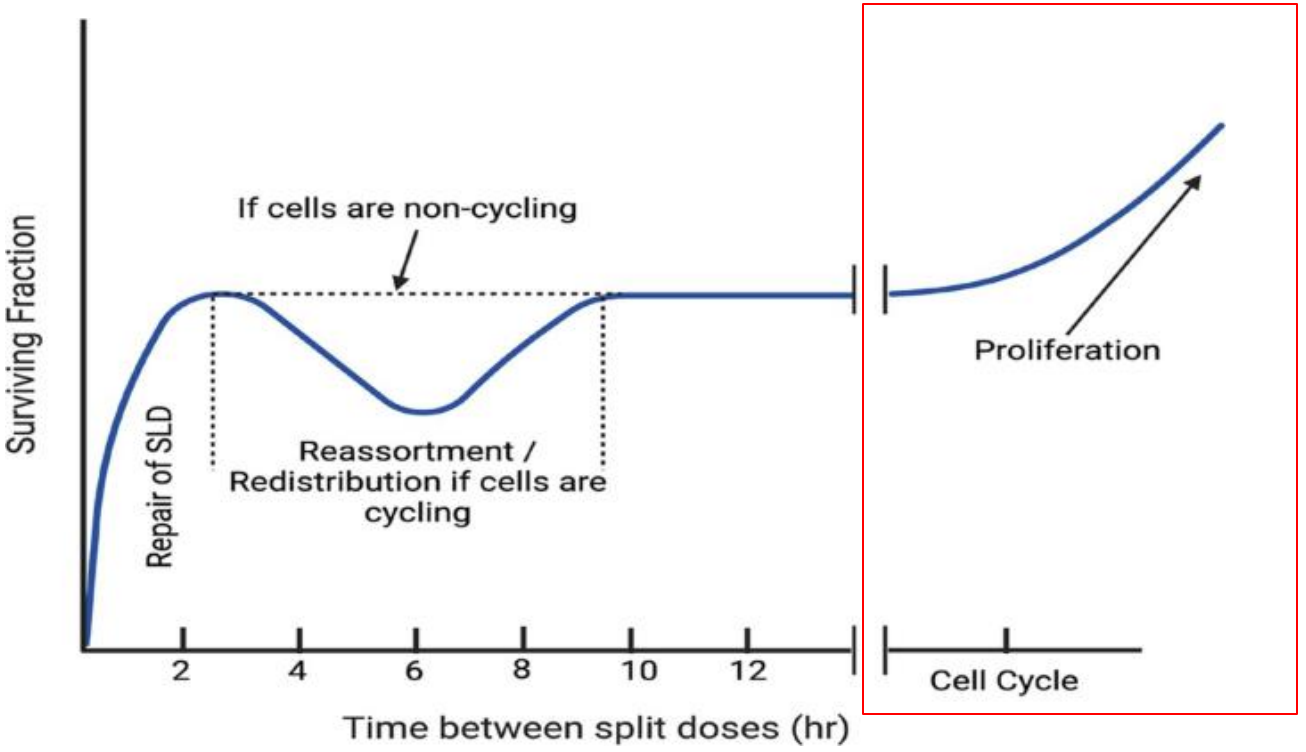
Repopulation



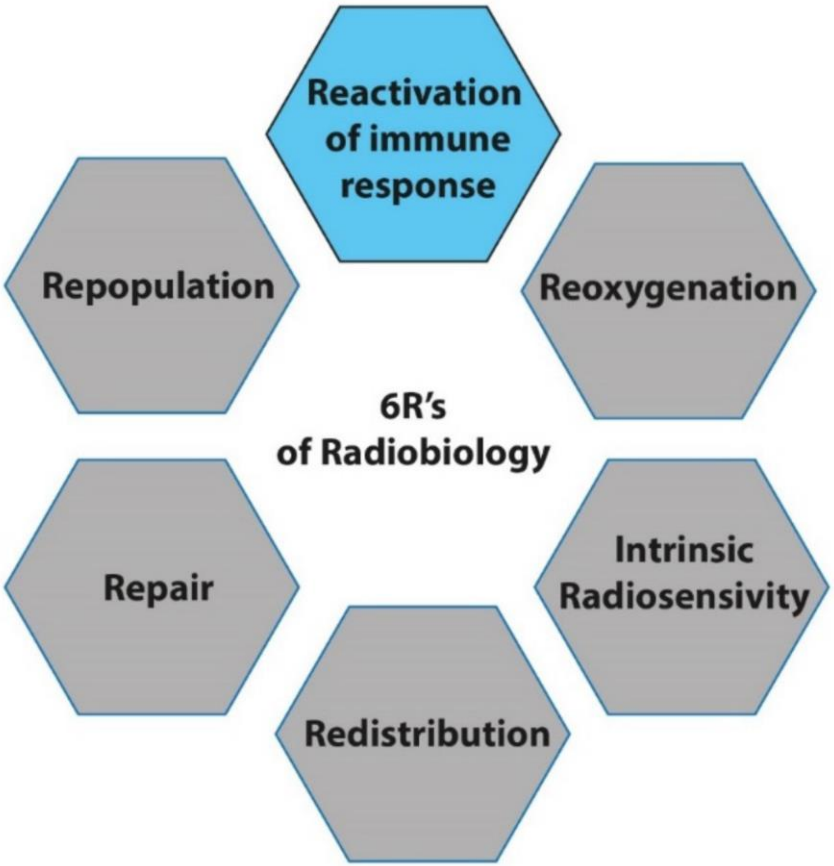


Repopulation



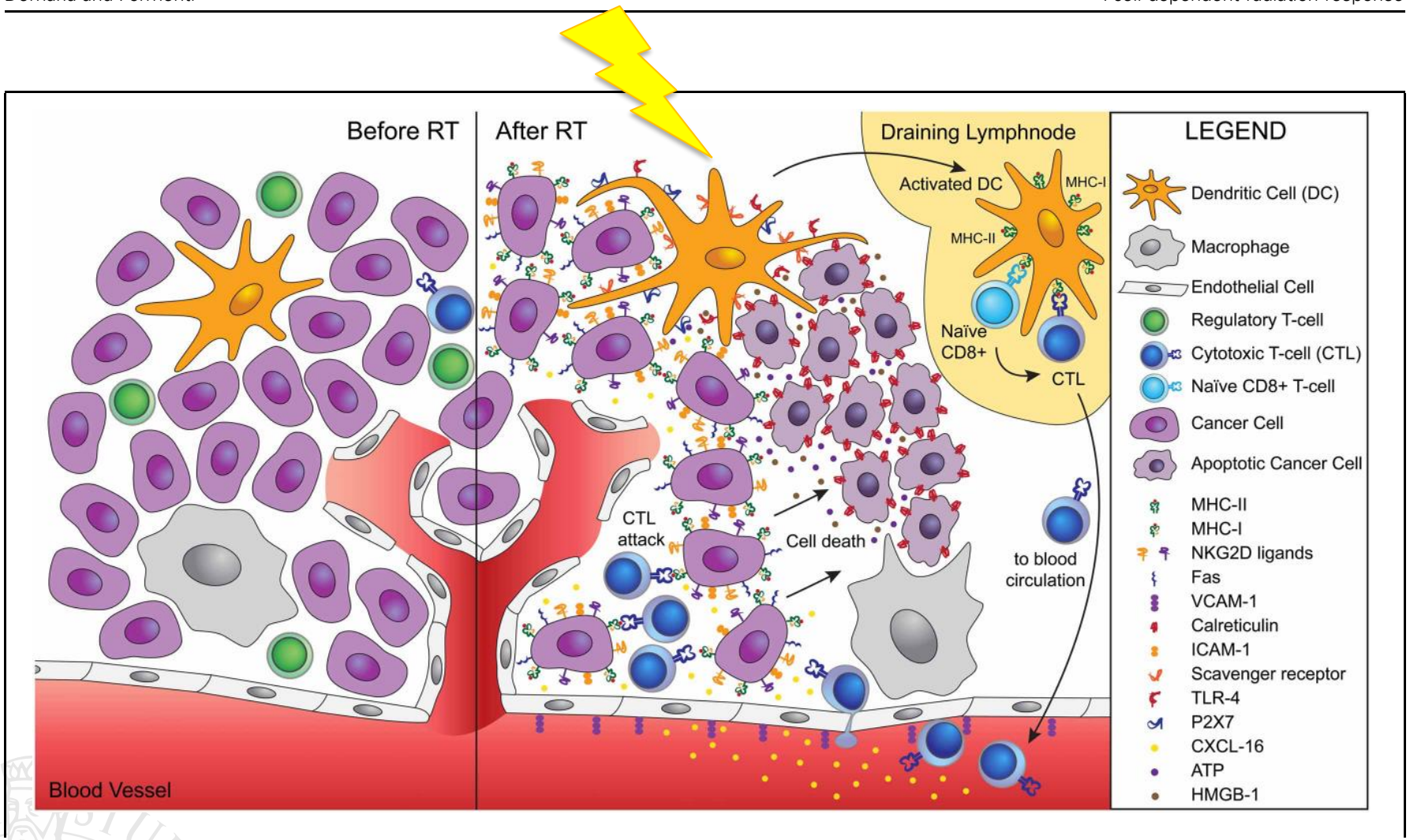


Antigen-induced damage and immune response



