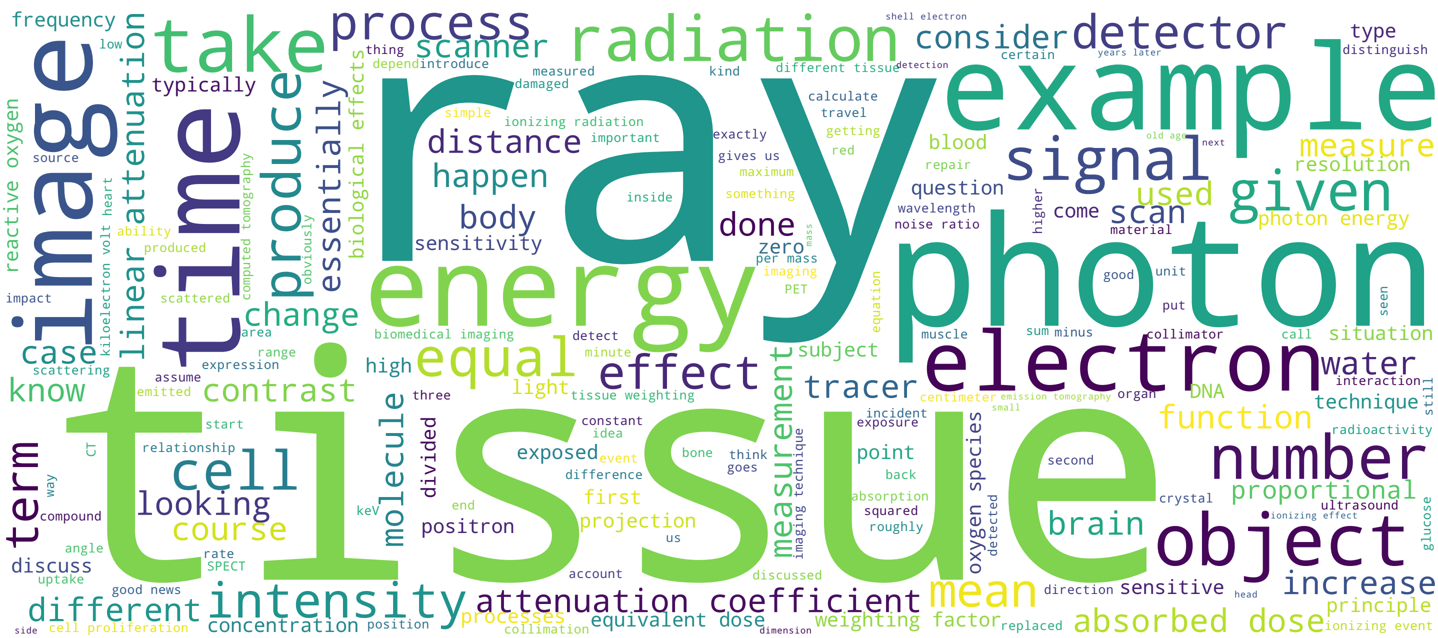
3.5 Biological effects of ionizing radiation

