Biological effects of ionizing radiation

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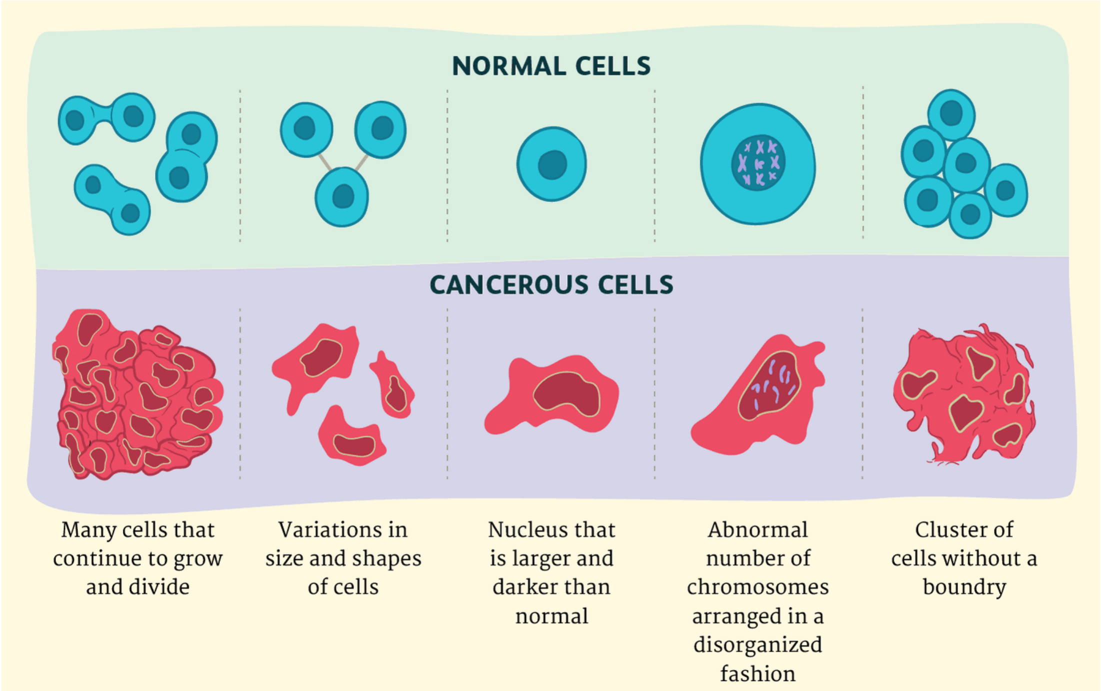
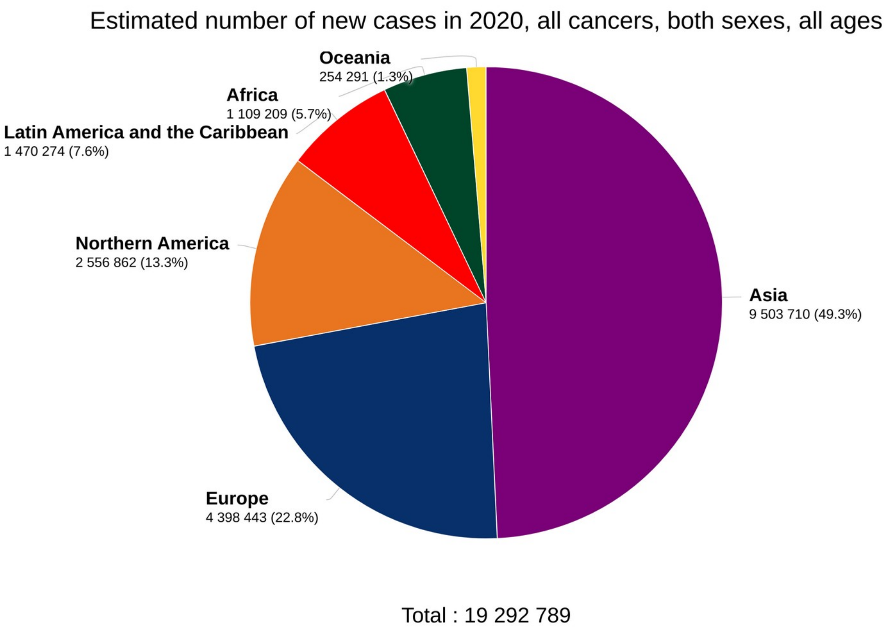
IPPOG-INFN International Particle Therapy Masterclass

Cancer in pills

Random mutation in cells

Uncontrolled proliferation





Still one of the leading cause of death worldwide

Radiation treatment

First idea at the end of XIX century:

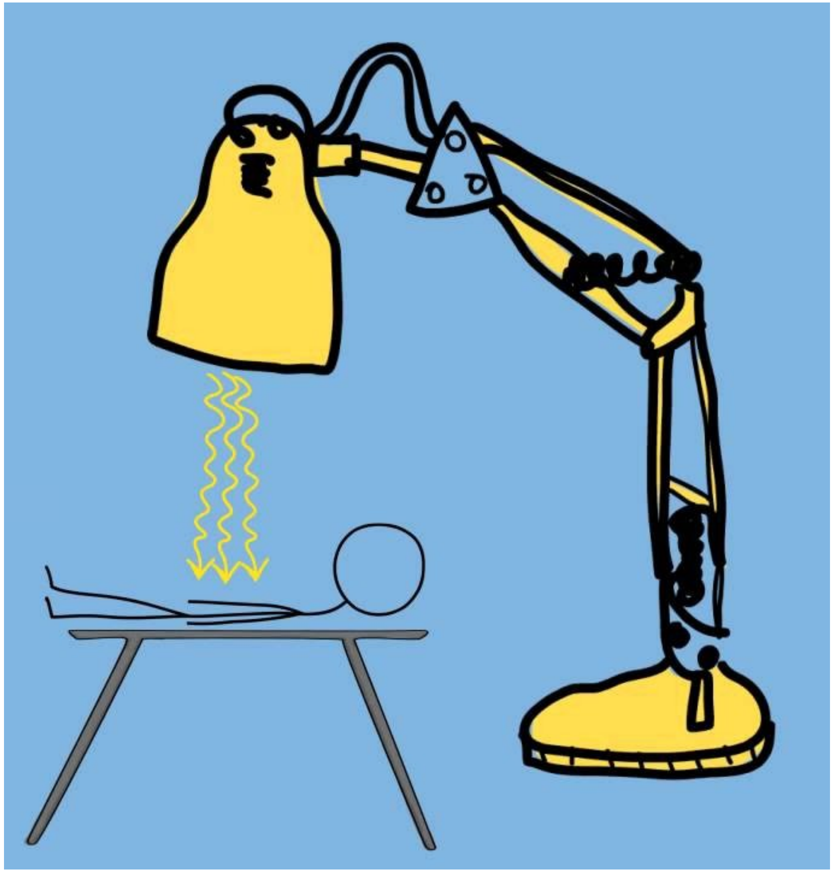
- Roentgen-therapy
- Radium salt applications/baths

But what does it mean to “treat” cancer with radiations?