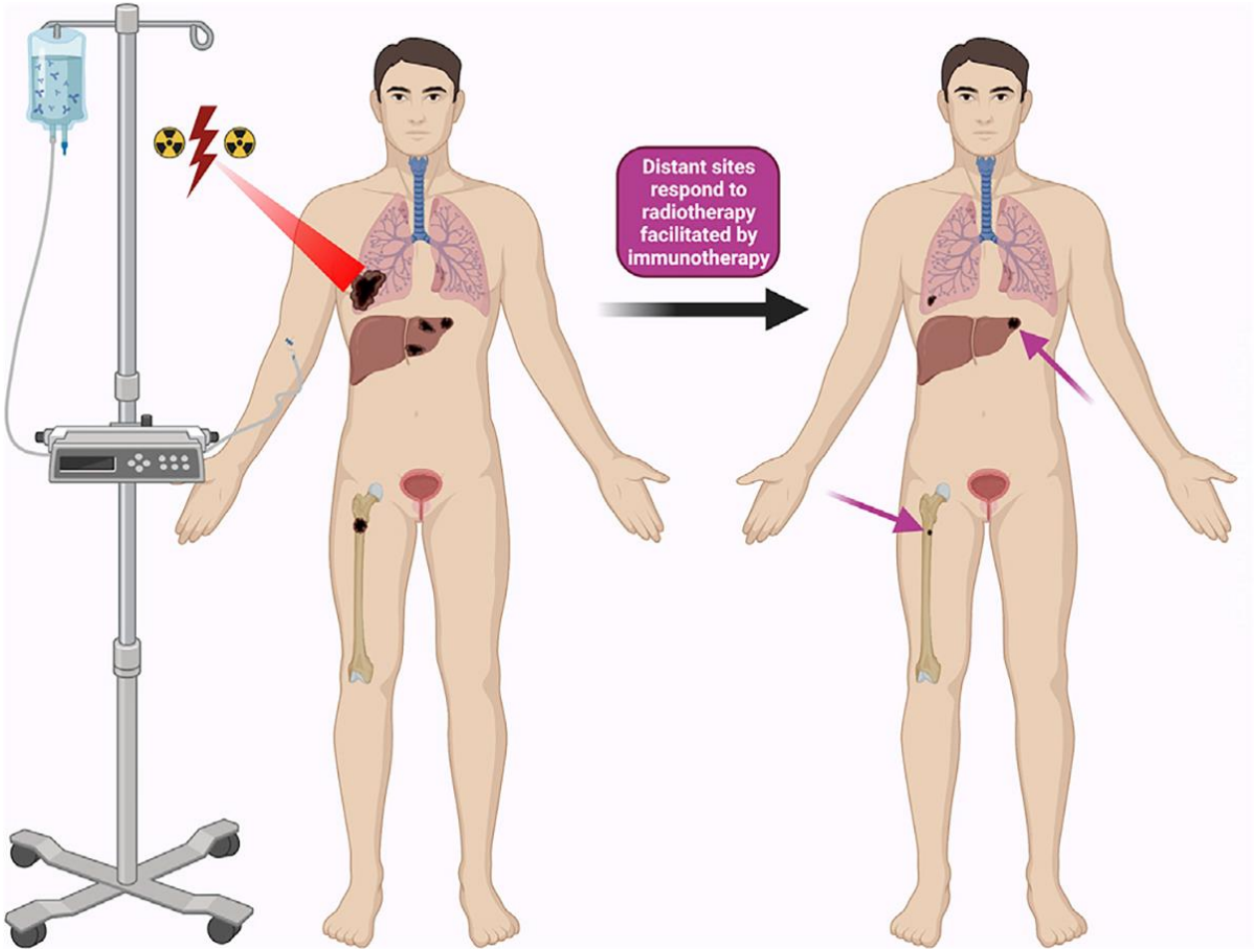
Boustani J, Grapin M, Laurent PA, Apetoh L, Mirjolet C.
The 6th R of Radiobiology: Reactivation of Anti-Tumor Immune Response. Cancers (Basel). 2019 Jun 20;11(6):860.