Fundamentals of Biomedical Imaging

Prof. Rolf Gruetter



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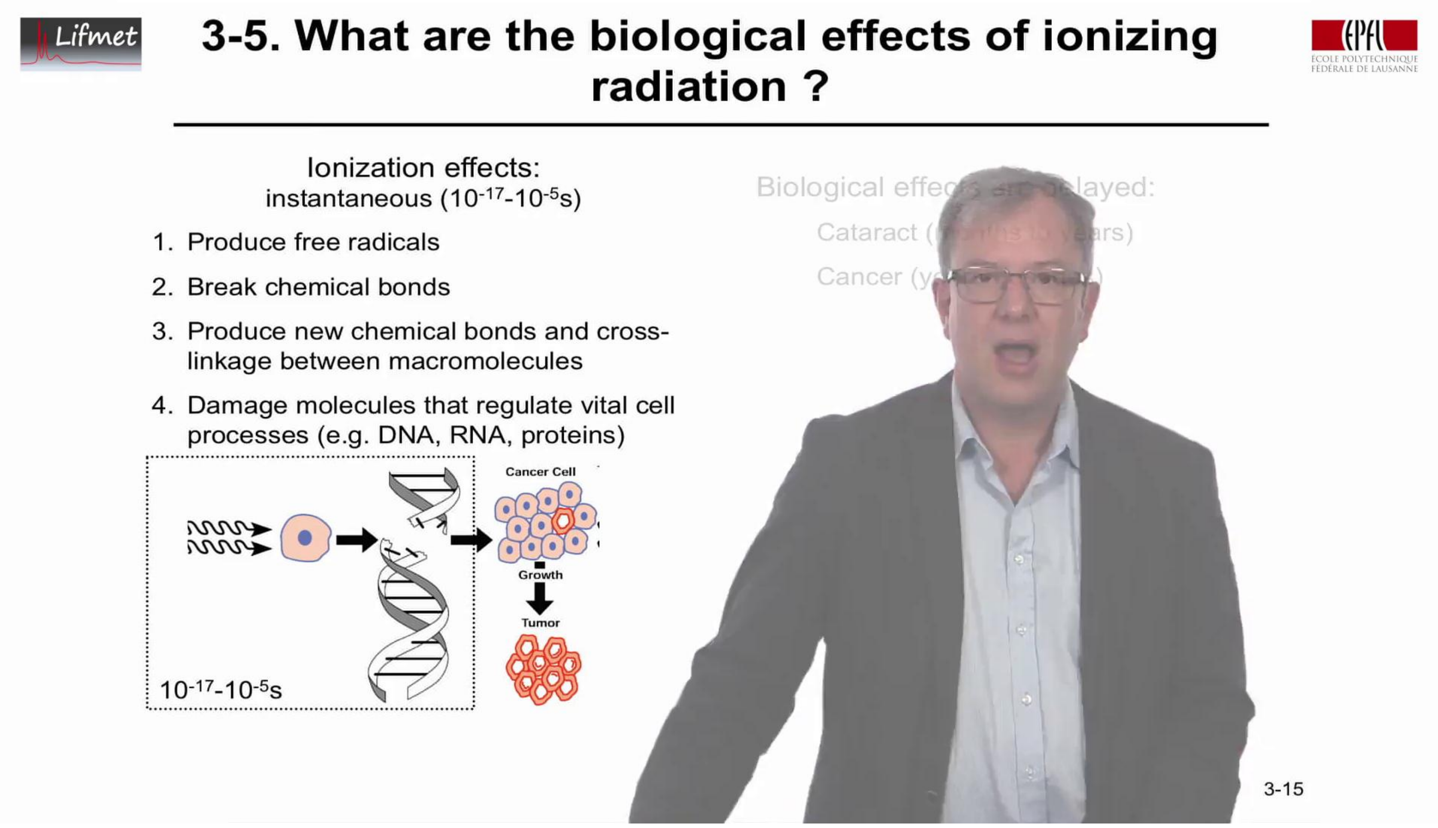


For today's segment, we want to now also discuss the biological effects of ionizing radiation, and exactly what are these biological effects? We have all a fairly good understanding that x-rays are not very healthy as we've discussed. We need to put on sunscreen to minimize ionizing radiation. And it is actually exactly those ionizing effects that are at the center stage here. The ionizing effects that are pretty much instantaneous. The minute the photon hits our molecule, it produces an ionizing effect, produces a molecule with a charge, it's ionized. This happens today and now. This can produce free radicals. This can break chemical bonds. This can produce new chemical bonds or cross linkage between macromolecules, for example in the eye. Or it can damage molecules that regulate vital processes, for example, certain proteins, RNA and DNA. So what we have is the x-ray that impacts on our cell, for example in this graphic here, it breaks the DNA structure. This happens instantaneously. It is now, if you're exposed to the x-ray this happens now. However, and this is one of the difficulties here is that the biological effects are delayed.

Notes

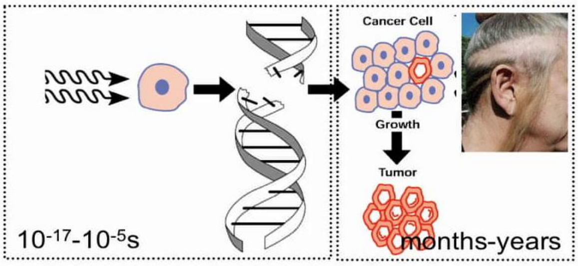
Summary

0m 04s

3-5. What are the biological effects of ionizing radiation ?

