



UNIVERSITÀ DEGLI STUDI  
DI GENOVA

Università degli Studi di Genova

# L'importanza della Radiobiologia in clinica

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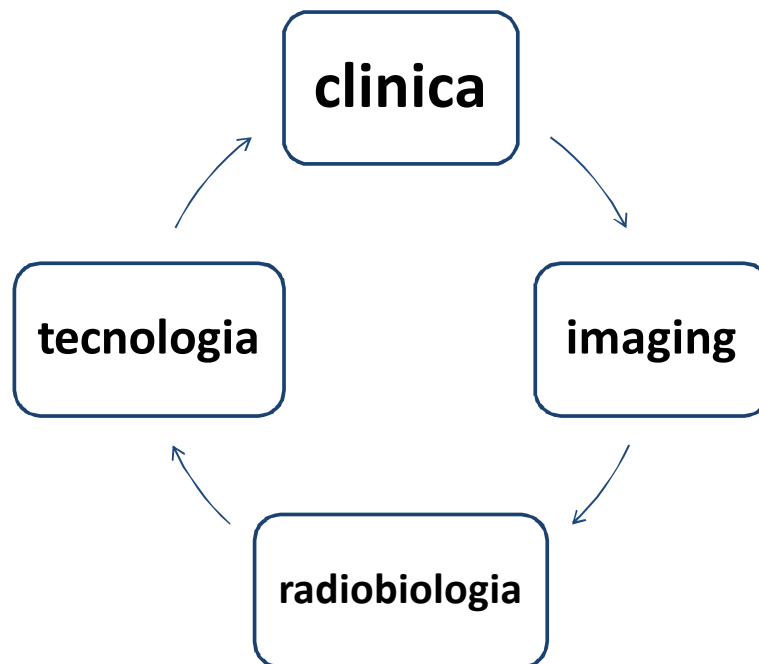


## **RADIOBIOLOGIA**

**Studio degli effetti biologici derivati dall' interazione  
delle radiazioni elettromagnetiche e corpuscolari  
sugli organismi viventi**

- Effetti delle alte dosi sui tessuti sani del paziente e sul tumore maligno
- Effetti delle basse dosi sul personale esposto alle radiazioni, sui pazienti e sulla popolazione

## L'apprendimento di base del Medico Specializzando dell'Area Radiologica



## La dose radiante di 2 Gy (dose standard) induce:

- 4000 ionizzazioni per cellula
- 2000 rotture di una singola elica (DNA)
- 80 rotture della doppia elica (DNA)
- 6000 basi del DNA danneggiate

Learch et al, Cancer Res. 2001

→ Frazionamento standard:

2 Gy x 35 frazioni in 7 settimane

# La dose radiante di 10 Gy (RT stereotassica) induce:

- 20.000 ionizzazioni per cellula
- 10.000 rotture di una singola elica (DNA)
- 400 rotture della doppia elica (DNA)
- 30.000 basi del DNA danneggiate

Leach et al, Cancer Res. 2001

## RADIAZIONI IONIZZANTI



**TUMORE**

Inefficace riparo  
del danno



Apoptosi  
Catastrofe mitotica  
Necrosi cellulare  
(Regressione clinica e  
strumentale)

**CURA DEL TUMORE**



**CELLULE SANE**

Efficace riparo  
del danno



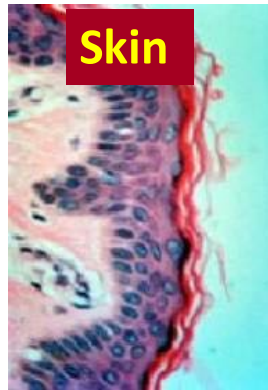
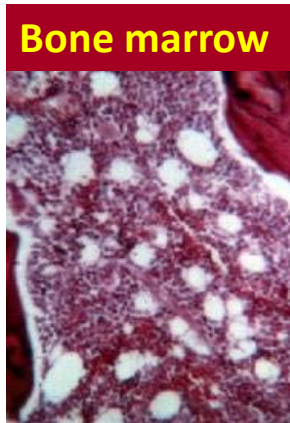
Danno tessutale  
(morte cellulare/apoptosi)



ripopolamento/  
proliferazione

**TOSSICITA' →  
restitutio ad integrum**

# Radioensitivity of tissues



## Highly radiosensitive

- Lymphoid tissue
- Bone marrow
- Gastrointestinal epithelium
- Gonads
- Embryonic tissues

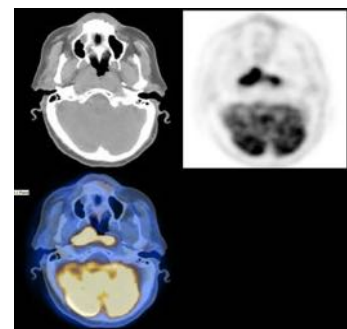
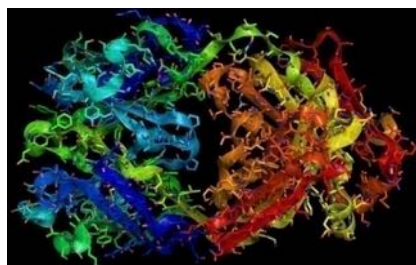
## Moderately radiosensitive