Damage cancerous cell structures in order to

Kill them (directly/apoptosis)

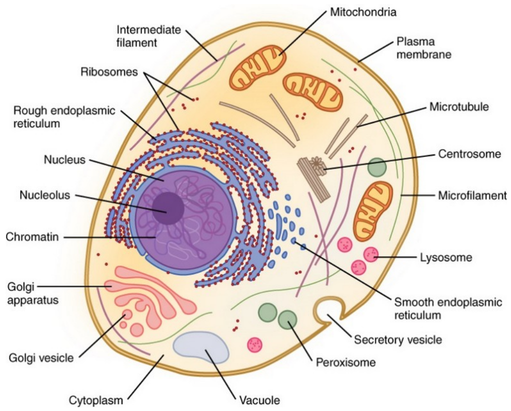
Remove their clonogenic capability

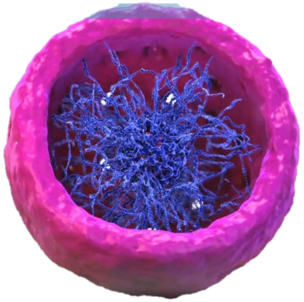


Radiation damage

How does radiation damage cells? **Ionization** → break molecular bonds in DNA

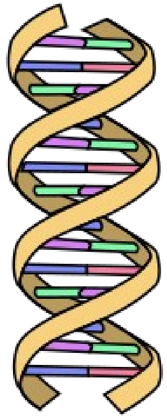
Cell





Nucleus

Chromosome

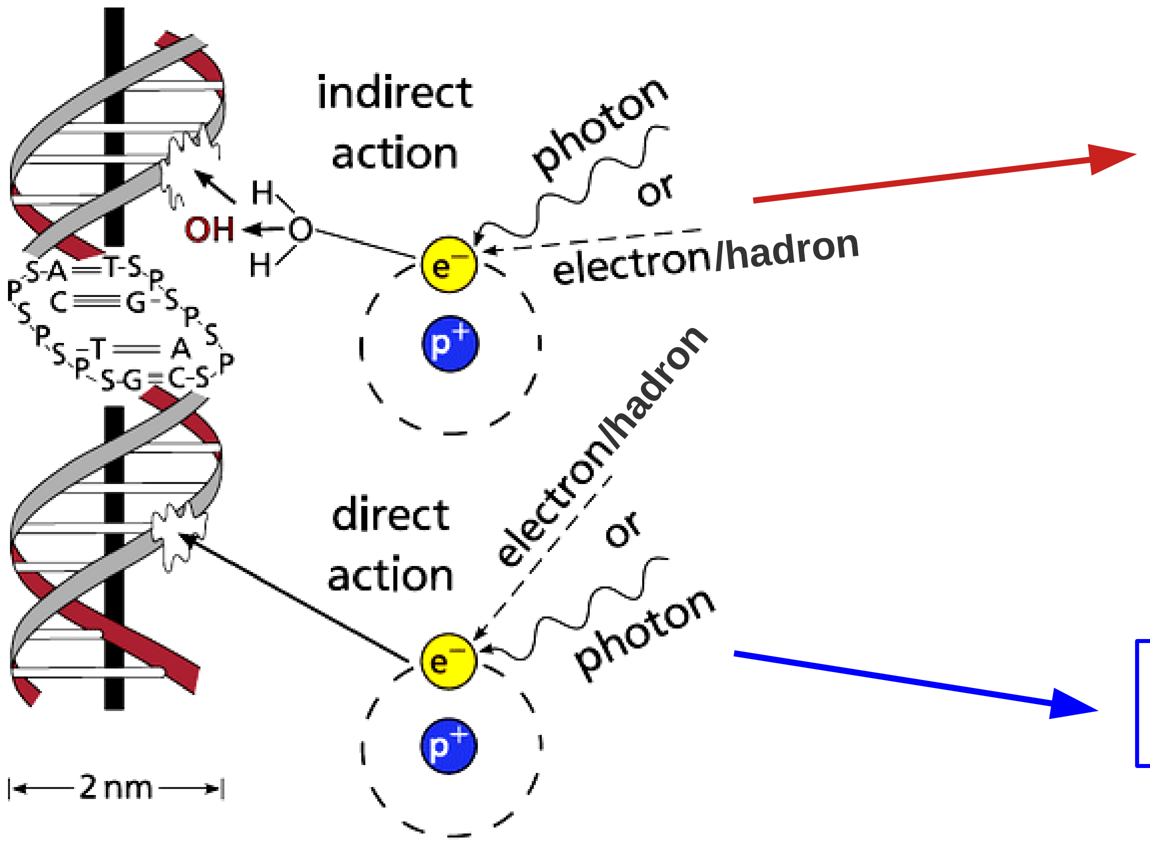


DNA

Complex molecule, difficult to repair:

1) DNA strand break (single/double)
2) N base alteration
3) Sugar destruction
4) Cross-bonds

