





Biological effects of ionizing radiation

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IPPOG-INFN International Particle Therapy Masterclass

Cancer in pills

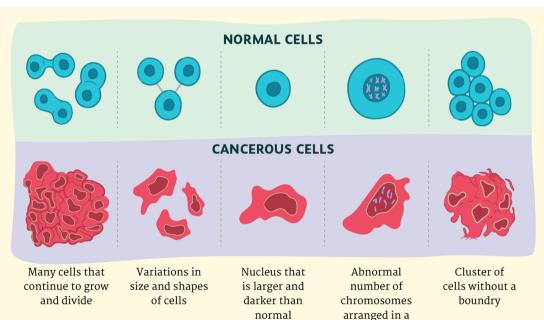


Random mutation in cells

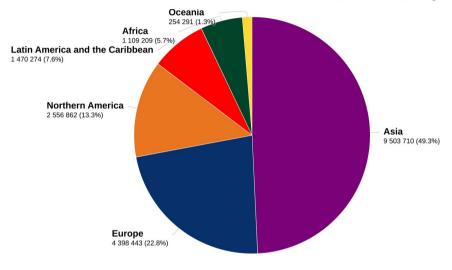


Uncontrolled proliferation

disorganized fashion



Estimated number of new cases in 2020, all cancers, both sexes, all ages



Total: 19 292 789

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

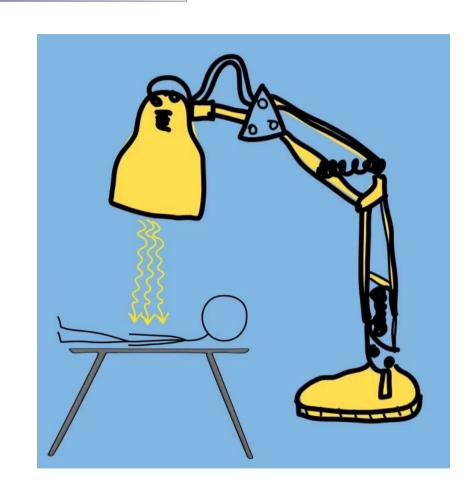
But what does it mean to "treat" cancer with radiations?

Damage cancerous cell structures in order to



Kill them (directly/apoptosis)