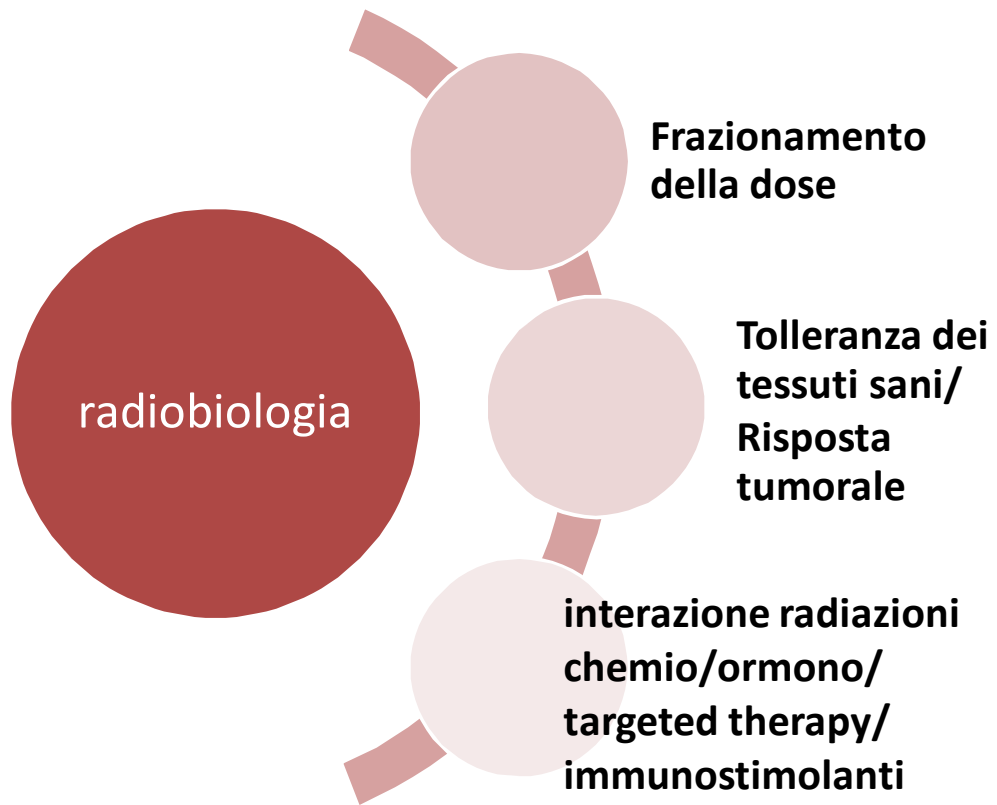
- Skin
- Vascular endothelium
- Lung
- Kidney
- Liver
- Lens (eye)

## Least radiosensitive

- Central nervous system (CNS)
- Muscle
- Bone and cartilage
- Connective tissue

## COMPLEXITY IN RADIOBIOLOGY: FROM LABORATORY TO CLINICAL TREATMENT AND ... FROM CLINICAL RESULTS TO LABORATORY

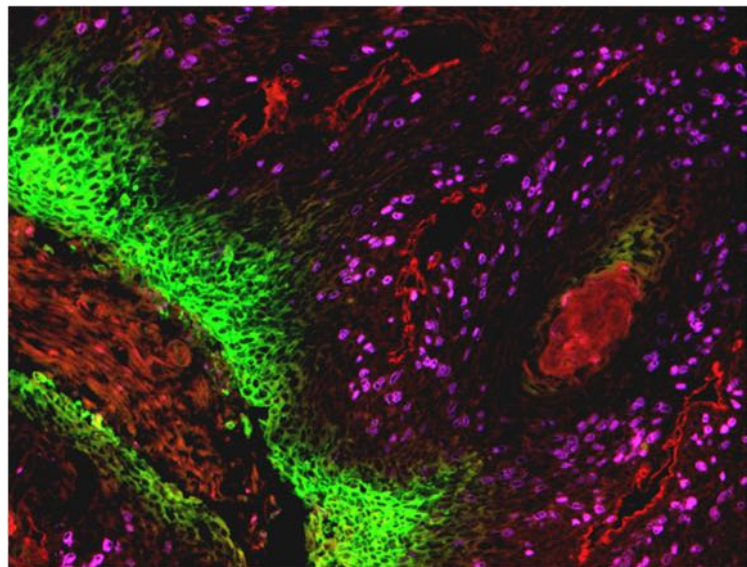




## **The five Rs of radiobiology meet the hallmarks of cancer**

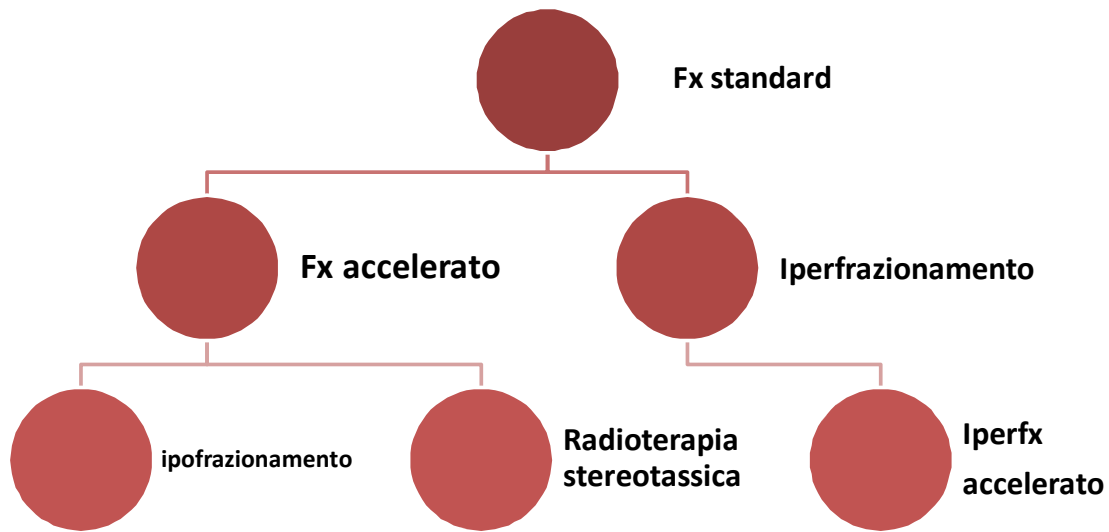
Harrington K et al, Clin Oncol 19:561-571, 2007

