Future impact on medical radiation protection from radiobiological advances

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Commissioner

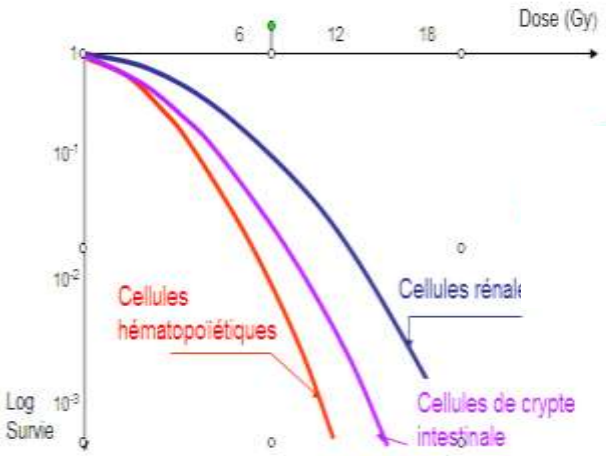
The French Nuclear Safety Authority (ASN)

International conference on radiation protection in medicine

Setting the scene for the next decade - BONN 6 Dec 2012

Factors of radiosensitivity

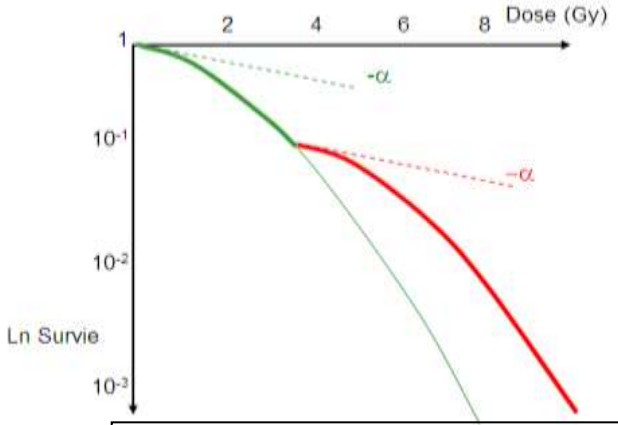
Young age of cells



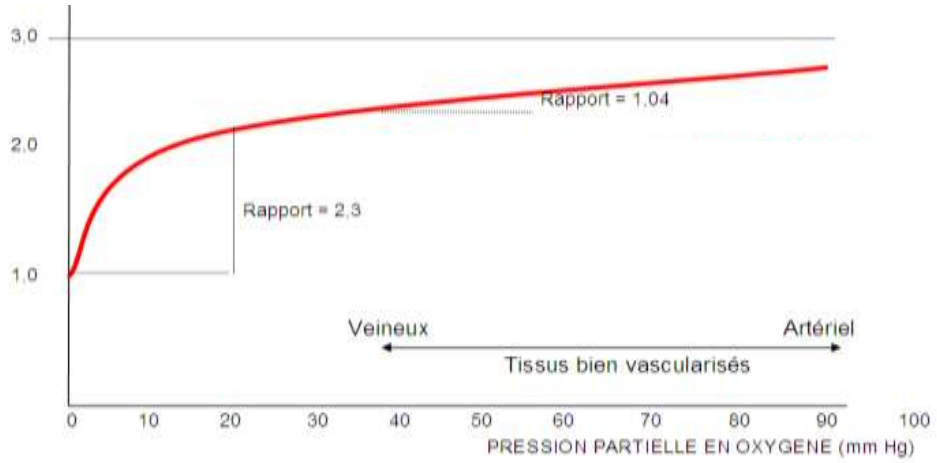
Cellular type => W_T

Dose rate

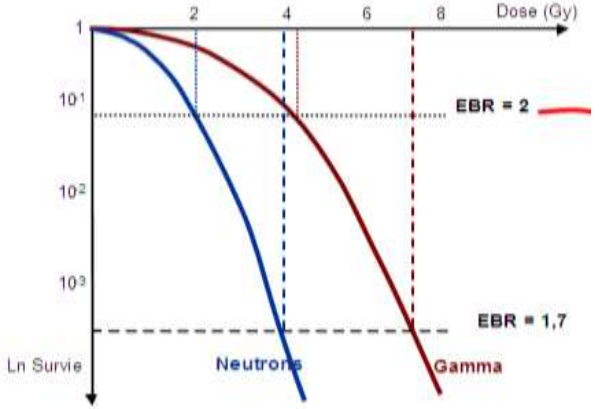
DDREF



Dose fractionation



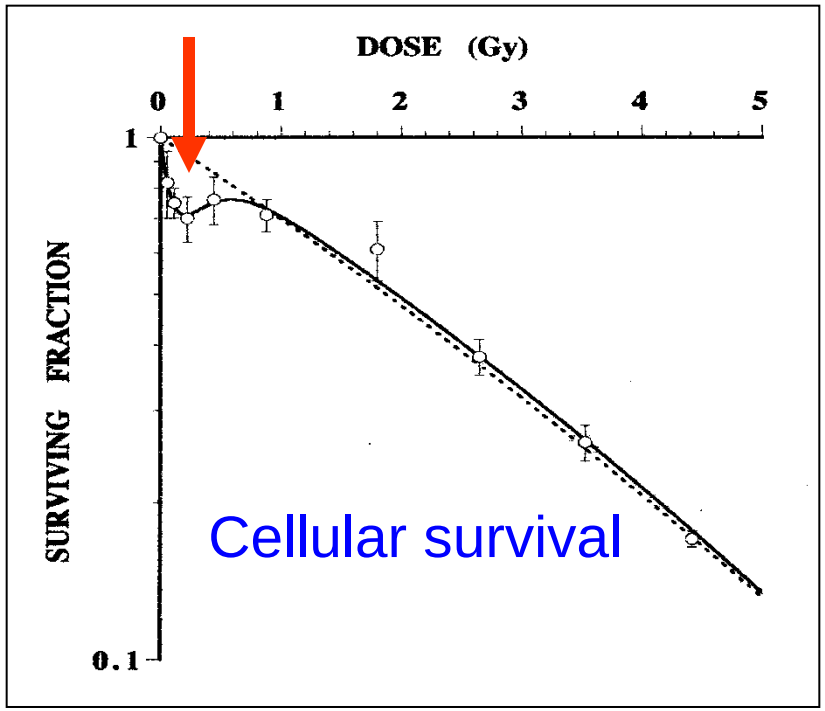
O_2 pressure



Type of radiations => W_R

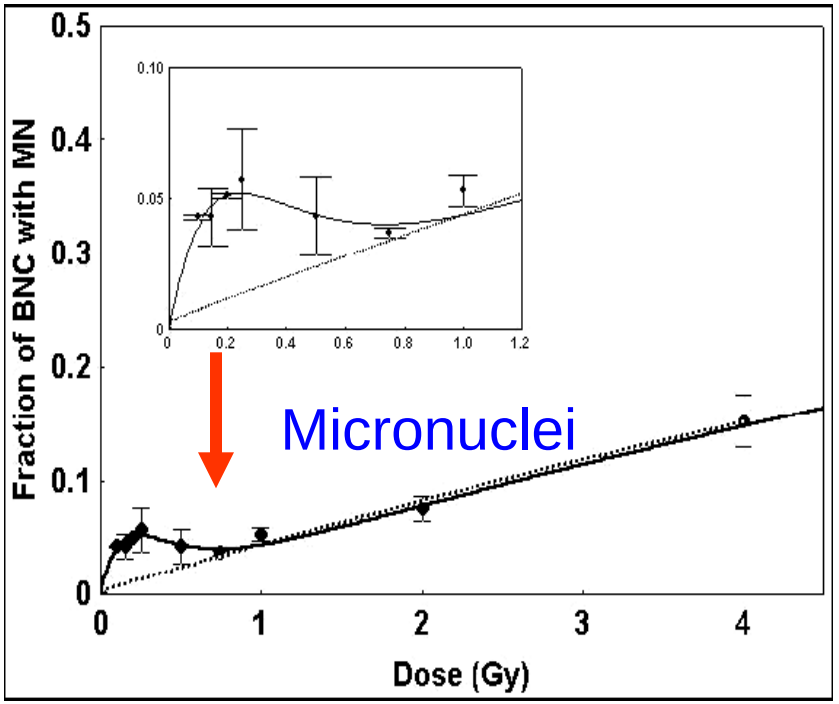
Global hyper-radiosensitivity at low doses