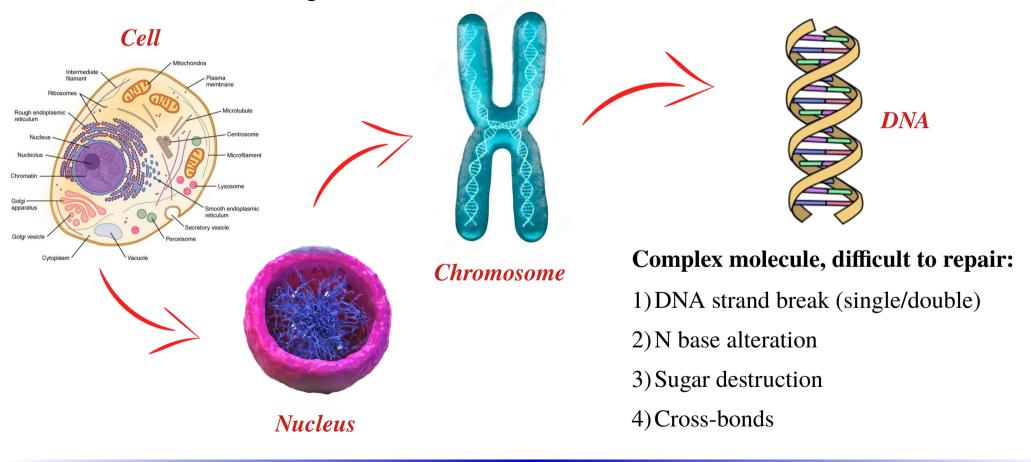
Remove their clonogenic capability



Radiation damage

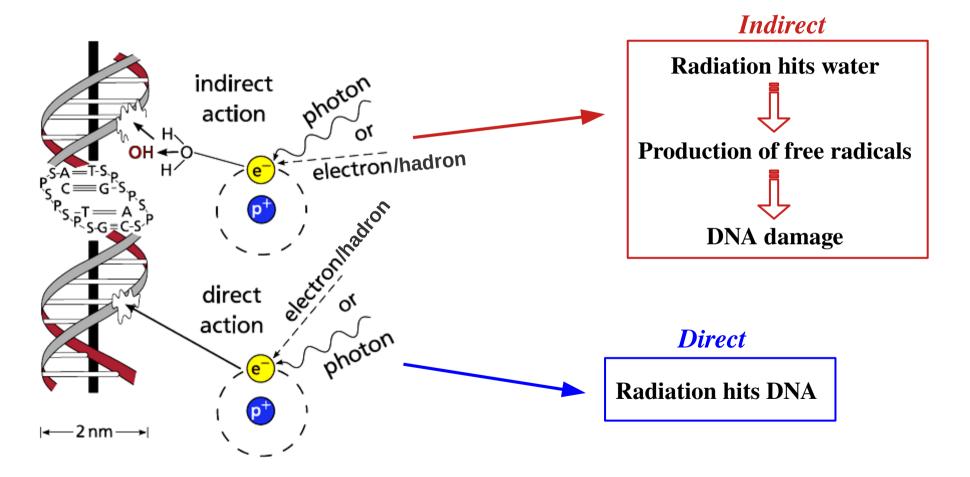


How does radiation damage cells? **Ionization** → break molecular bonds in DNA



DNA damage





Direct DNA damage

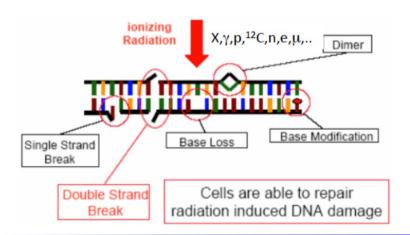


DNA is found in cell nucleus and mitochondria



Different types of direct damage

Usually only SSB is repairable



Single and clustered damage sites

single strand break



base damage/sugar damage



clustered damage



Double strand breaks (prompt DSB)

simple DSB





complex DSB

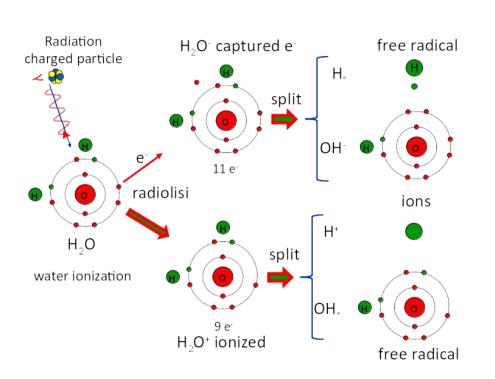




Indirect damage



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





- Ionization of bio-molecules (mainly H₂O)
- Production of free radicals → highly reactive
- Reaction with other molecules

Ex. $H_2O \rightarrow OH^{\circ}$, H° 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



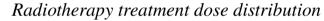
How do we measure radiation exposure? **Absorbed Dose**

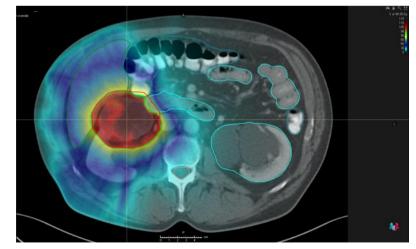
$$D = \frac{dE}{dm} \qquad \to \qquad [D] = 1Gy = \frac{1J}{1kg}$$

Energy deposited by ionizing radiation per kg of mass

Dose does NOT measure damage, only energy deposition

Typical treatment dose ~ 60-70 Gy



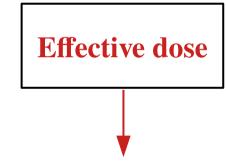


What influences damage?



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...