REPAIR  
REPOPULATION  
REDISTRIBUTION  
REOXYGENATION  
RADIOSENSITIVITY

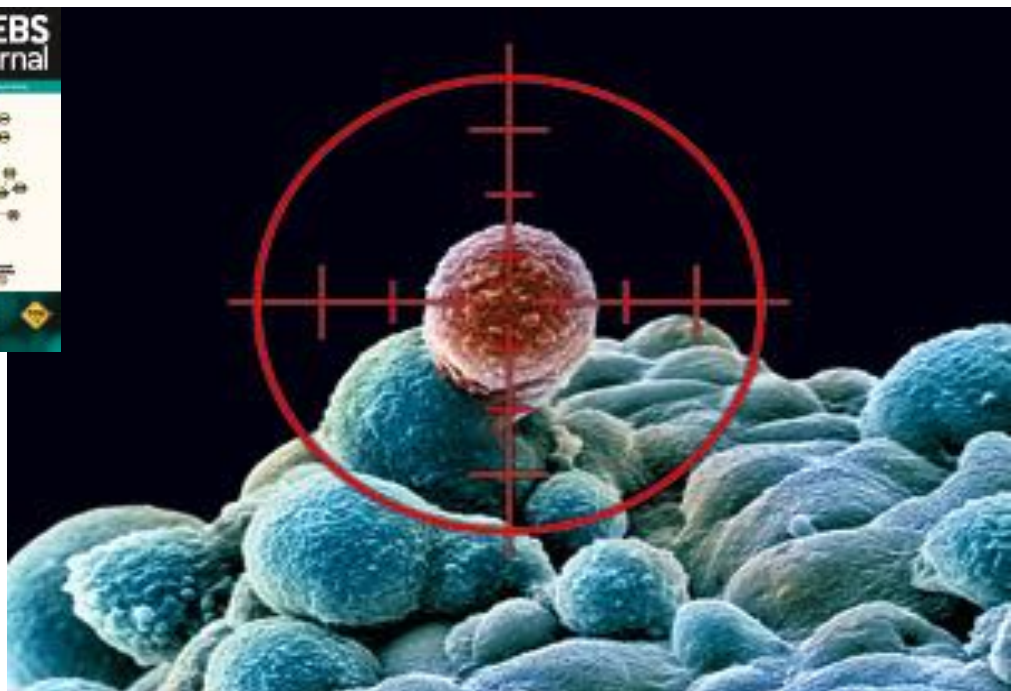


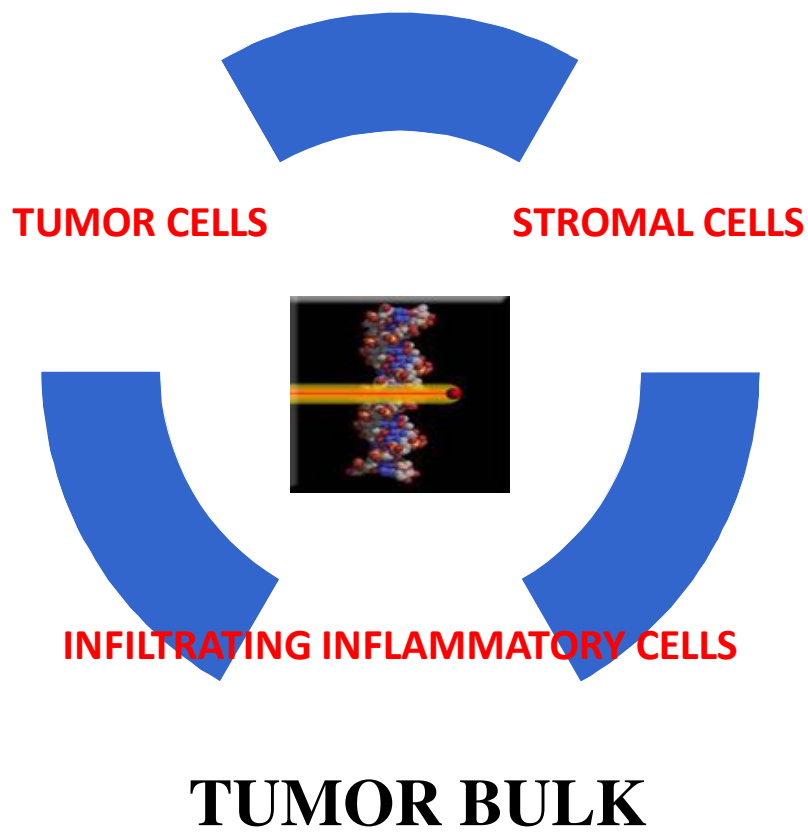
INVASION AND METASTASIS

# Evoluzione radiobiologica del frazionamento della dose