Ionization effects:
instantaneous (10^{-17}-10^{-5}s)

1. Produce free radicals
2. Break chemical bonds
3. Produce new chemical bonds and cross-linkage between macromolecules
4. Damage molecules that regulate vital cell processes (e.g. DNA, RNA, proteins)



Biological effects are delayed:

Cataract (months to years)

Cancer (years-decades)

Tissue sensitivity to radiation

proportional: rate of cell proliferation
inversely prop.: degree of cell differentiation

3-15

In the eye, we can have cataract formation that's cross-linkage between molecules, macromolecules, that's cataract. This can happen months later or years later, and if the cell is losing its ability to autoregulate, this can produce cancer. This can happen years later or decades later. And this is the difficulty in managing the x-rays. We cannot immediately see the effect. We cannot immediately judge it, and it is detached from the original event. So the disregulation of a cell, when it loses autoregulation, it starts to grow uncontrolled, that's cancer-- develops into a tumor, that happens months to years later. Sometimes it's relatively short, and here's an example of a person who underwent actually an angiogram in a CT scanner. So as you can see here on the hair, the hair cells on the surface they were exposed to very high radiation in this case and this created radiation damage in the skin of this person who lost the ability to grow hair. This was most likely temporary, but it is an effect that happened in the next few months after the scan. Now what complicates the assessment of biological effects is that not all tissues are equally sensitive to radiation.

Notes

Summary

1m 31s

3-5. What are the biological effects of ionizing radiation ?

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instantaneous (10^{-17}-10^{-5}s)

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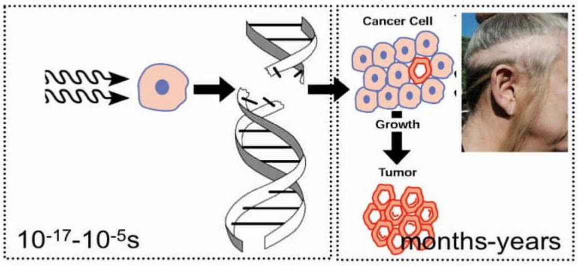


Biological effects are delayed:

- Cataract (months to years)
- Cancer (years-decades)

Tissue sensitivity to radiation

proportional: rate of cell proliferation
inversely prop.: degree of cell differentiation