A significant effect between 100 and 300 mGy



Joiner & Marples 2001, Thomas 2005

- Human glial cells T98G
- X Rays 240 kV



Slonina, 2006, 2007

- Human fibroblasts & keratinocytes
- Gamma Rays

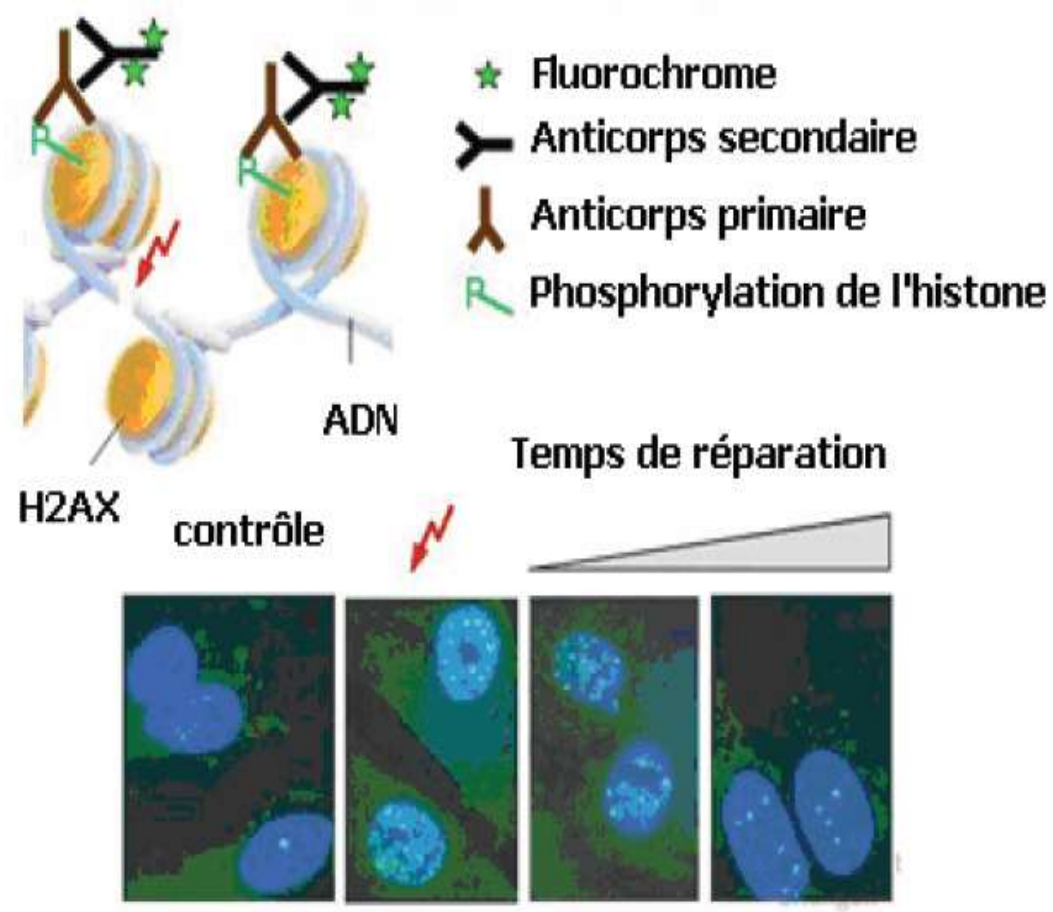
New investigation techniques

Immunofluorescence

Demonstration of DNA double strand breaks with fluorescent antibodies anti-histones γ-H2AX :

- increase sensitivity by a factor 100
- threshold : 1 mGy
- the effects of one single Xray examination can be seen !