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

Radiation damage effects



SOMATIC

(exposed person)



Deterministic

 $Effect \propto Dose \ over \ threshold$



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

GENETIC

(heirs, gonads)



Stocastic

Probability of effect $\propto Dose$

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

Radiation damage effects

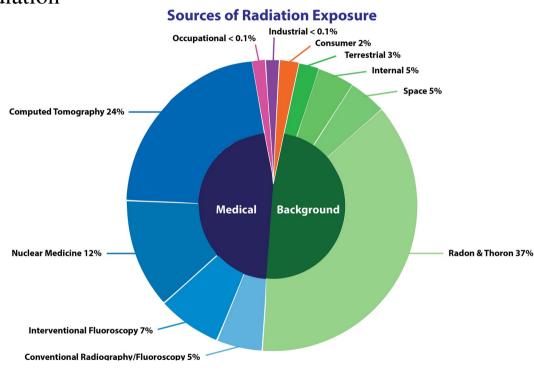


Remember that we are continuously exposed to radiation

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

That sounds like a lot of stuff... should we worry about this??





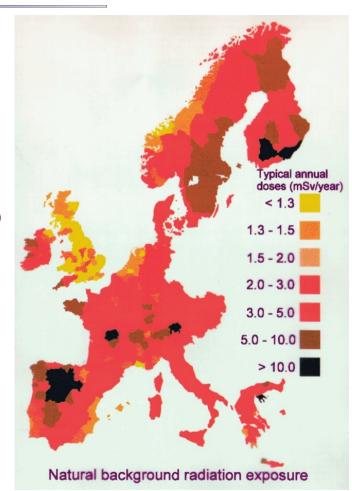
Radiation exposure limits



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?

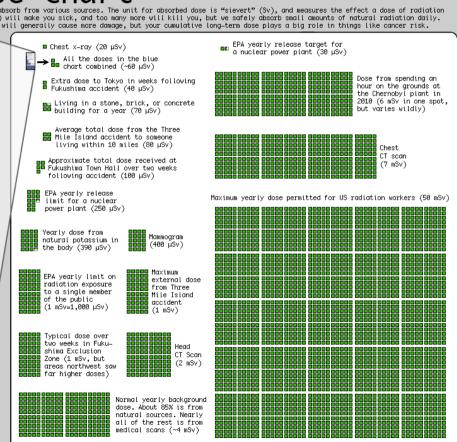


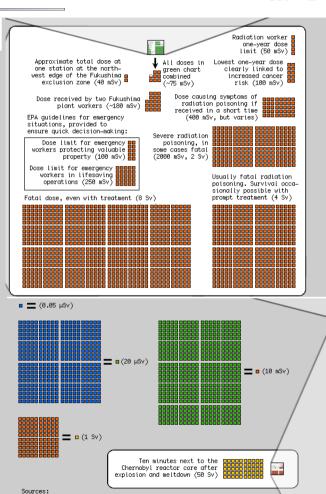


Radiation Dose Chart

This is a chart of the ionizing radiation dose a person can absorb from various sources. The unit for absorbed dose is "sievert" (Sv), and measures the effect a dose of radiation will have on the cells of the body. One sievert (all at once) will make you sick, and too many more will kill you, but we safely absorb small amounts of natural radiation daily. Note: The same number of sieverts absorbed in a shorter time will generally cause more damage, but your cumulative long-term dose plays a big role in things like cancer risk.