In situ vaccine

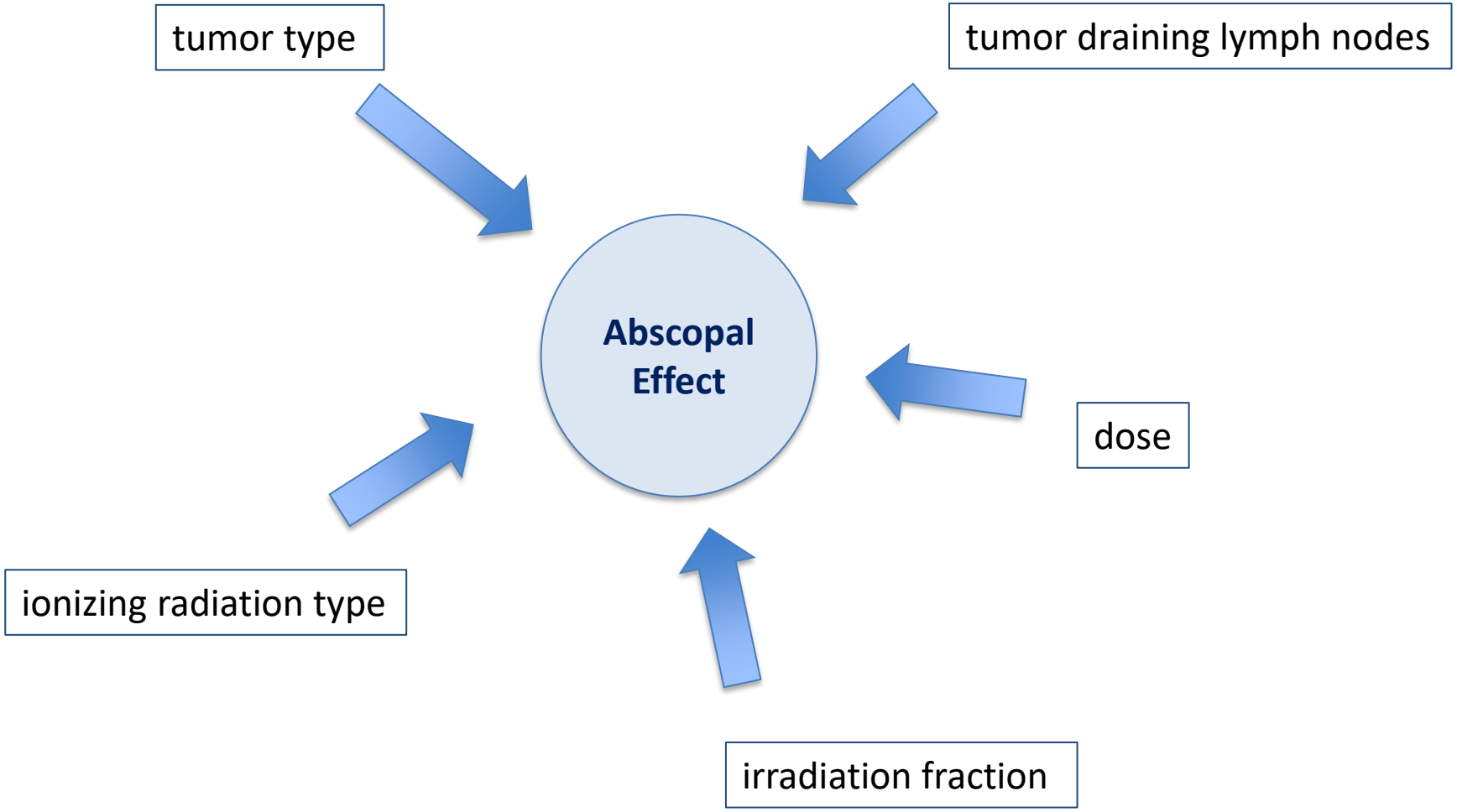


Demaria S, Frontiers in Oncology 2012

Abscopal effect



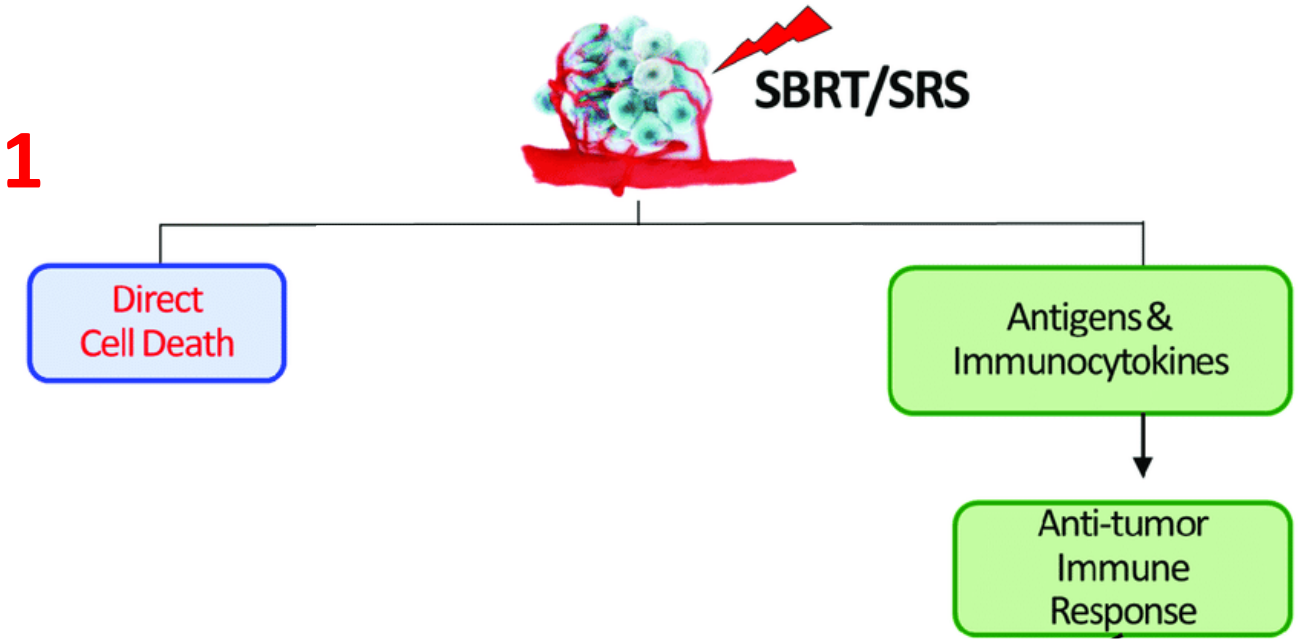
RT + immunotherapy



Rev in