DNA damage



Indirect

Radiation hits water

⇩

Production of free radicals

⇩

DNA damage

Direct

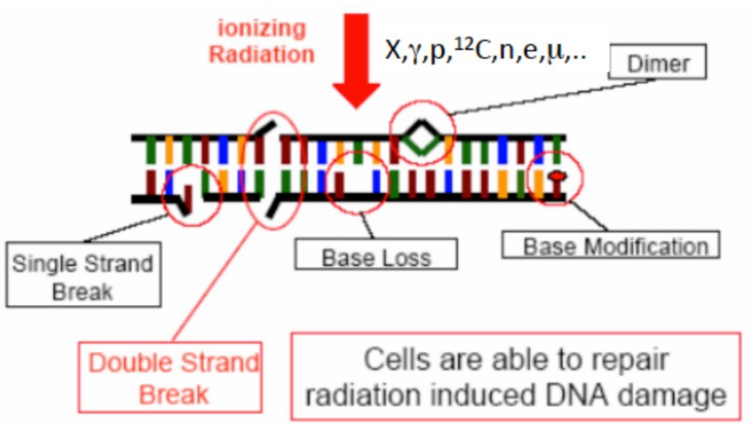
Radiation hits DNA

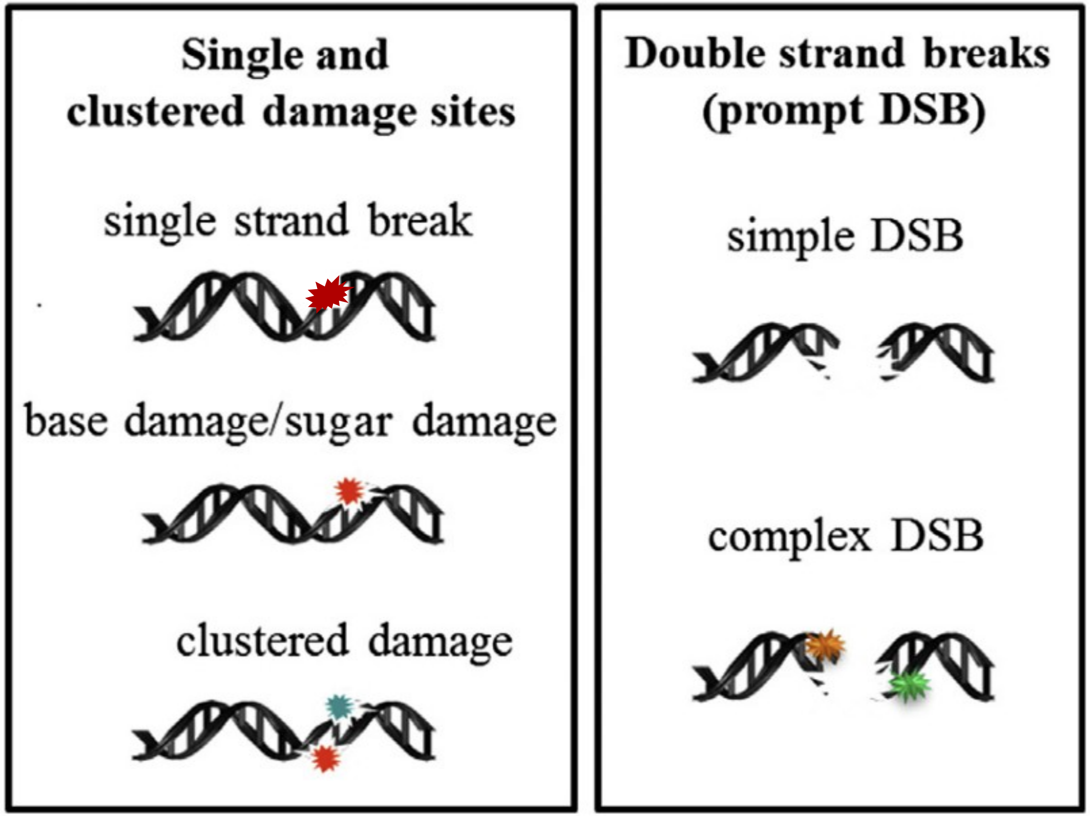
Direct DNA damage

DNA is found in cell nucleus and mitochondria  

Different types of direct damage

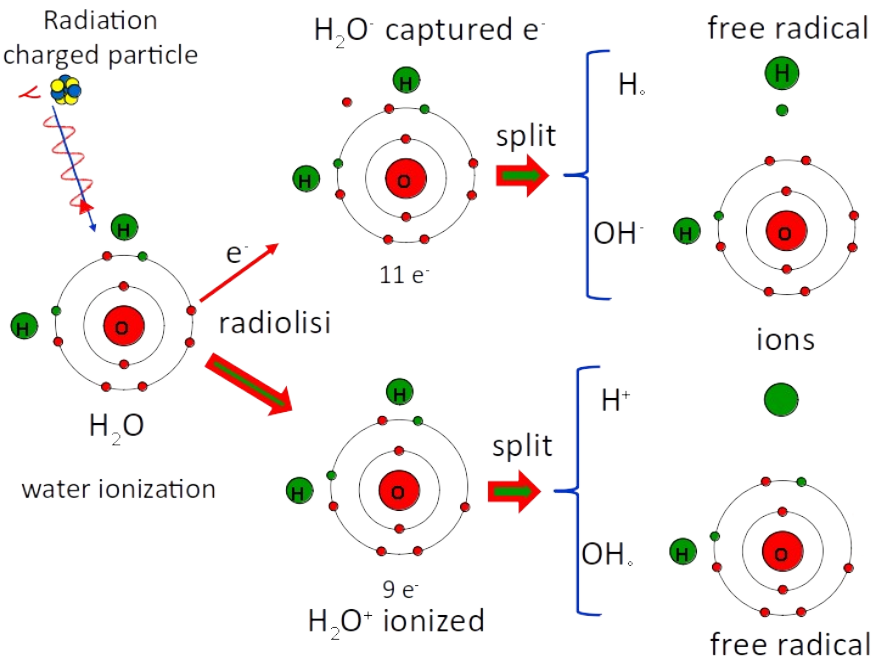
Usually only SSB is repairable





Indirect damage

DNA is a very small target, but not the nucleus!



- Ionization of bio-molecules (mainly H_2O)
- Production of free radicals → highly reactive
- Reaction with other molecules

Ex. $H_2O \rightarrow OH^\circ, H^\circ$ radicals $\rightarrow H_2O_2$

$\rightarrow HO_2$ (high [O])

Free radicals are the main responsible for ionizing radiation damage to biological tissues

Absorbed dose

How do we measure radiation exposure? **Absorbed Dose**

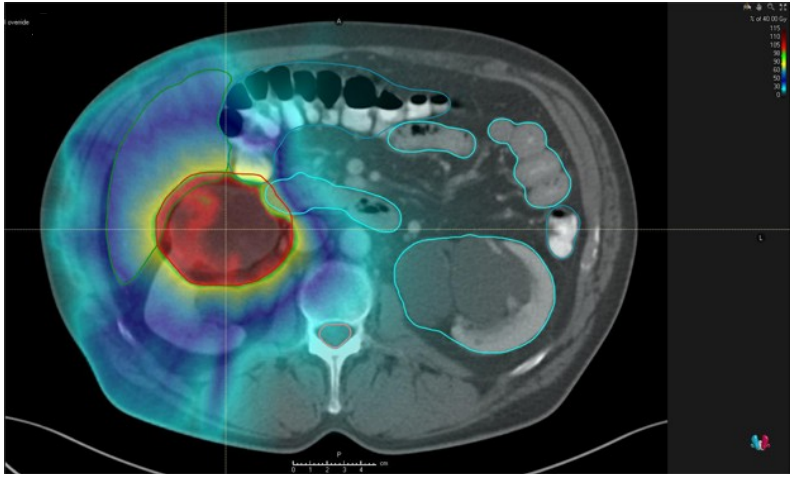
$$D = \frac{dE}{dm} \qquad \rightarrow \qquad [D] = 1Gy = \frac{1J}{1kg}$$

Energy deposited by ionizing radiation per kg of mass

Dose does NOT measure damage, only energy deposition

Typical treatment dose ~ 60-70 Gy

Radiotherapy treatment dose distribution



What influences damage?

Very complex topic, but mainly:

- Dose
- Type of radiation (X-rays, electrons, hadrons, etc.)
- Tissue radiosensitivity
- Oxygen concentration (up)
- Tissue cell replication (up)
- Cell differentiation (down)
- Cell cycle
- Many more…

Effective dose

- Measured in Sievert (Sv)
- Measures radiation damage/effect!