radiante

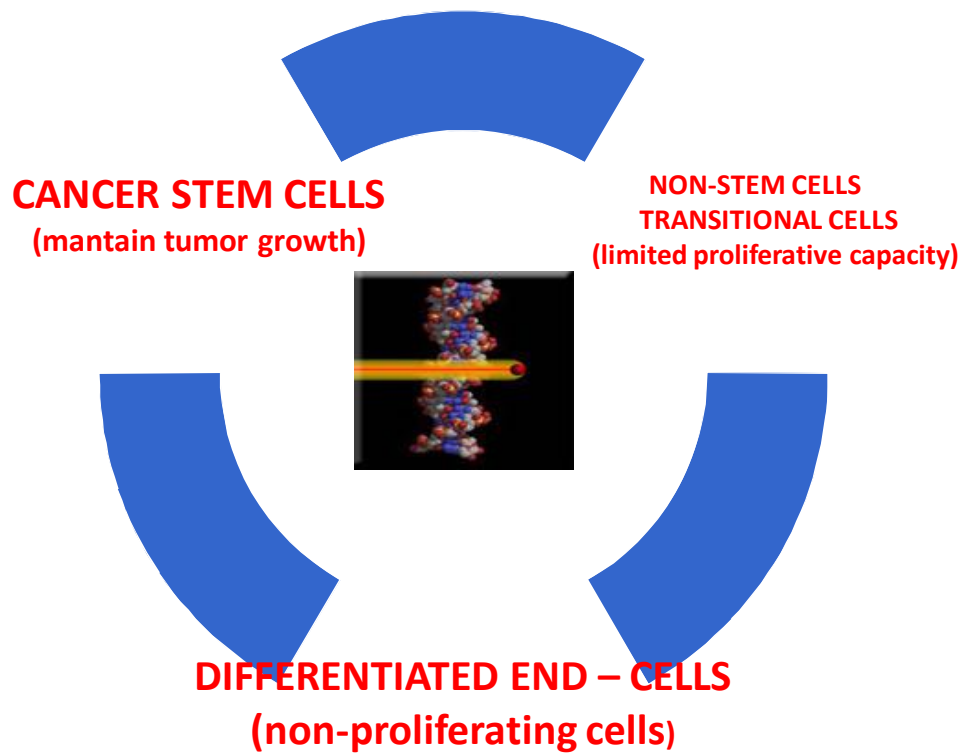


## Cancer Stem Cell important players in tumor cell resistance





**TUMOR CELLS: HIERARCHICAL MODEL**

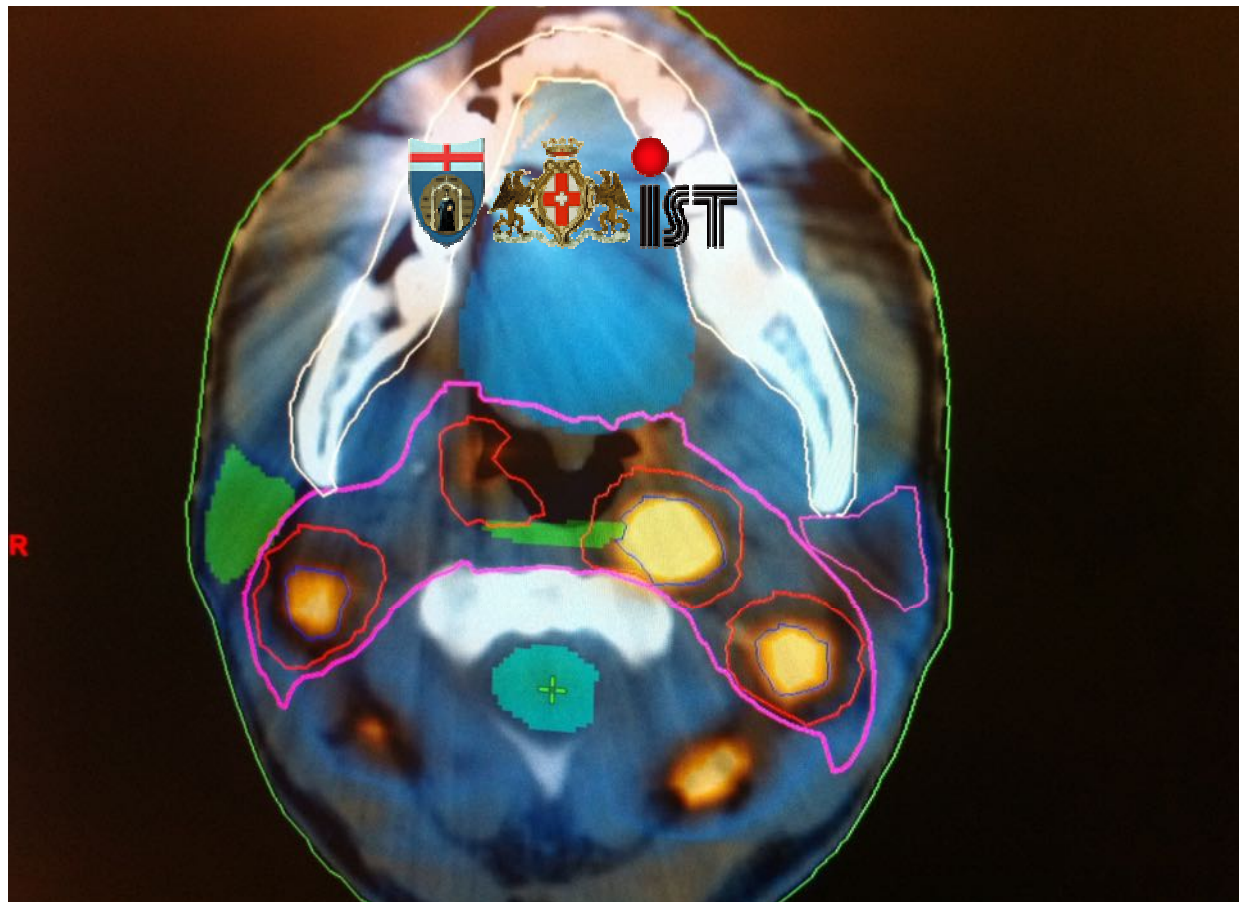
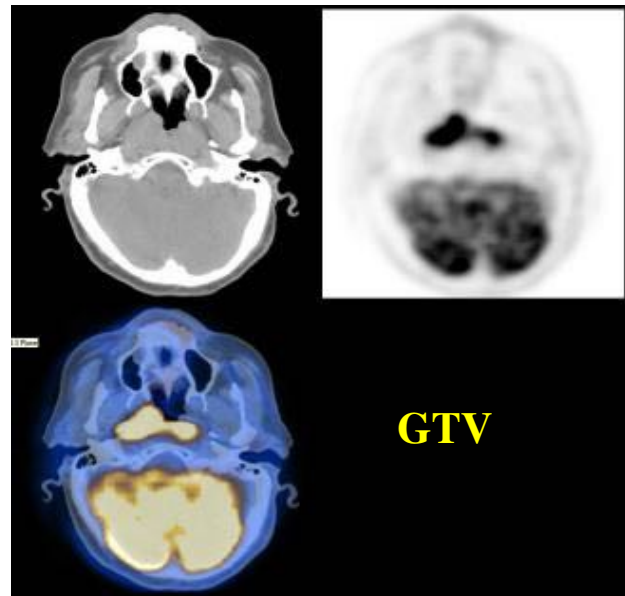