(Rothkamm & Löbrich 2003)



Visualization of radiation induced DNA DSBs by foci γ-H2AX (green) of non transformed human fibroblasts

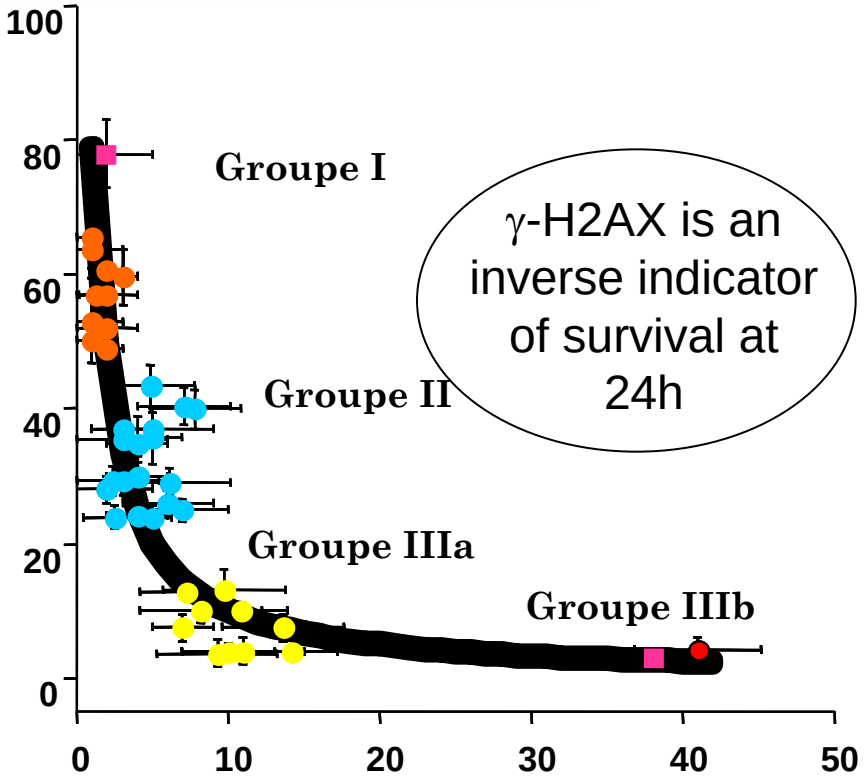
Individual radiosensitivity

- Known in radiotherapy for high doses (side effects & complications)
- Due to abnormal DNA lesion signalisation and repair
- Recently demonstrated for low doses
- ≈ 5-15% of the population
- Significant effect (range 1 to 10)

Individual radiosensitivity at 2 Gy

Characterization of 40 lines of skin fibroblasts of syndroms of known radiosensitivities (N.Foray)