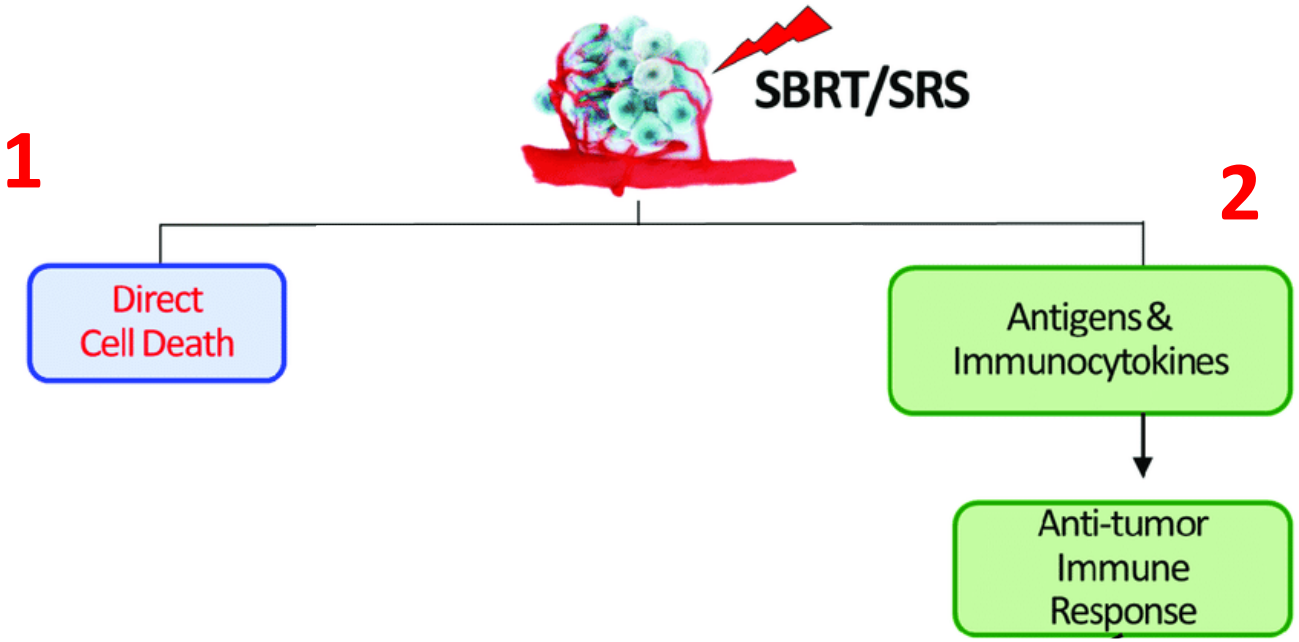
B. Yu et al. ”Killing two birds with one stone: Abscopal effect mechanism and its application prospect in radiotherapy” *Critical Reviews in Oncology / Hematology (2024)*