Radiation damage effects

SOMATIC
(exposed person)

GENETIC
(heirs, gonads)

Deterministic
$Effect \propto Dose\ over\ threshold$

- Erythema, radiation poisoning, etc.
- Very very high threshold

Stocastic
$Probability\ of\ effect \propto Dose$

- Mutations, cancer, etc.
- Very very low probability

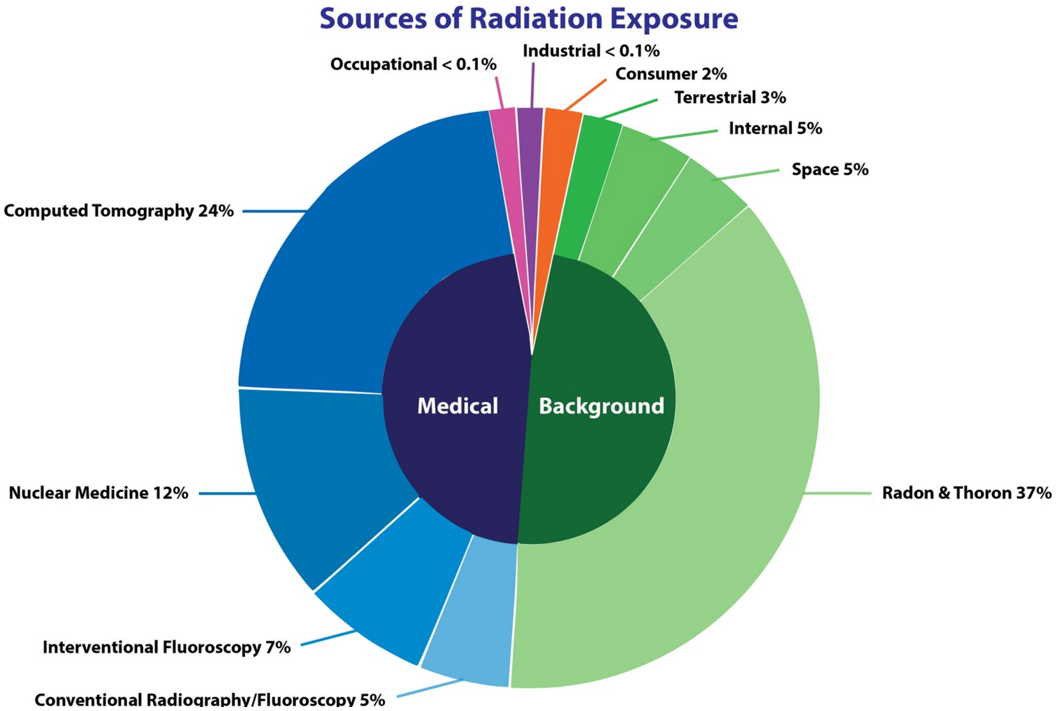
Radiation damage effects

Remember that we are continuously exposed to radiation

- Cosmic rays
- Natural radioactivity (food, soil, etc…)
- Nuclear medicine and diagnostics
- Etc…

That sounds like a lot of stuff…

should we worry about this??

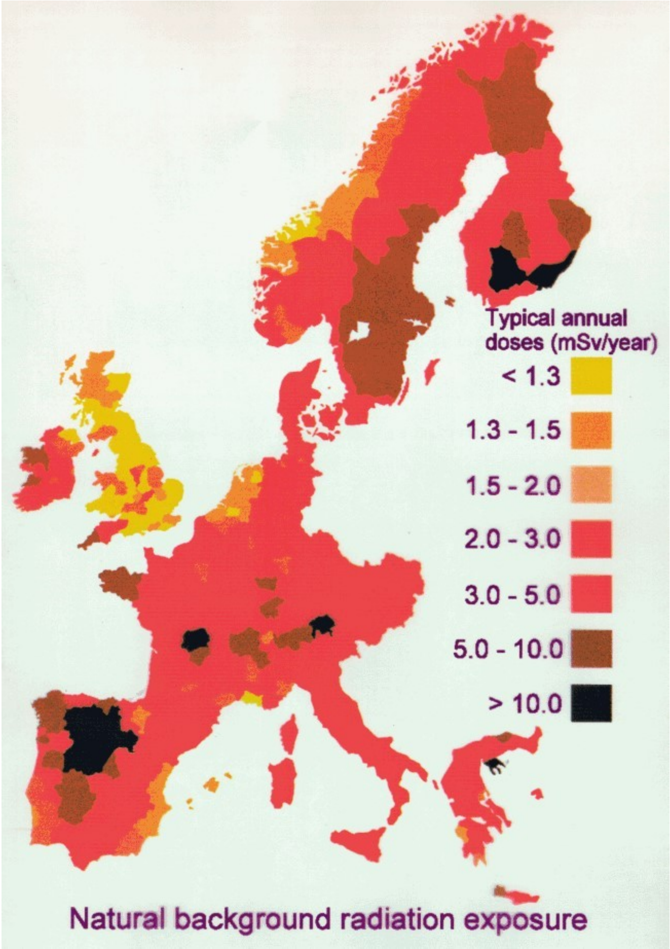


Radiation exposure limits

Quantity makes the poison!