# Gross Tumor Volume (GTV)

- Small subset of cancer stem cells
- Large subset of cancer non-stem cells

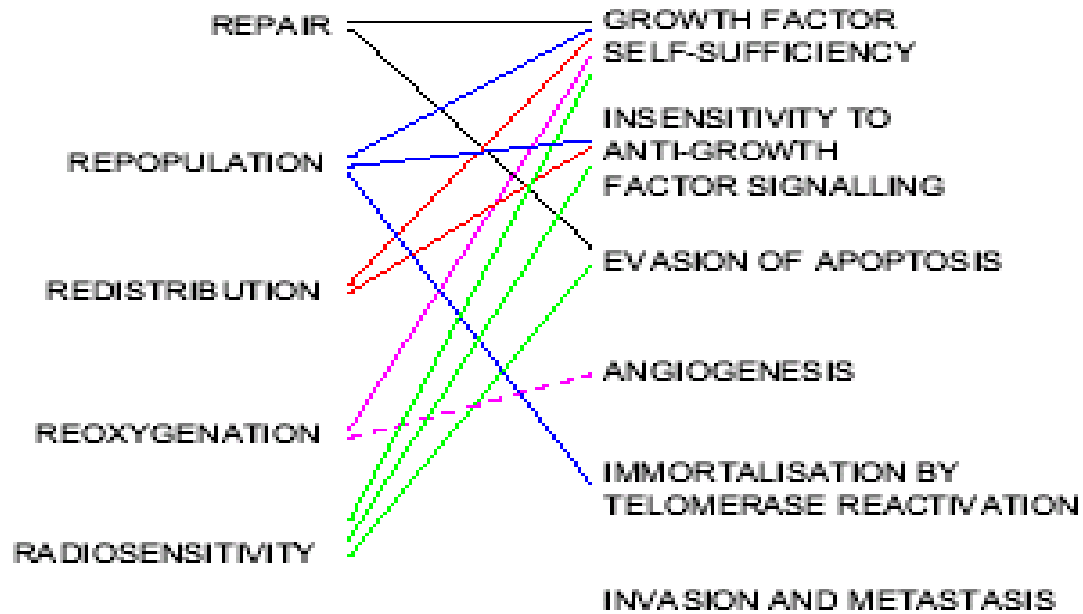
Burden of cancer stem cells may modulate response



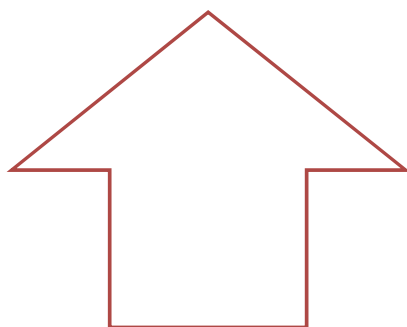


## The five Rs of radiobiology meet the hallmarks of cancer

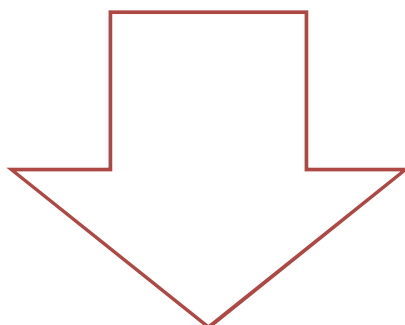
Harrington K et al, Clin Oncol 19:561-571, 2007



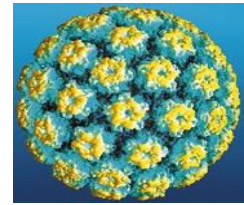
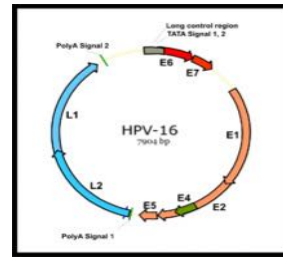
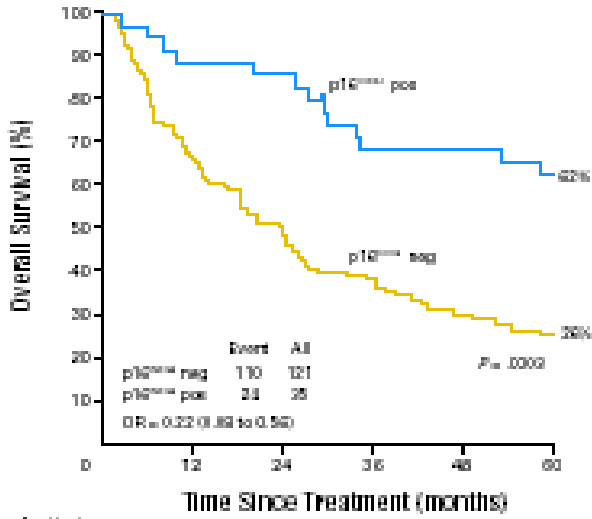
## La ricerca traslazionale in radiobiologia



**Reverse translation research**  
dalla clinica al laboratorio



**Forward translation research**  
dal laboratorio alla clinica



VOLUME 27 • NUMBER 12 • APRIL 20 2009

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

### Effect of HPV-Associated p16<sup>INK4A</sup> Expression on Response to Radiotherapy and Survival in Squamous Cell Carcinoma of the Head and Neck

Berndt Lassen, Jesper G. Erikson, Stephen Hamilton-Duoss, Trine Traenen, Jost Alster, and Jens Overgaard