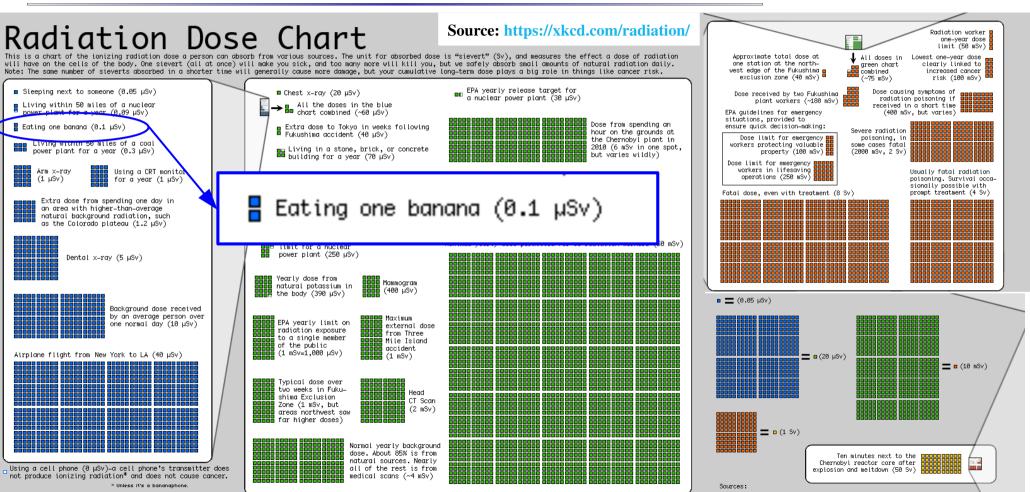
- Sleeping next to someone (0.05 µSv) Living within 50 miles of a nuclear power plant for a year (0.09 uSv) Eating one banana (0.1 μSv) Living within 50 miles of a coal power plant for a year (0.3 µSv) Arm x-ray Using a CRT monitor (1 µSv) for a year (1 uSv) Extra dose from spending one day in an area with higher-than-average natural background radiation, such as the Colorado plateau (1.2 µSv) Dental x-ray (5 µSv) Background dose received by an average person over one normal day (10 uSv) Airplane flight from New York to LA (40 µSv)
- Using a cell phone (0 µSv)-a cell phone's transmitter does not produce ionizing radiation* and does not cause cancer. × Unless it's a bananaphone



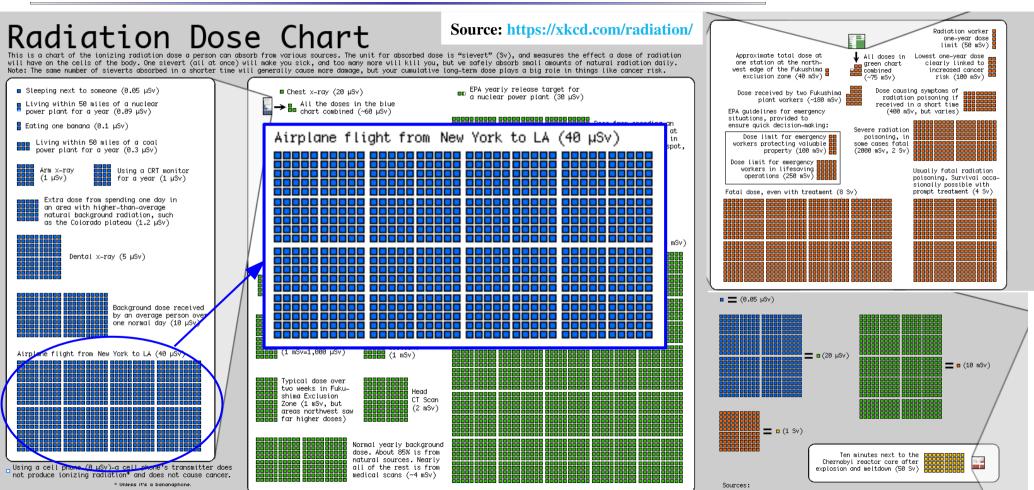


Source: https://xkcd.com/radiation/









Using a cell phone (0 µSv)-a cell phone's transmitter does

not produce ionizing radiation* and does not cause cancer.