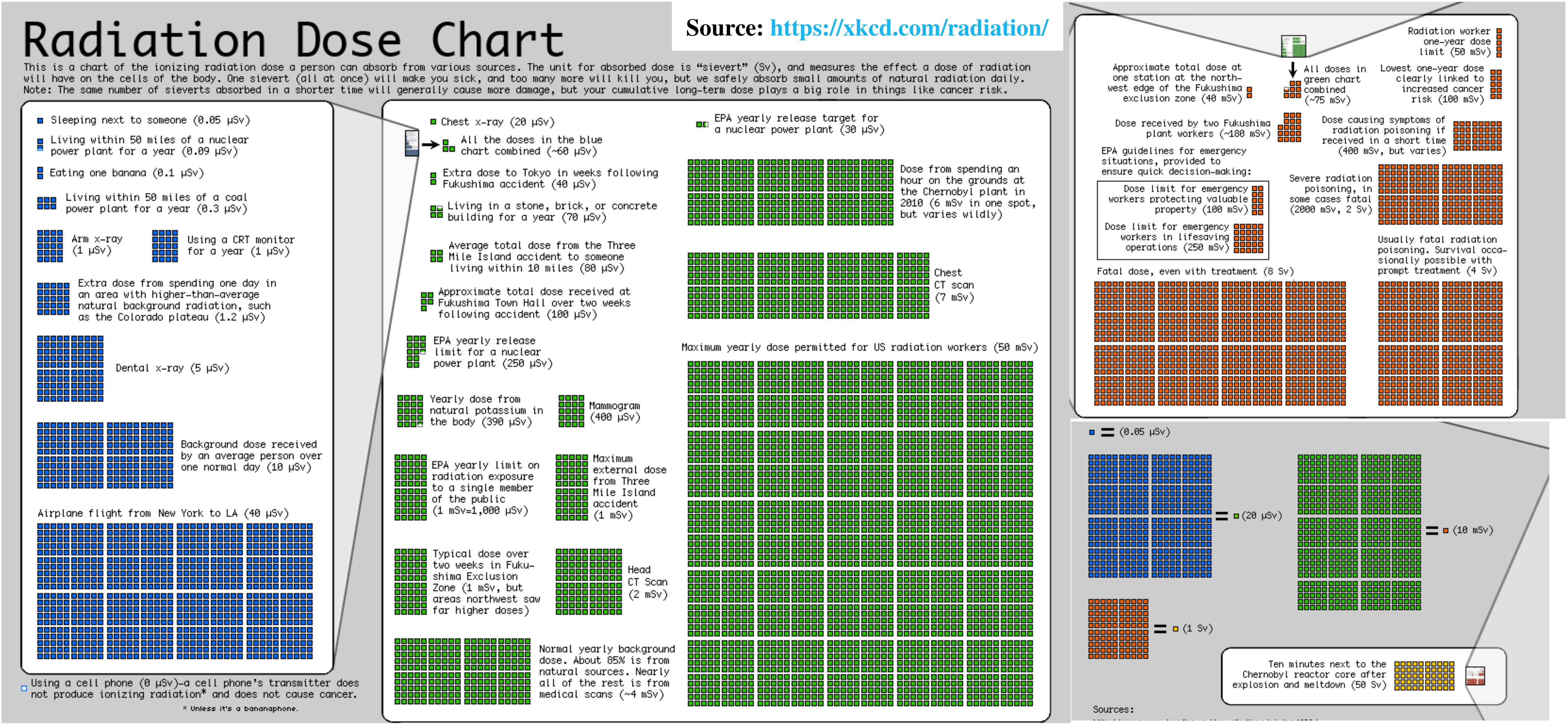
- Radiation exposure is well known and strictly regulated by now
- Yearly limits for public (1 mSv) and workers (6-20 mSv) way below threshold of proven increased cancer probability (200 mSv)
- Natural background is not the same everywhere!

But what do these numbers mean?



Some examples

Source: https://xkcd.com/radiation/



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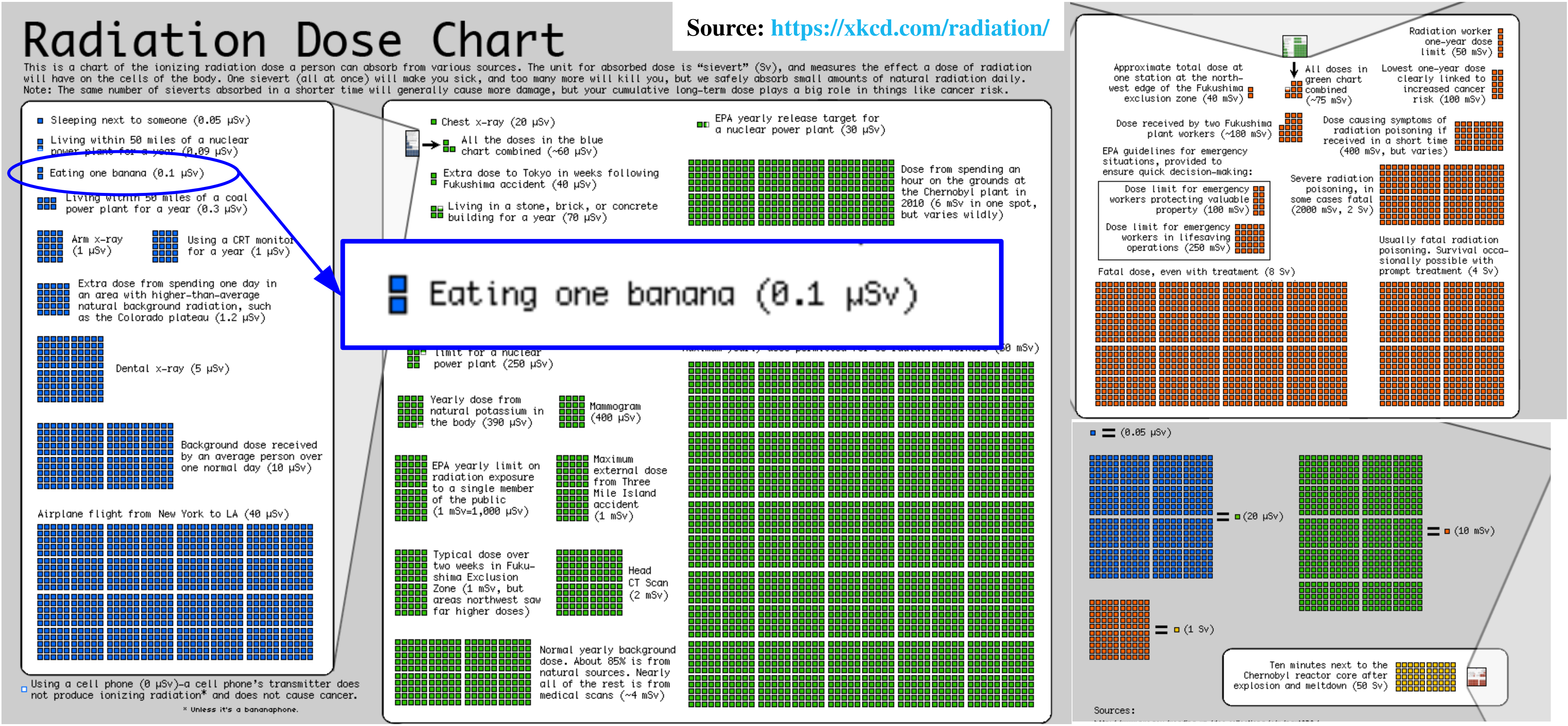