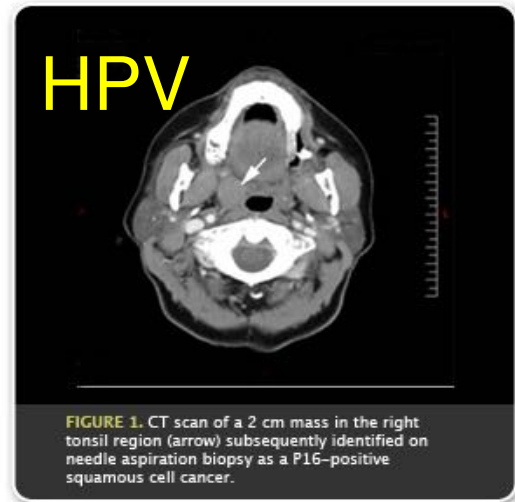
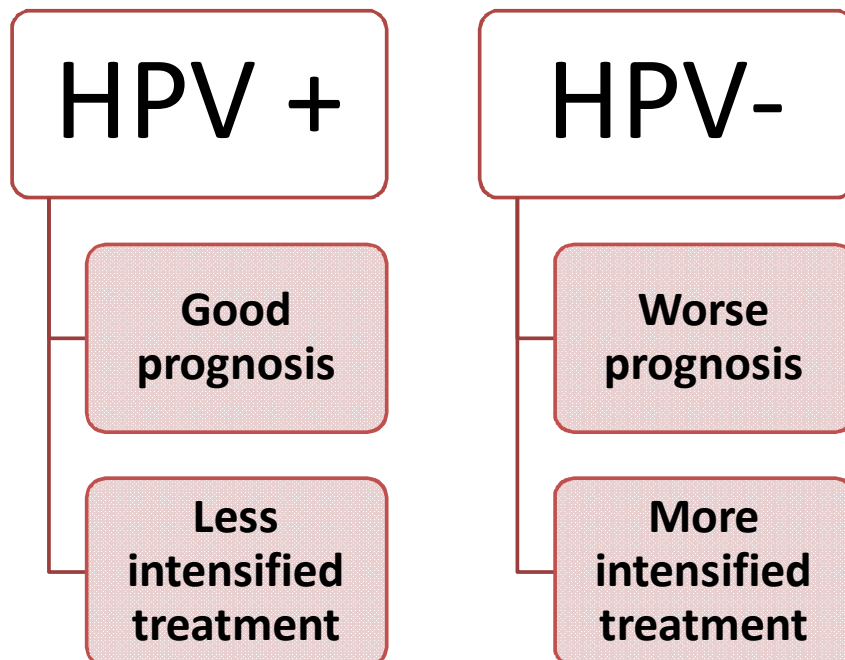


FIGURE 1. CT scan of a 2 cm mass in the right tonsil region (arrow) subsequently identified on needle aspiration biopsy as a P16-positive squamous cell cancer.

## Oropharyngeal/ Anal Cancer



# Effect of Radiotherapy on immune response

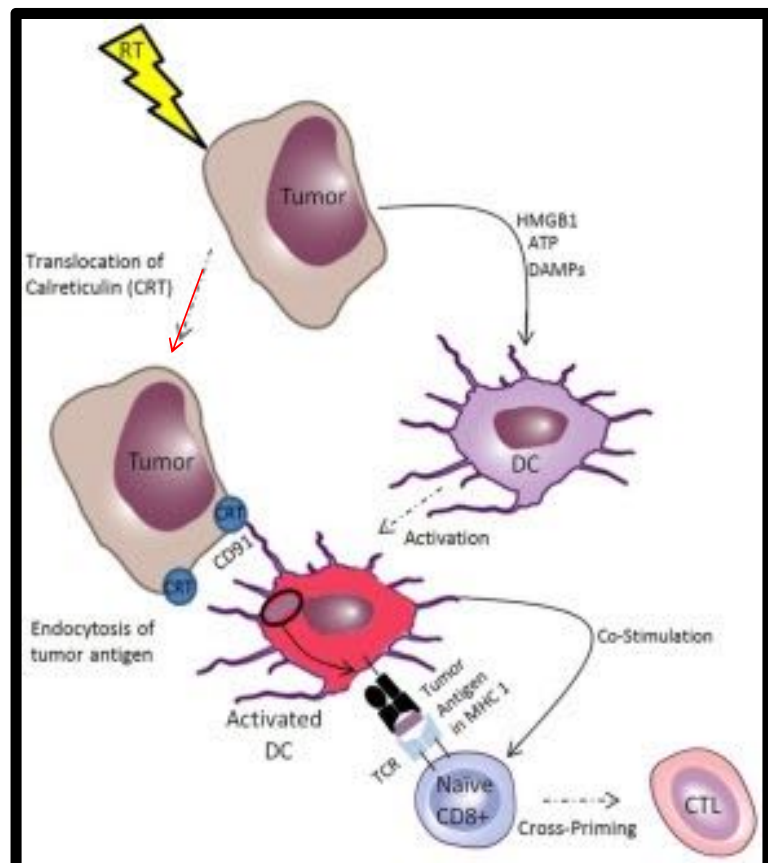
- Immunosuppressive role for bone marrow cell
- Immunostimulation after stereotactic RT or RT
- **50 clinical trials now active in USA**



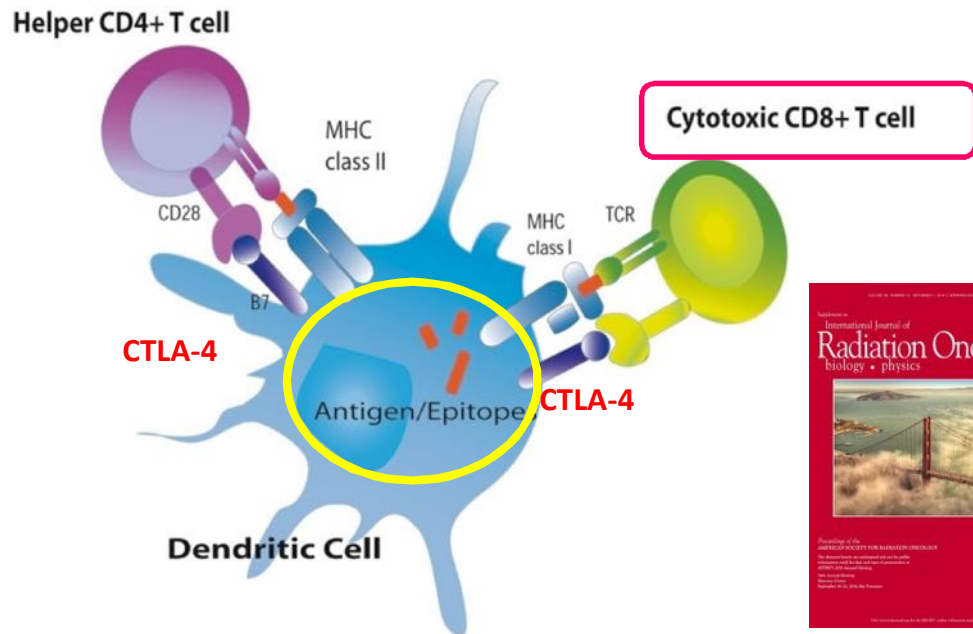
**Ionizing Radiations**  
→ tumor cells

→ «eat me»  
membrane signal to  
**Dendritic Cells**

radiating the tumor  
seems to activate  
immune cells in the  
surrounding  
**lymphnodes**