× Unless it's a bananaphone



Radiation Dose Chart Source: https://xkcd.com/radiation/ Radiation worker one-year dose limit (50 mSv) This is a chart of the ionizing radiation dose a person can absorb from various sources. The unit for absorbed dose is "sievert" (Sv), and measures the effect a dose of radiation Approximate total dose at Lowest one-year dose L All doses in will have on the cells of the body. One sievert (all at once) will make you sick, and too many more will kill you, but we safely absorb small amounts of natural radiation daily. one station at the northareen chart west edge of the Fukushima Note: The same number of sieverts absorbed in a shorter time will generally cause more damage, but your cumulative long-term dose plays a big role in things like cancer risk. combined increased cancer exclusion zone (40 mSv) risk (100 mSv) ~75 mSv) EPA yearly release target for Sleeping next to someone (0.05 µSv) ■ Chest v_ray (20 uSv) Dose causing symptoms of Dose received by two Fukushima ose causing symptoms of radiation poisoning if Living within 50 miles of a nuclear plant workers (~180 mSv) received in a short time power plant for a year (0.09 µSv) EPA quidelines for emergency (400 mSv. but varies) situations, provided to Dose from spending an Eating one banana (0.1 μSv) ensure quick decision-making: hour on the grounds at Severe radiation Dose limit for emergency poisoning, in the Chernobyl plant in Living within 50 miles of a coal workers protecting valuable property (100 mSv) some cases fatal 2010 (6 mSv in one spot. power plant for a year (0.3 µSv) (2000 mSv, 2 Sv) Head but varies wildly) Dose limit for emergency workers in lifesaving Arm x-ray Using a CRT monitor Usually fatal radiation operations (250 mSv) (1 µSv) for a year (1 uSv) poisonina. Survival occasionally possible with Fatal dose, even with treatment (8 Sv) prompt treatment (4 Sv) Chest Extra dose from spending one day in CT scan an area with higher-than-average (7 mSv) natural background radiation, such as the Colorado plateau (1.2 µSv) US radiation workers (50 mSv) Dental x-ray (5 µSv) Yearly dose from Mammog natural potassium in (400 % the body (390 uSv) ■ (0.05 µSv) Background dose received by an average person over EPA vearly limit on one normal day (10 uSv) external dose radiation exposure from Three to a single member Mile Island of the public ident (1 mSv=1,000 µSv) Airplane flight from New York to LA (40 µSv) (1 mSv) □ (20 µSv) Typical dose over two weeks in Fuku Head shima Exclusion

(1 Sv)

Sources:

Ten minutes next to the

Chernobyl reactor core after

explosion and meltdown (50 Sv)

CT Scan

(2 mSv)

Normal yearly background dose. About 85% is from

natural sources. Nearly

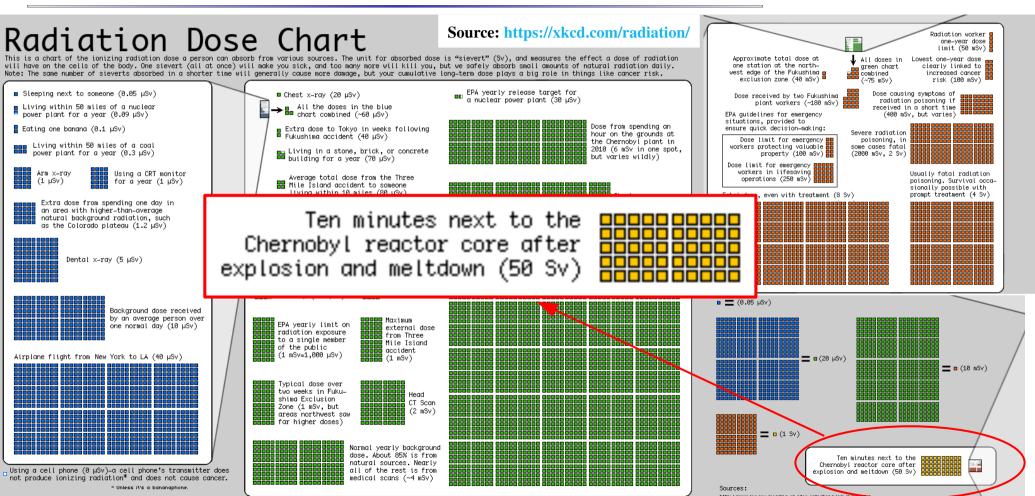
all of the rest is from

medical scans (~4 mSv)