Tumor cells killing



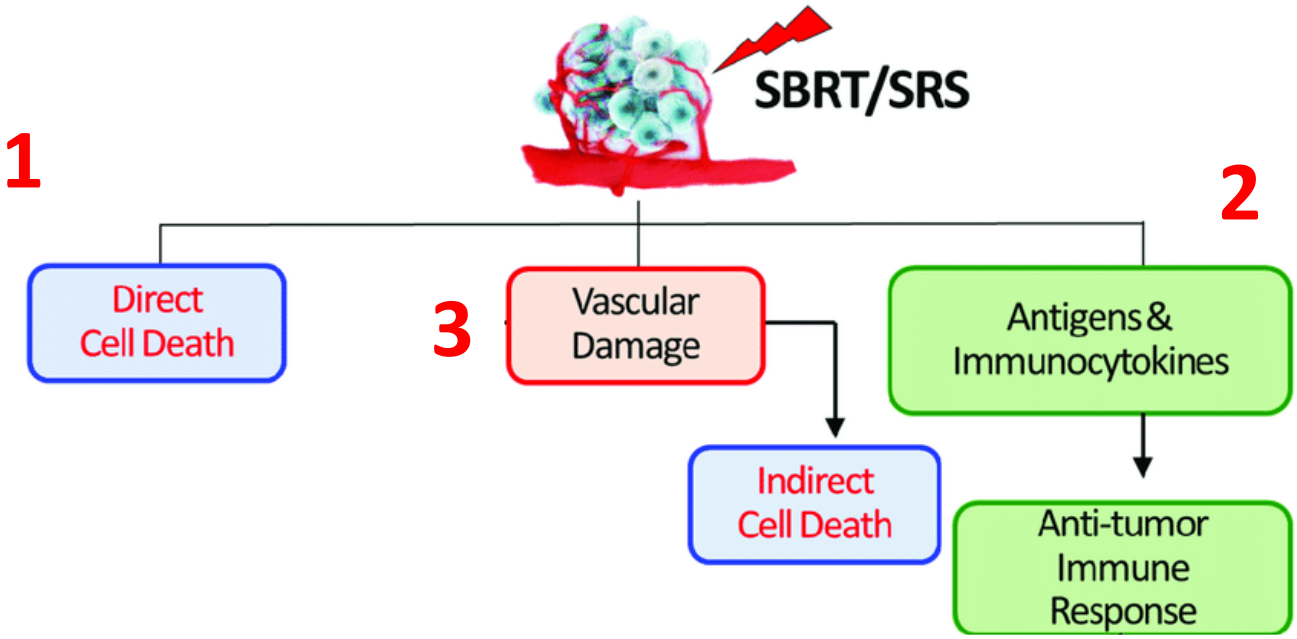
Song et al. Int J Radiation Oncol Biol Phys, Vol. 110, No. 1, pp. 21e34, 2021

Tumor cells killing

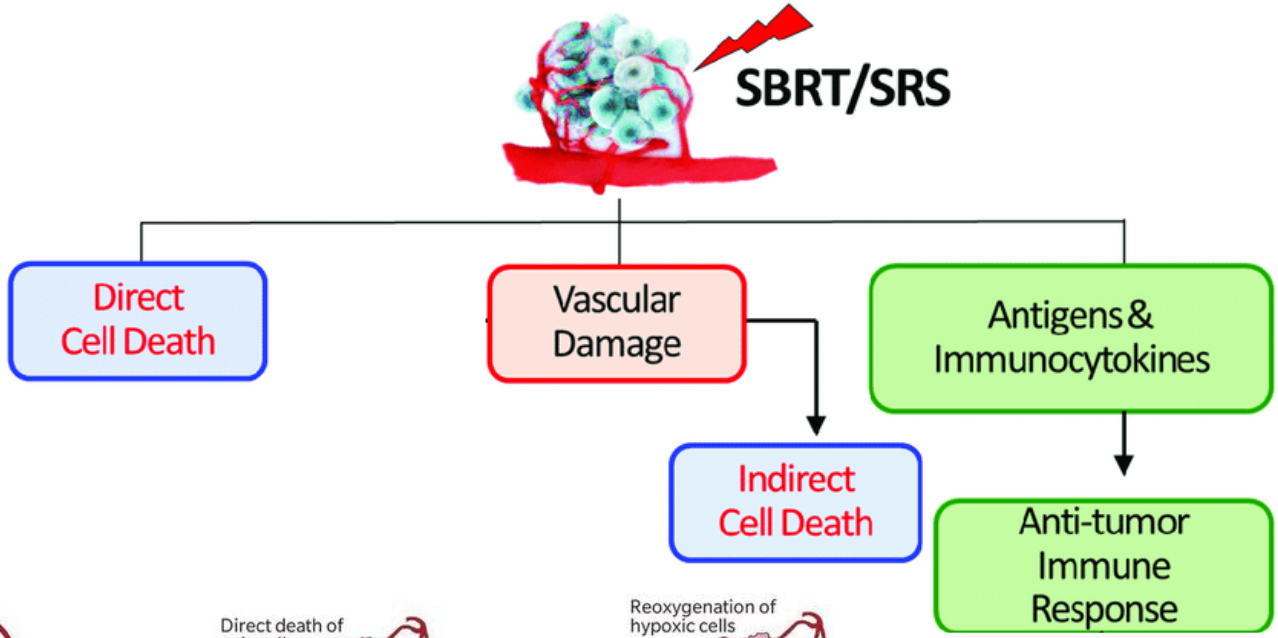


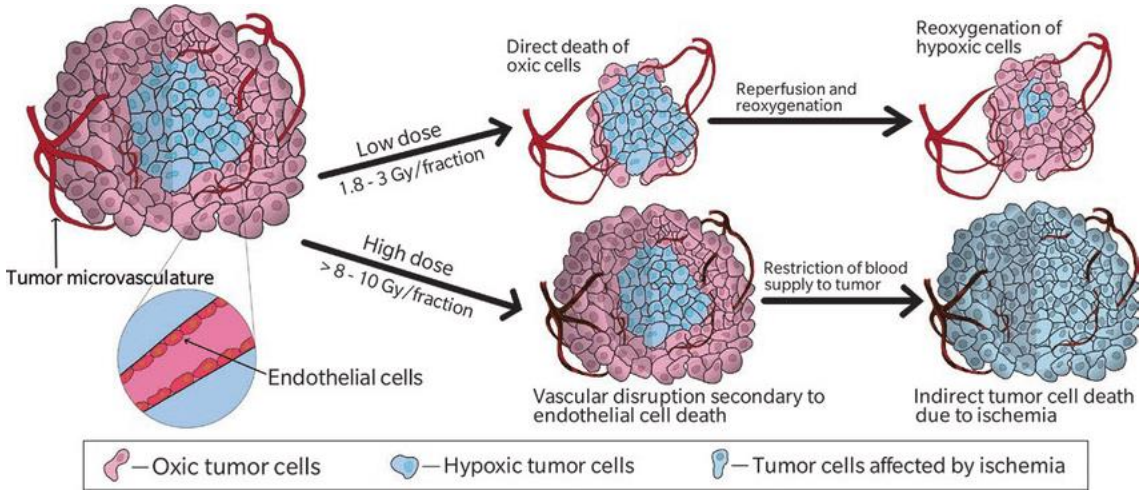
Song et al. Int J Radiation Oncol Biol Phys, Vol. 110, No. 1, pp. 21e34, 2021