Pregnancy vs. old age …

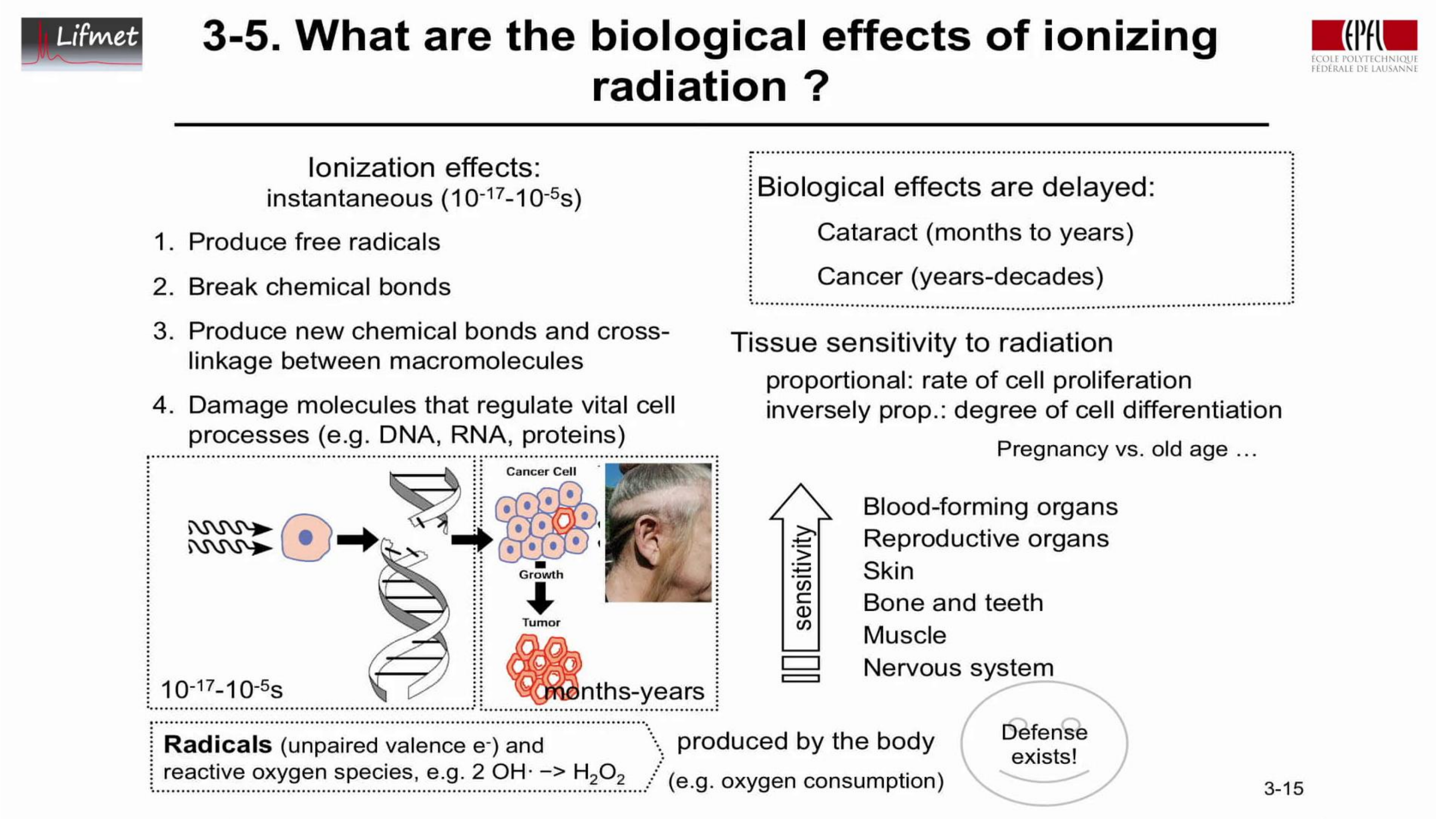
3-15

If you have a tissue that has a rapid cell proliferation, that divides the cells rapidly, then it is, the sensitivity of that tissue is proportional to the rate of cell proliferation, so it is high. So if you have a tissue that has a lot of cell proliferation, then it is more sensitive to radiation. On the other hand, if the tissue is highly differentiated, then it is less sensitive to radiation. And this is a very practical consideration, and actually we have a relatively high rate of cell proliferation in fetuses compared to old age, where our cells just don't divide as fast. So a young person is much more susceptible to the biological effects of radiation than an older person, where it is less important. So the damage that is created is less of a concern when you're increased in age. So this has considerations on exposure to radiation, but also in, for example, radiation cleanup, that is as in the cases of Fukushima where they have used, for the first firefighters that came to work on the cleanup of the site, they preferably selected people that were of older age than the younger firefighters exactly for that reason.

Notes

Summary

2m 57s



Another thing to consider is at old age even if you develop a cancer due to radiation exposure, the cancers tend to grow slower at old age, so there's a higher probability that you might die of a heart attack rather than of the cancer produced by the x-ray exposure. So if you look at sensitivity upwards then the nervous system is not very sensitive. The muscle is a bit more sensitive. Then we have bone and teeth. We have the skin. We have the reproductive organs, and finally the blood-forming organs which are the most sensitive to radiation. So one process is the production of radicals, that is compounds with unpaired valence electrons and reactive oxygen species such as-- we have 2 OH's that produce hydrogen peroxide. Radicals and reactive oxygen species are produced by processes that are naturally occurring in the body. One such process is oxygen consumption. It's the mitochondria that are responsible for that, and they are a powerhouse of radical formation and reactive oxygen species production. So it happens naturally in our body. And this is where the good news is: our body has to have, in order to survive these processes, has to have developed defense mechanisms against the production of radicals and reactive oxygen species, and this is what we are going to discuss next.