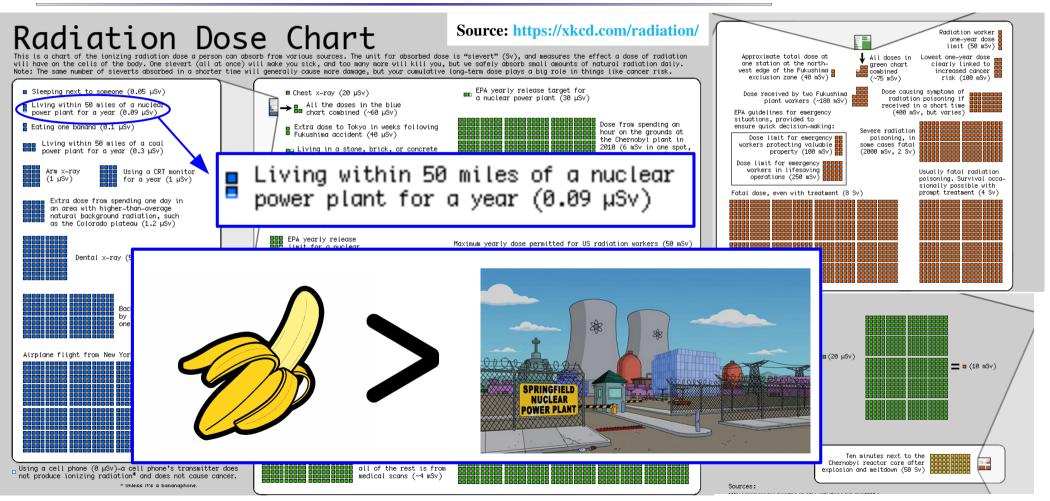
Zone (1 mSv. but

areas northwest saw far higher doses)





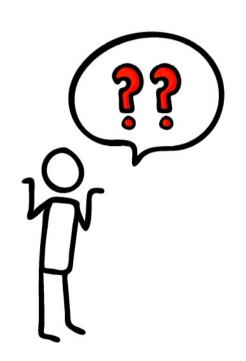




Radiation damage effects



So now a question...



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

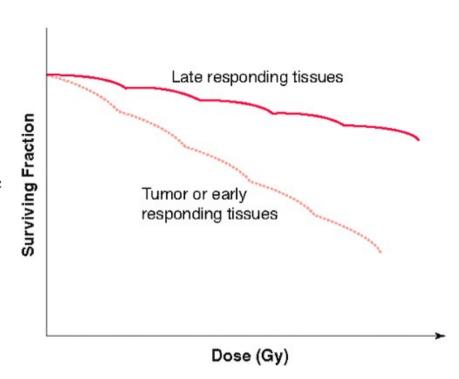
then why do we ask for 60-70 Gy in a normal radiation therapy treatment plan??

Dose fractionation and localisation



Total dose is fractioned and localised!!

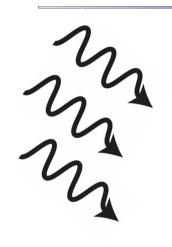
- We don't hit the whole body of the patient
- Healthy tissue better recover the radiation damage
- Cancer cells are less efficient in reparing the damage
- Radio resistent cancer cell move to a less resistent phase of the cell cycle
- Hypoxic cancer tissue can re-oxygenate improving the radio sensitivity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

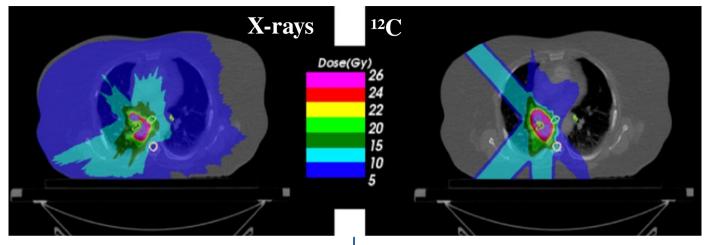


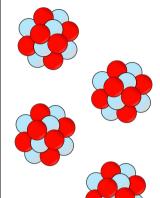
Optimization of exposure for treatment!

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!

But it is not our only weapon...

Indication	End point	Results photons	Results carbon HIMAC-NIRS	Results carbon GSI
Chordoma	local control rate	30 – 50 %	65 % Similar t	70 % o protons
Chondrosarcoma	local control rate	33 %	88 %	89 %
Nasopharynx carcinoma	5 year survival	40 -50 %	63 %	
Glioblastoma	av. survival time	12 months	16 months	Table by G. Kraft
Choroid melanoma	local control rate	95 %	96 % (*)	Results of carbon
Paranasal sinuses tumours	local control rate	21 %	63 %	ions
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 %	

Any question?