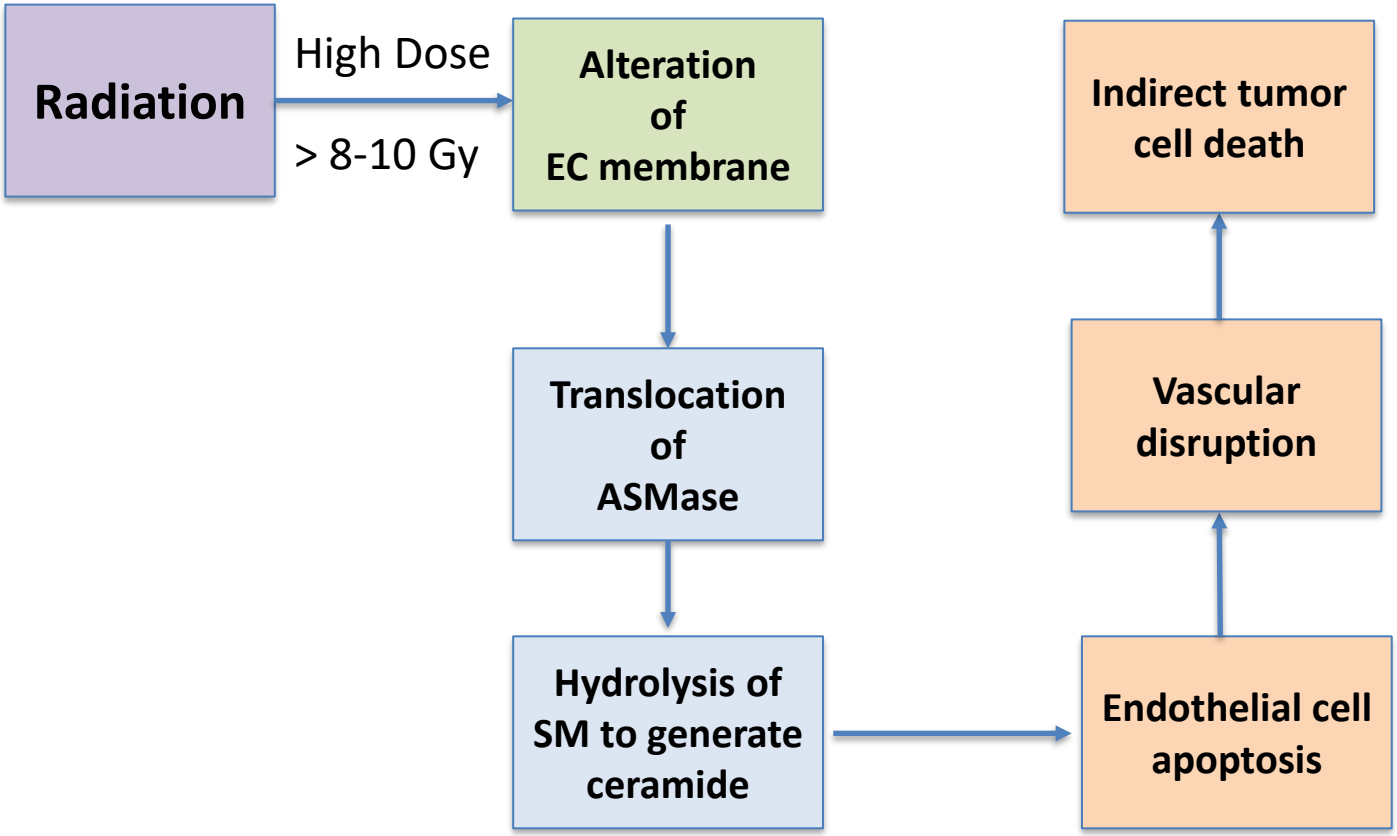
Indirect death

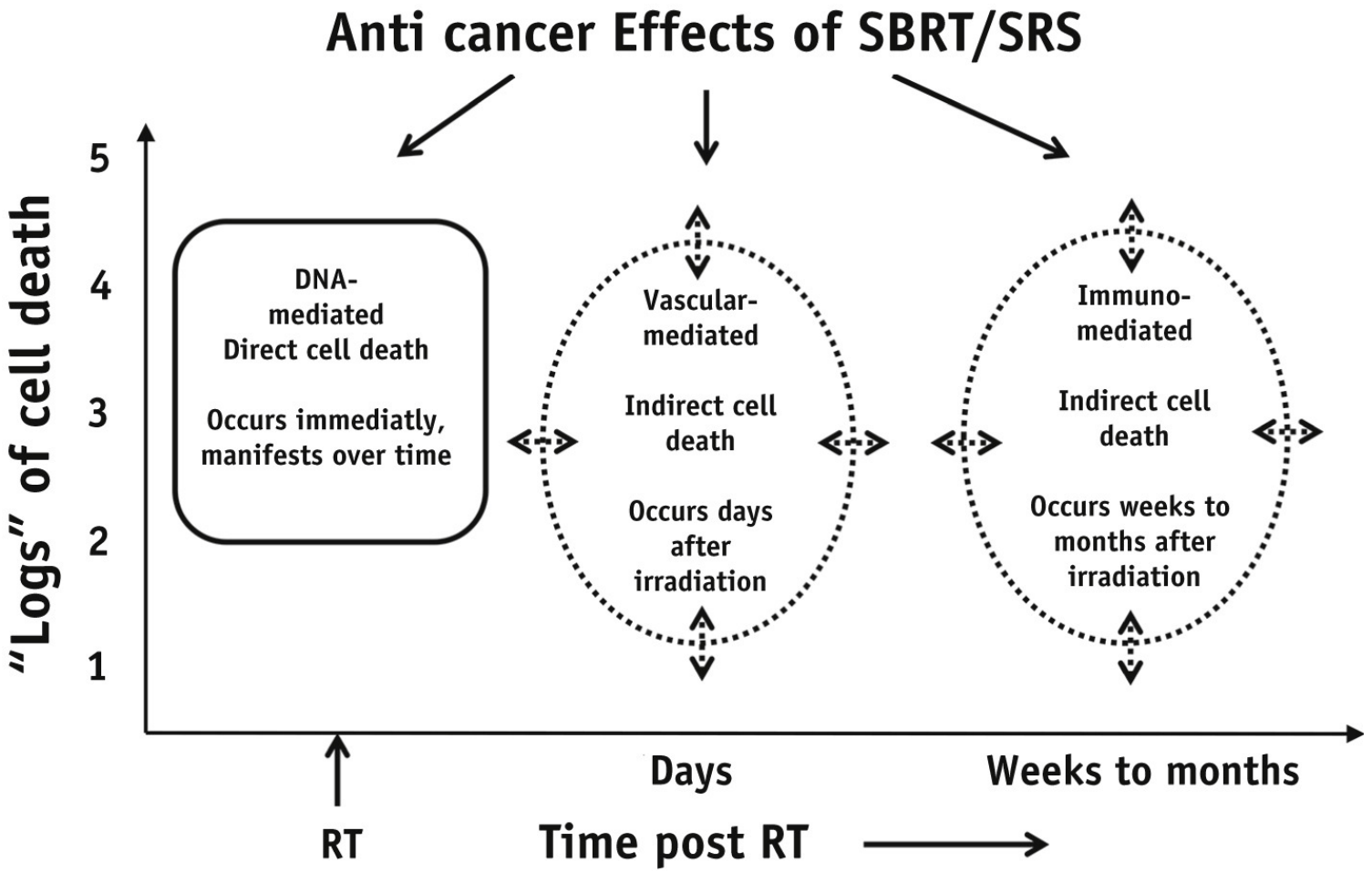


Indirect death

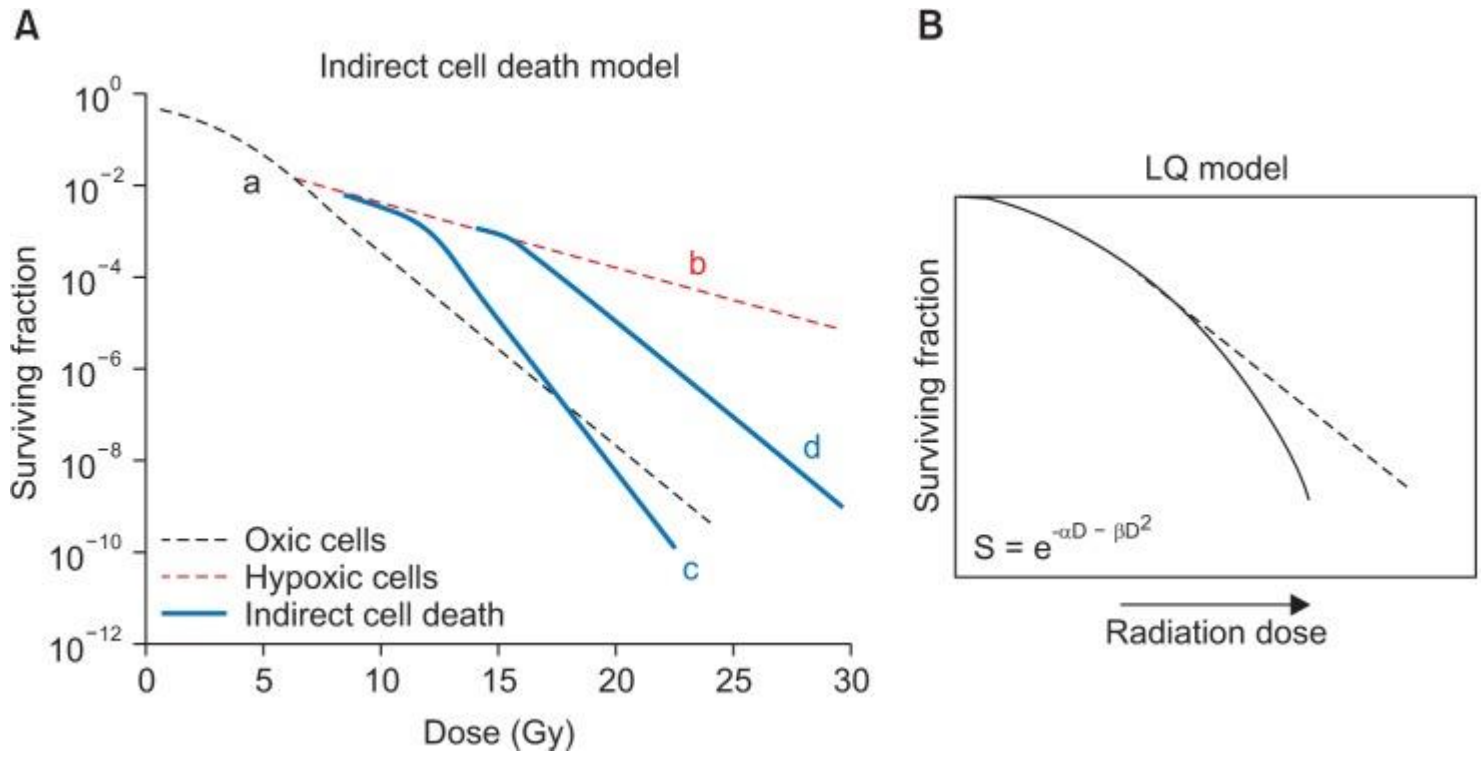





Radiation
High Dose
> 8-10 Gy
Alteration of EC membrane
Translocation of ASMase
Hydrolysis of SM to generate ceramide
Endothelial cell apoptosis
Vascular disruption
Indirect tumor cell death