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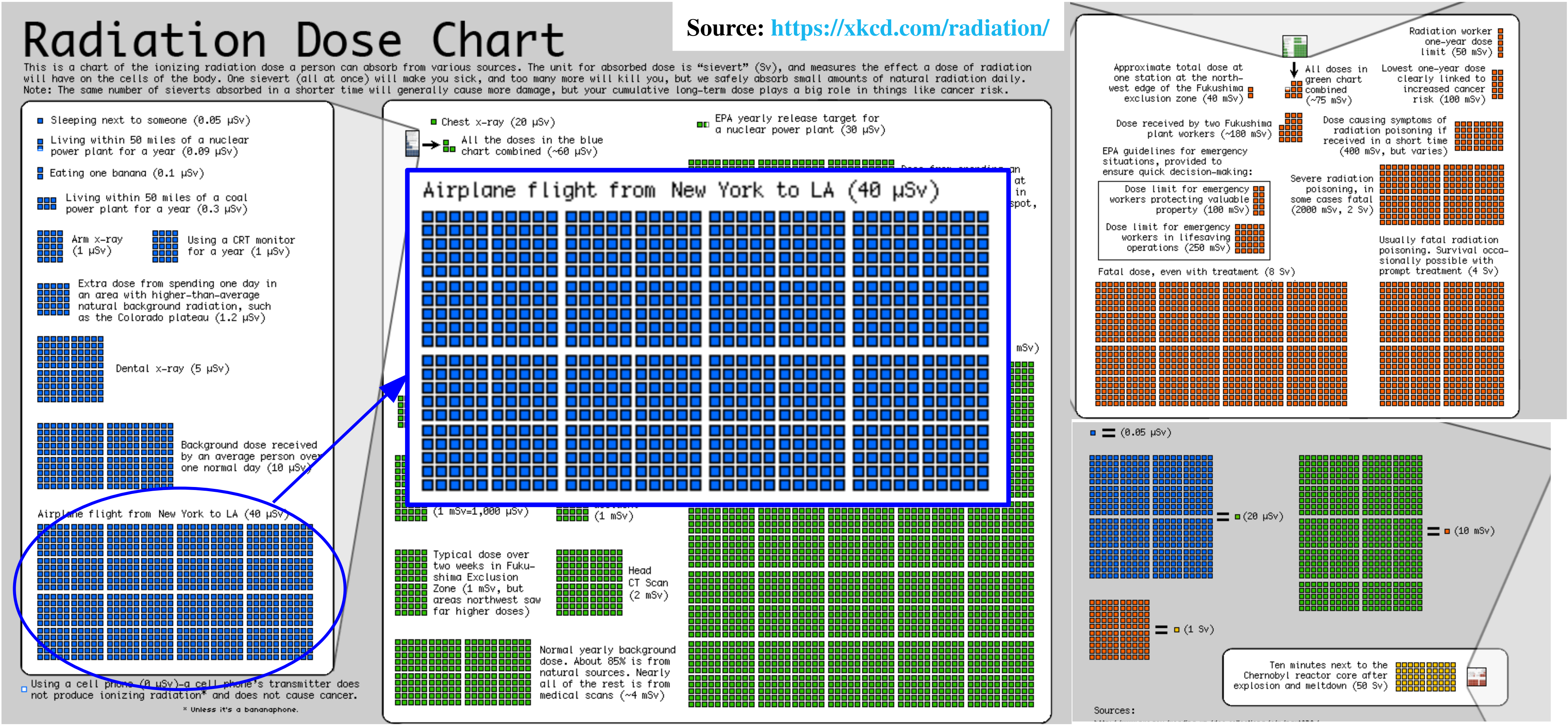

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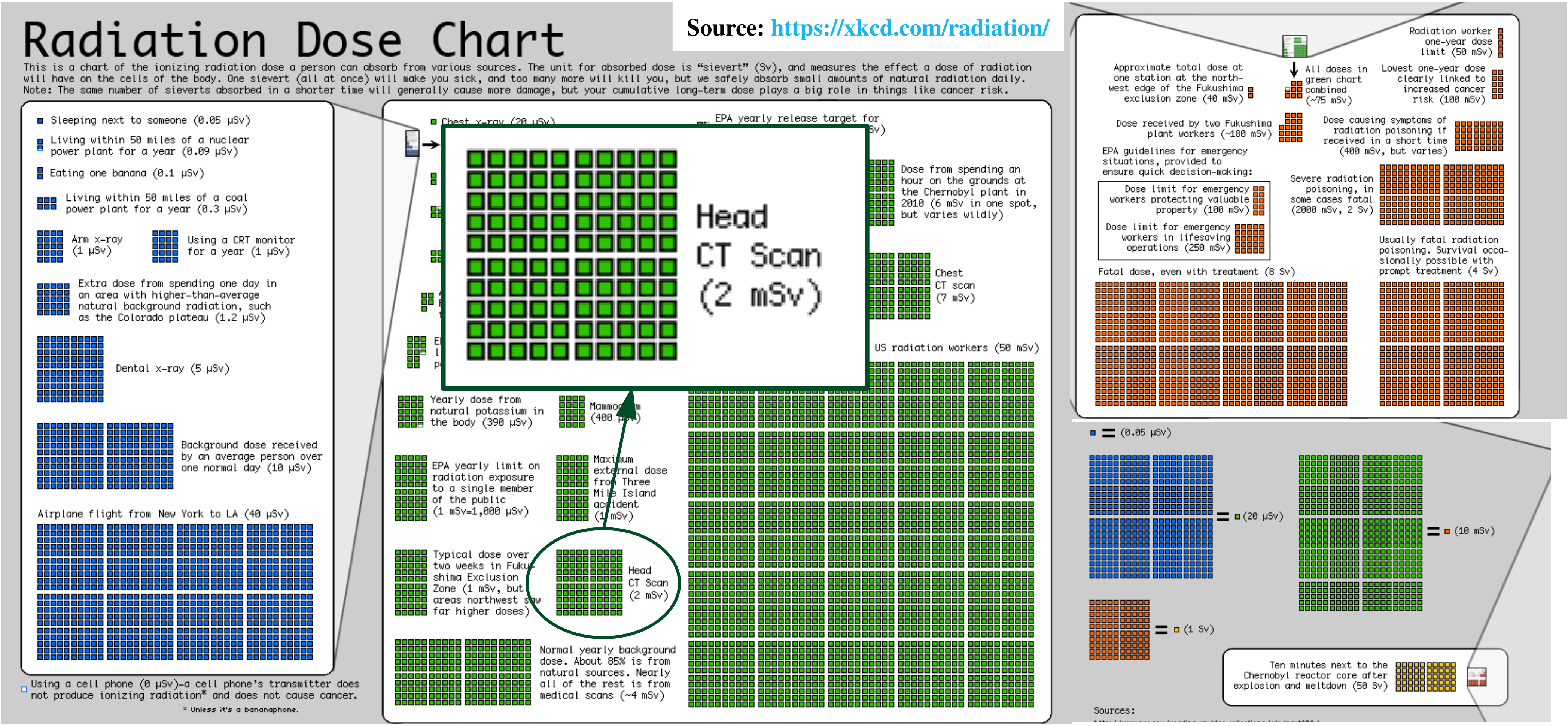