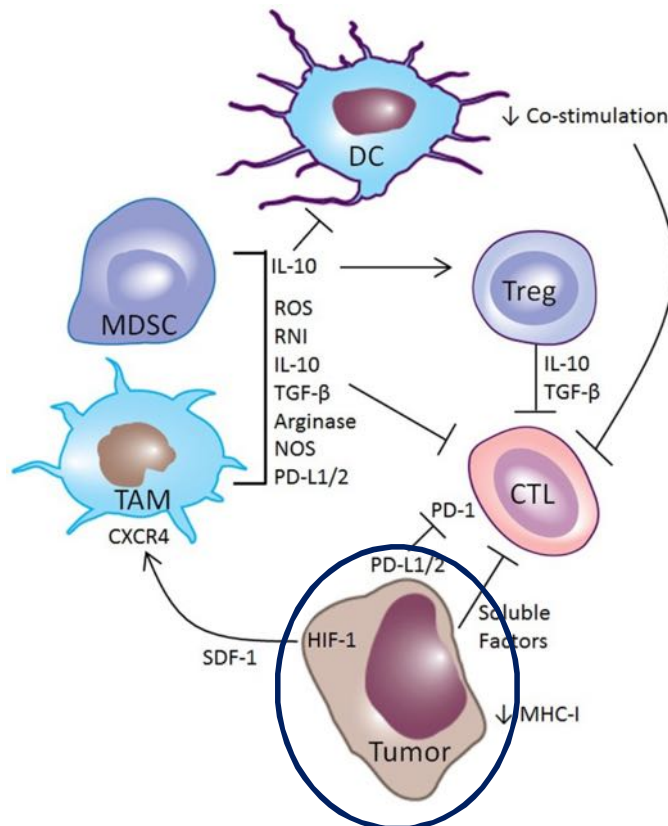
# Radiation Boosts Immunotherapy



**CTLA-4** (Cytotoxic T-Lymphocyte Antigen 4): protein receptor of downregulating immunoaction of Lymphocytes T CD4+ and CD8+

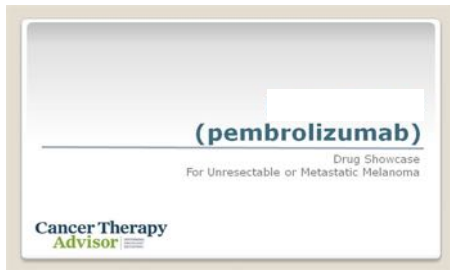
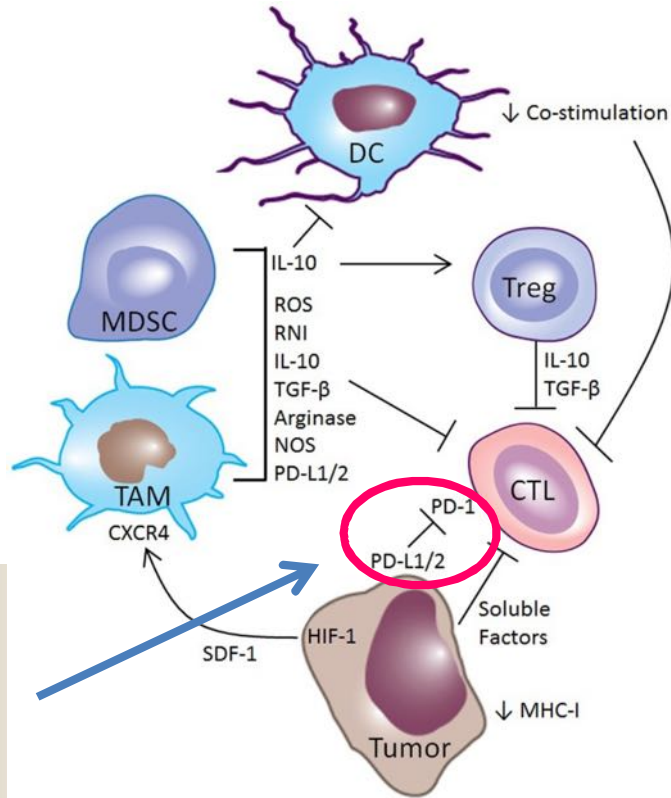
## Immuno-Evasion of Tumor Cell

- PD-1:** Programmed Death protein
- CTLs:** Cytotoxic T-lymphocytes
- Treg:** Regulatory suppressor T cells
- DC:** Dendritic cells
- TAM:** Tumor Associated Macrophages
- MDSC:** Myeloid-derived Suppressed Cells
- MHC I-II:** Major Histocompatibility Complex
- HIF-1:** Hypoxia inducible Factor -1
- SDF-1:** Stromal-Derived Factor -1

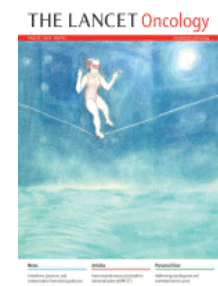
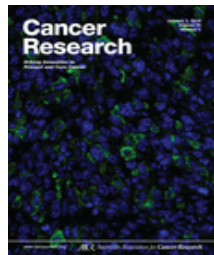