Anti cancer Effects of SBRT/SRS
"Logs" of cell death
5
4
3
2
1
DNA-
mediated
Direct cell death
Occurs immediatly,
manifests over time
Vascular-
mediated
Indirect cell
death
Occurs days
after
irradiation
Immuno-
mediated
Indirect cell
death
Occurs weeks to
months after
irradiation
RT
Days
Weeks to months
Time post RT

The linear quadratic model

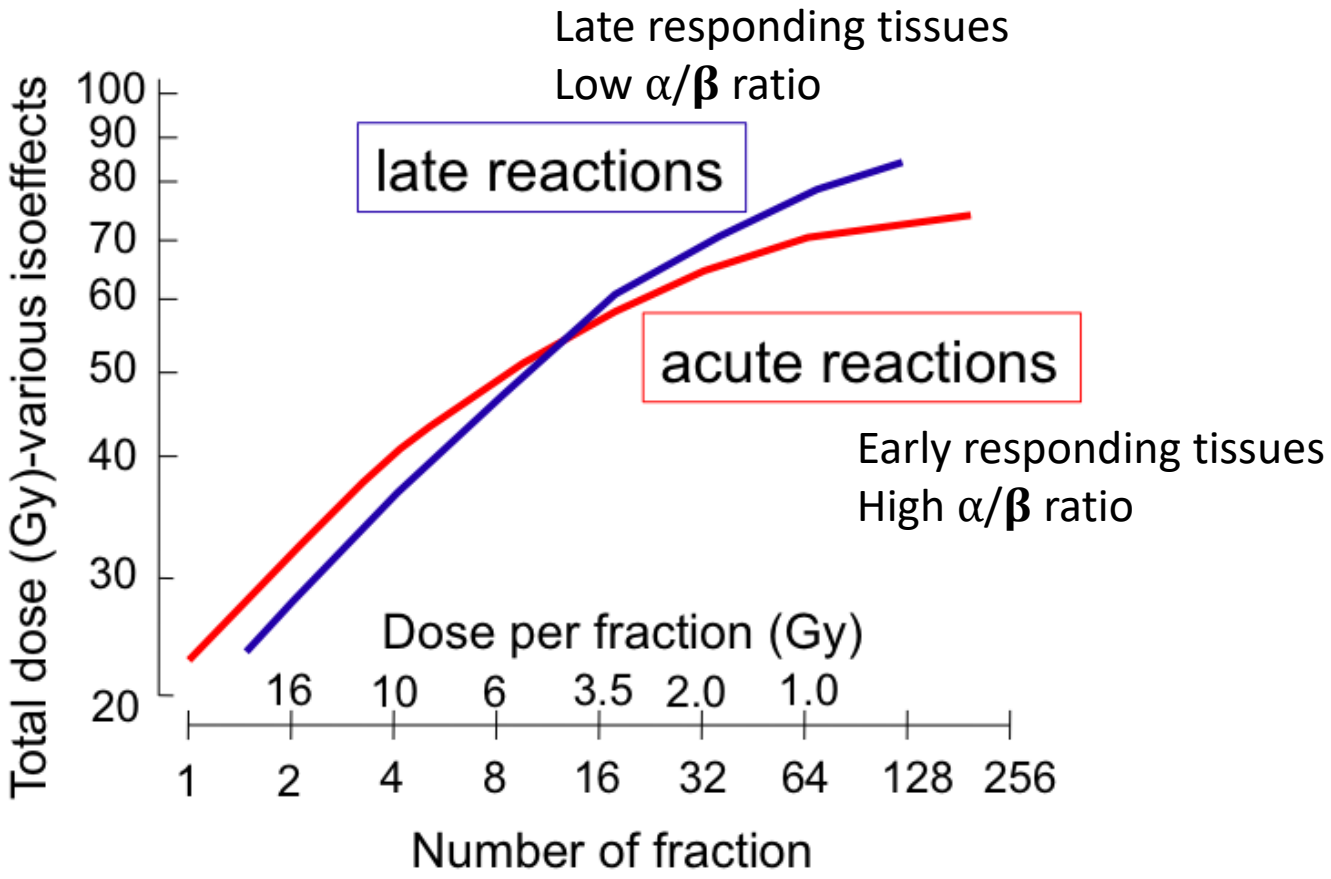


Kim MS, et al. Radiobiological mechanisms of stereotactic body radiation therapy and stereotactic radiation surgery. Radiat Oncol J. 2015

Implications of high dose per fraction on normal tissue

Relationship between isoeffective dose and dose per fraction

Implications of high dose per fraction on normal tissue



Relationship between isoeffective dose and dose per fraction

Implications of high dose per fraction on normal tissue

"vascular mediated" mechanisms have been suggested as the primary mode of radiation-induced late normal-tissue effects

Implications of high dose per fraction on normal tissue

- radiation-induced vascular damage in normal tissue progresses slowly
- ischemic cell death and necrotic breakdown will gradually develop in normal tissues
- later cell death and tissue damage occur in a dose-dependent manner in normal tissues
- take measures to avoid normal-tissue damage: patient selection, target delineation, dose prescription, and treatment delivery accuracy during SBRT/SRS.
- imperative to limit the volume of normal tissues exposed to high doses per fraction