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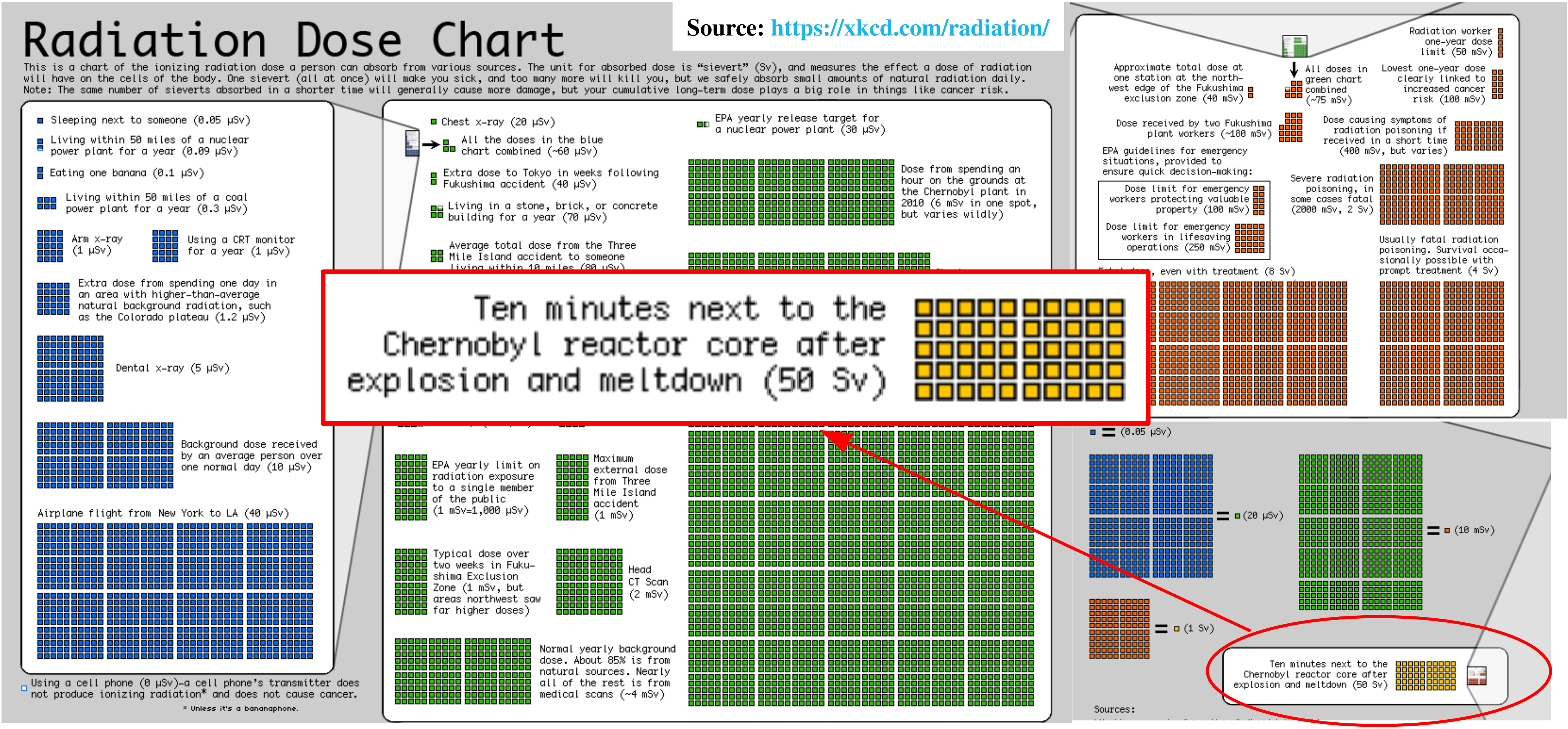

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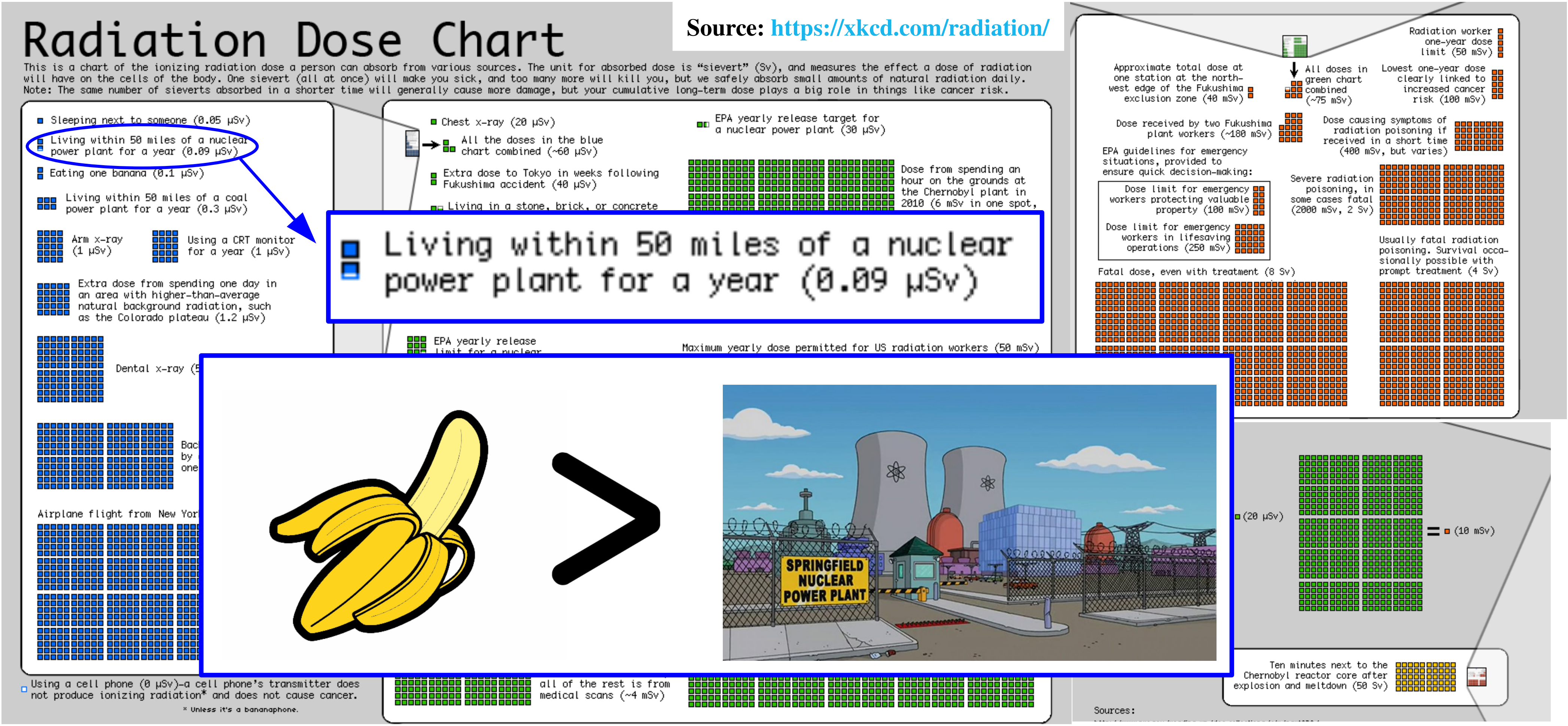


Radiation damage effects

So now a question...