% cell survival at 2 Gy



γ-H2AX is an inverse indicator of survival at 24h

% unrepaired DNA DSBs

Immunofluorescence
3 specific Antibodies

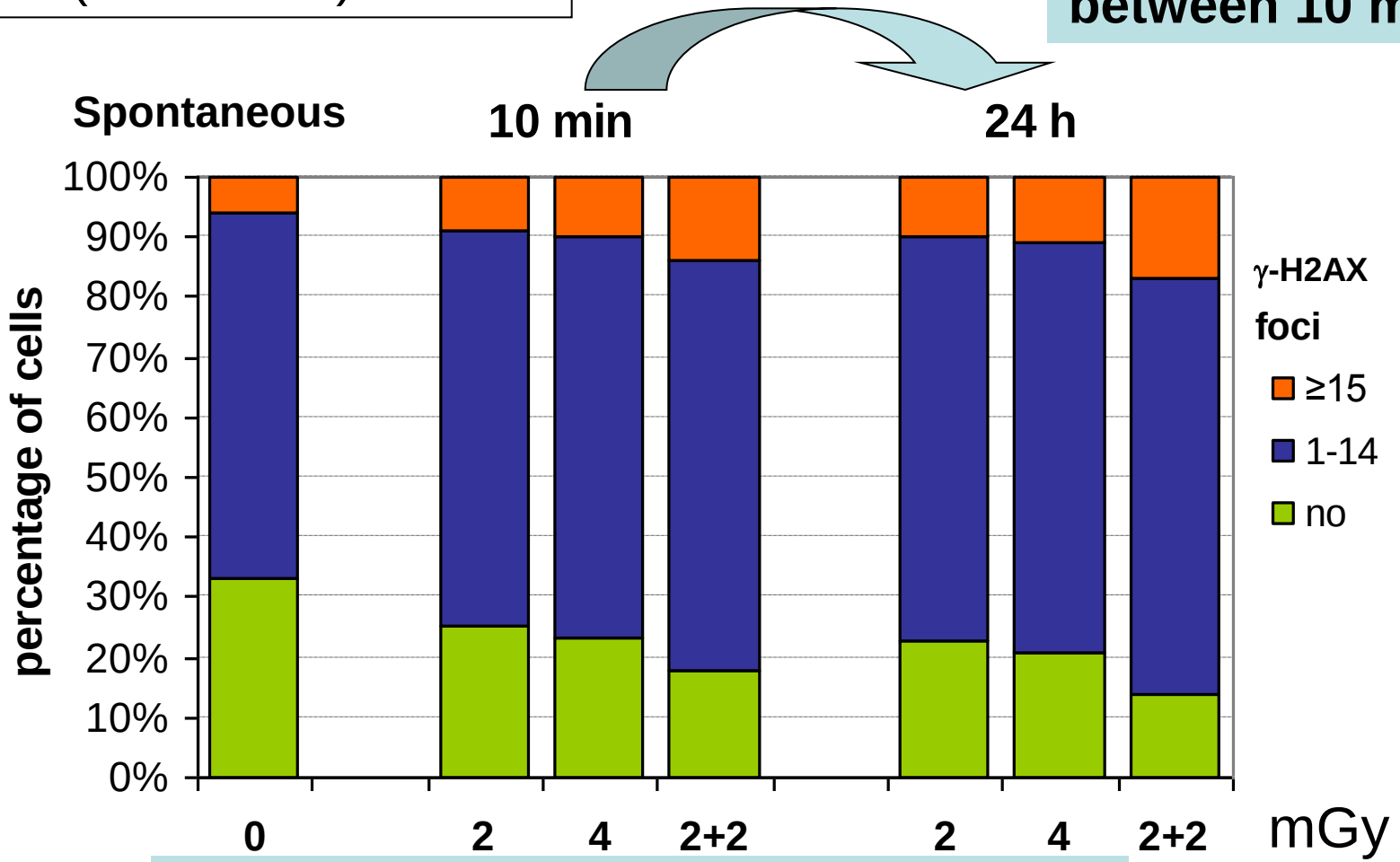
- γ-H2AX :
  recognition and accurate repair by joining
- ATM :
  signalization (from cytoplasm to nucleus)
- MRE11 :
  poor DNA DSB repair & genomic instability

3 groups of radiosensitivity and genomic instability

Individual radiosensitivity at low doses

Study on human mammary epithelium exposed ex vivo to ionizing radiations in the conditions of mammography (Colin 2011)