**ANTIBODY blocking immunosuppressive PD-1 checkpoint protein**

- PD-1:** Programmed Death protein
- CTLs:** Cytotoxic T-lymphocytes
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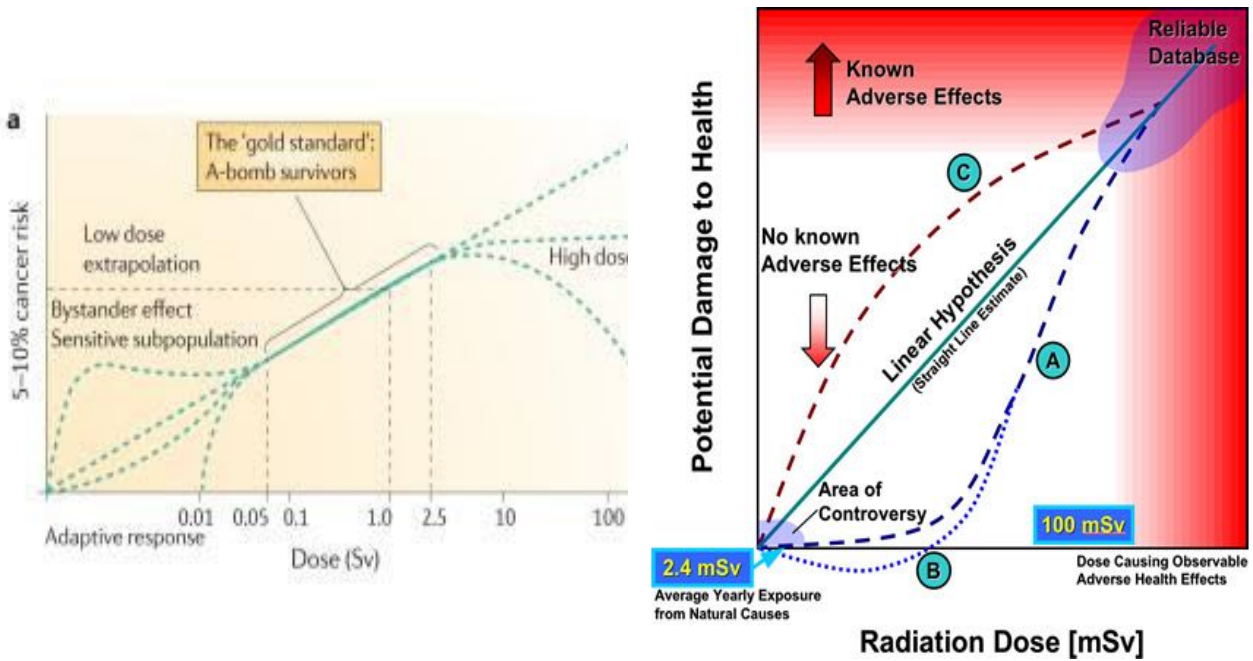


*Published in 2015*





# Incertezze sul reale rischio di effetti biologici dopo esposizione a basse dosi di radiazioni



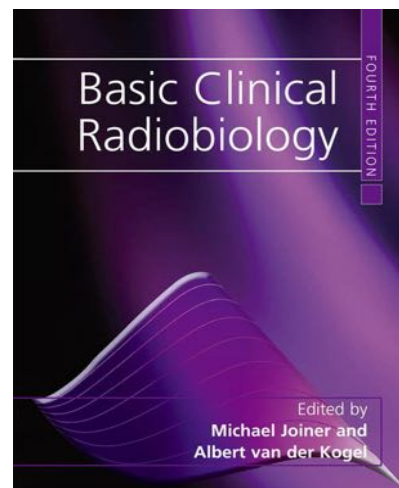
EUROPEAN SOCIETY FOR RADIOTHERAPY & ONCOLOGY (ESTRO)  
**BASIC CLINICAL RADI BIOLOGY COURSE**

ESTRO School

The Royal Australian and New Zealand College of Radiologists  
 The Faculty of Radiation Oncology

21st-24th November 2015 STAMFORD PLAZA, BRISBANE, AUSTRALIA

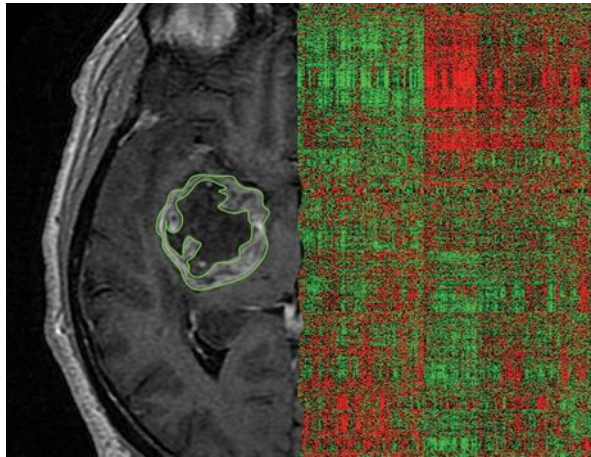
**Società Italiana di Radiobiologia**



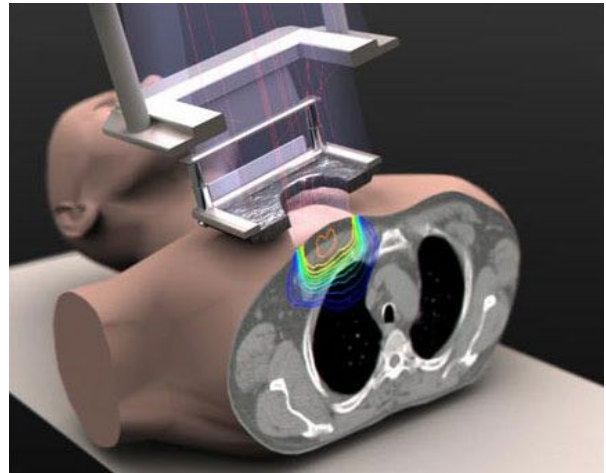


# Many others Highlights in 2015

## RADIOGENOMICS



## TECHNOLOGY




## Dalla Clinica alla Radiobiologia: due fenotipi dello stesso genotipo

**Il clinico**



**Il radiobiologo**





JOINT MEETING  
1<sup>st</sup> ADVANCED AIRB COURSE IN RADIOBIOLOGY  
BRESCIA MEETINGS IN RADIATION ONCOLOGY - 2015 EDITION

# THE POWER OF BIOLOGY

Brescia – October 8<sup>th</sup>/9<sup>th</sup>, 2015