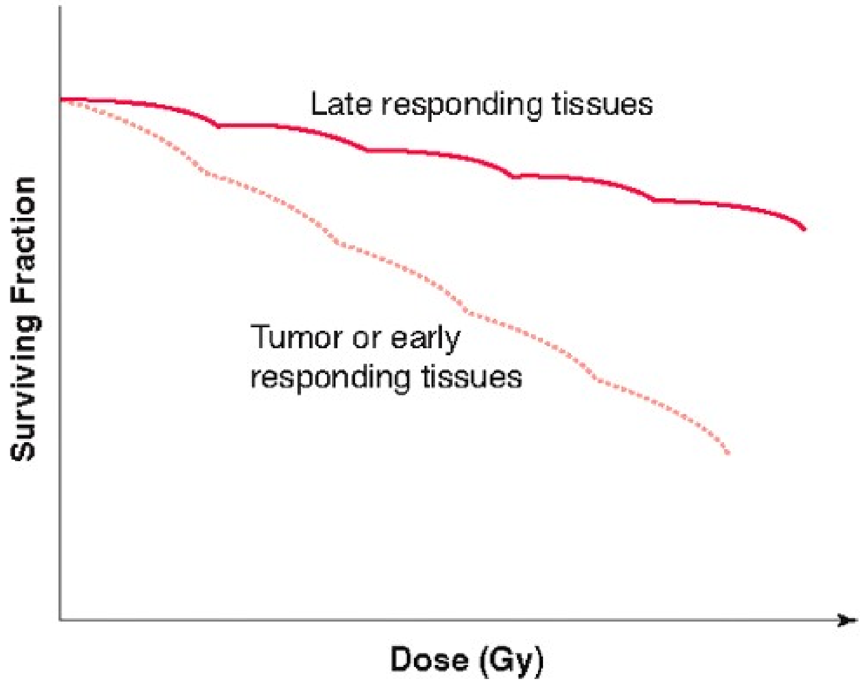
Knowing that people in Hiroshima received about 6 Gy of dose…

then why do we ask for 60-70 Gy in a normal radiation therapy treatment plan??

Dose fractionation and localisation

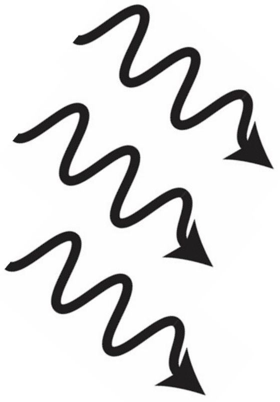
Total dose is fractioned and localised!!

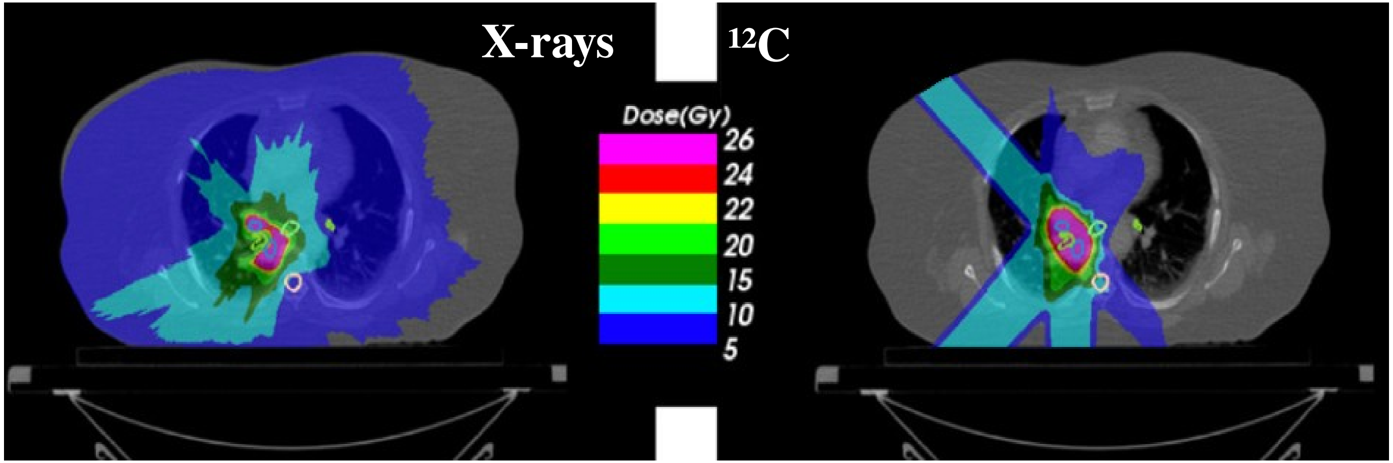
- **We don’t hit the whole body of the patient**
- Healthy tissue better recover the radiation damage
- Cancer cells are less efficient in reparing the damage
- Radio resistent cancer cell move to a less resistent phase of the cell cycle
- Hypoxic cancer tissue can re-oxygenate improving the radio sensitivity
- **Danger of providing the dose all together**

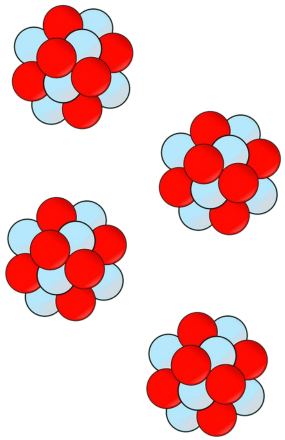


Optimization of exposure for treatment!

Radiotherapy vs Hadrontherapy







- More dose to healthy tissues
- Less conformal dose
- Indirect damage dominant
- More dependent on oxygen effect
- Way easier to carry out

- Less dose to healthy tissues
- More conformal dose (better for OAR)
- Direct damage dominant
- Less dependent on oxygen effect
- More difficult (and expensive) to carry out

Hadrontherapy vs Radiotherapy

Hadrontherapy works!

Indication	End point	Results photons	Results carbon HIMAC-NIRS	Results carbon GSI
Chordoma	local control rate	30 – 50 %	65 %	70 %
Chondrosarcoma	local control rate	33 %	88 %	89 %
Nasopharynx carcinoma	5 year survival	40 -50 %	63 %	
Glioblastoma	av. survival time	12 months	16 months	
Choroid melanoma	local control rate	95 %	96 % (*)	
Paranasal sinuses tumours	local control rate	21 %	63 %	
Pancreatic carcinoma	av. survival time	6.5 months	7.8 months	
Liver tumours	5 year survival	23 %	100 %	
Salivary gland tumours	local control rate	24-28 %	61 %	77 %
Soft-tissue carcinoma	5 year survival	31 – 75 %	52 -83 %	

Similar to protons

Table by G. Kraft 2007

Results of carbon ions

Geneva - 16.10.13 - UA

But it is not our only weapon...

Any question?