Induction of DNA-DSB between 10 min & 24 h

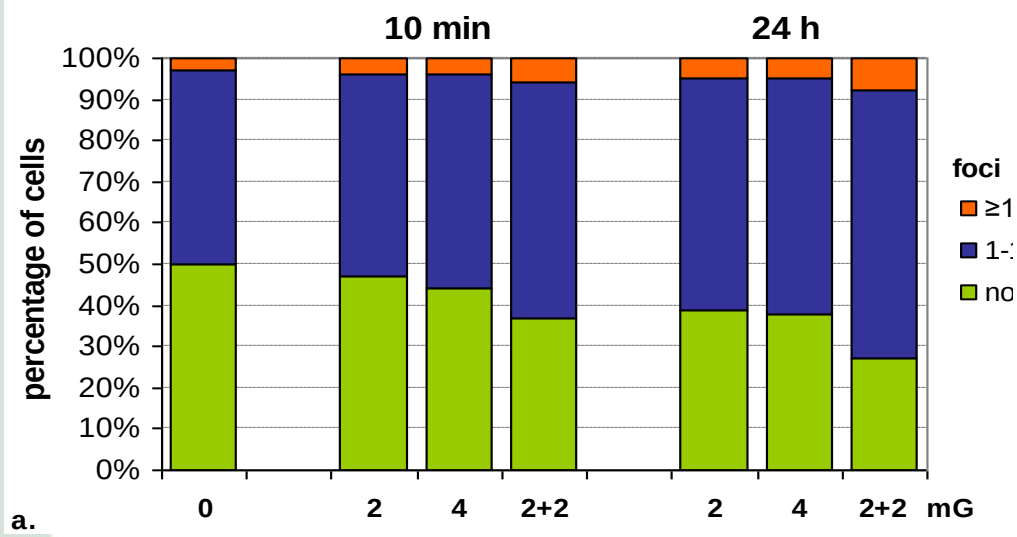


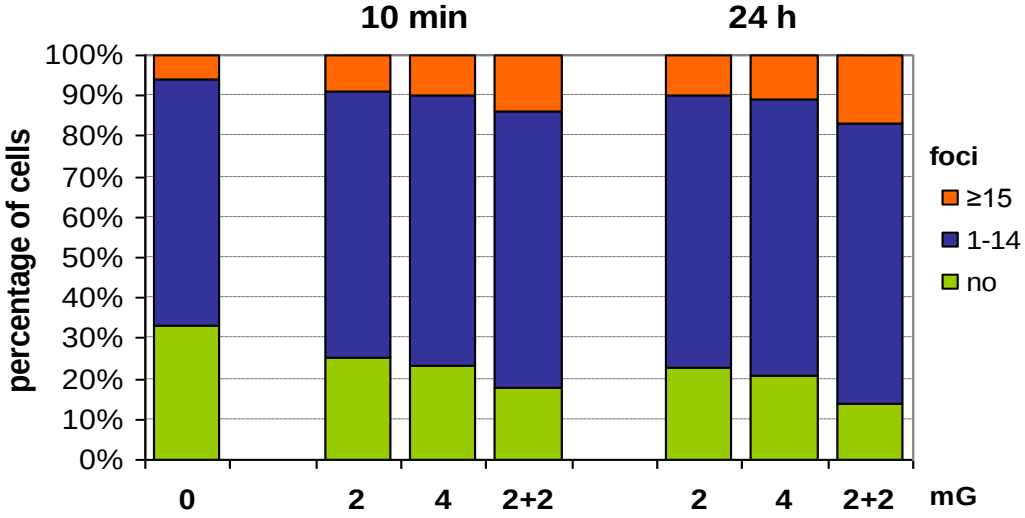
Dose effect & Repetition of doses effect

Patients with low risk of cancer / high familial risk (C.Colin 2011)

Individual radiosensitivity at low doses

3 effects increased in HR patients $p < 0{,}001$





Low risk patients

High Risk patients

Radiobiological advances paving the way for the next decade (1)

- Global hypersensitivity to low doses of medical imaging to be further explored
  - Immunofluorescence techniques
  - Effects of 30 kV mammography / 120 kV CT
  - Impact of dose rate
  - Effects of iodinated contrast agents
  - Global hypersensitivity and bystander effect
  - Comprehension of pathways : DNA-PK…

Radiobiological advances paving the way for the next decade (2)

- Individual radiosensitivity to low doses of medical imaging to be further explored
  - Signaling & repair pathways of DNA lesions : immunofluorescence, other techniques …
  - Lymphocyte CD4/CD8 apoptosis
  - Other biomarkers : cytogenetic, polymorphism… ?
  - Impact of repetition of exposure after short interval (second view)
  - % population : 5-15 % ? … 20 %
  - Transfer from research laboratory to routine testing

Radiobiological advances paving the way for the next decade (3)

- Individual radiosensitivity / oncogenesis
  - DNA injuries : physicochemical process
  - DNA lesions result from poor signalization and repair of injuries
  - DNA lesions do not mean cancer but cancers result from poor combinations of DNA lesions (how many?)
  - Individual radiosensitivity and oncogenesis have many mechanisms in common (but do not superimpose completely) : studying one = studying the other

Radiobiological advances paving the way for the next decade (4)

- Need to focus on key issues in the context of increase medical doses
  - Most sensitive patients : children, family risk of cancer patients, hyper-radiosensitive patients, …
  - Most sensitive tissues : breast, thyroid…
  - Most dosing examinations : CT (neck, chest, abdomen & pelvis)
  - Most frequent examinations : CT, mammography
  - Subgroup of patients with repetition of examinations (screening) and good life expectancy : women (breast), cardiac patients, backbone problems

Radiobiological advances paving the way for the next decade (5)

- Probable need to review the Radiation Protection system
  - So far the RP system takes into account sensitivity factors : age, W_R, W_T, O_2, fractionation, DDREF
  - Need to include ASAP individual radiosensitivity as a factor : W_S and global sensitivity to low doses
  - Justification and optimization remain as milestones because the risk of medical exposure is very low but is (much) greater in radiosensitive patients and in patients with repeated exposures in whom epidemiology may become demonstrative !