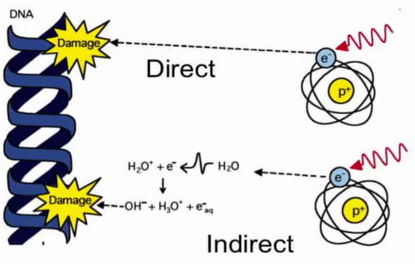
Notes

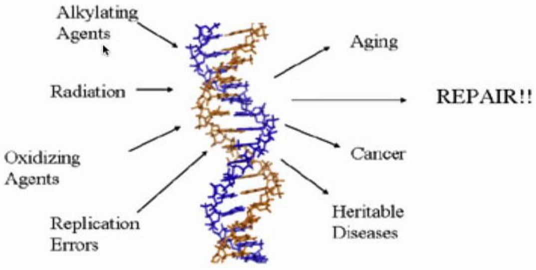
Summary

4m 28s

How does the tissue defend itself against radiation damage ?

DNA repair





Healing

3-16

So how does the tissue defend itself against radiation damage? We can distinguish basically two processes. We have the x-ray that produces an ionizing event. This ionizing event happens directly on the molecule of interest, so that would be the direct effect. We have ionizing event directly on the DNA here in this example and that's direct damage. We can also have an ionizing event in another molecule. This produces then water and an electron. This produces then H3O + and a free electron, and through this reactive oxygen species, we have the indirect effect through a chemical reaction. To look at DNA, which is what we are mainly concerned with, the DNA is constantly subjected to processes that menace, that threaten its integrity. We have alkylating agents. We have oxidizing agents. We have replication errors. We have aging, we have radiation, natural radiation. We have diseases. And so the cells, our cells have developed mechanisms to provide for repair of the DNA, so there are, to account for all these effects, there are repair mechanisms that exist. Now if you look at the healing of the tissue that's been exposed to x-ray we are looking at essentially two fundamental ways.

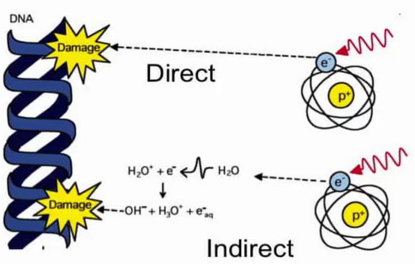
Notes

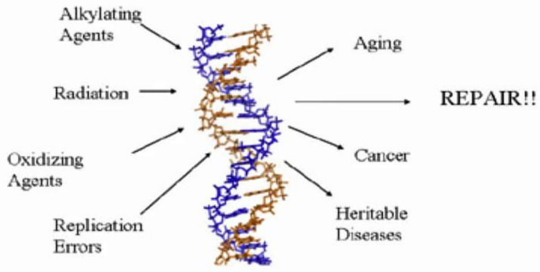
Summary

6m 13s

How does the tissue defend itself against radiation damage ?

DNA repair





Healing

Repair	Regeneration
Replace damaged cells with different cell type (fibrosis)	Replace damaged cells by same
Organ not returned to original state	Organ returned to original state
Radioresistant tissues (muscle, brain): only repair possible	Radiosensitive tissues (skin, digestive system, bone marrow)

3-16

One is repair. In repair, the cells in the tissue are being replaced with a different cell type. Typically, it's fibrosis. In this case, the organ is not returned to the original state. We take a liver cell, replace it with a fiber cell. There's not a liver cell again in that tissue or in the brain, for example. In radioresistant tissues, the tissues are less likely to be damaged by radiation, such as muscle and brain. We can only do repair. This is the only mechanism that happens. So in the brain, a cell that is being damaged by x-rays is not being replaced by a cell of the same kind. The other process of healing that happens is regeneration. In this case, the cells that are damaged by the x-rays are replaced by the same type of cells. The organ is therefore returned to its original state. It still has the proper cells in there, and this, the process of regeneration, happens in tissues that are more sensitive to radiation such as skin. Skin regrowth, as we all know, we have all cut ourselves, it happens in the digestive system and bone marrow.

Notes

Summary

7m 40s

How are the effects of ionizing radiation quantified ?

Three forms of radiation dose

Absorbed dose D:
energy deposited by ionizing radiation per unit mass of material:

D = Energy/mass

Units: [Gray[Gy]=1J/kg]

Equivalent dose *H*:

Absorbed dose D depends on

1. Intensity of incident x-ray
2. Duration of exposure

3-17

These are the fundamental processes of interaction of x-rays with tissue, the damage how it's done, but we still do not know how to relate this to quantities that we can measure for our imaging techniques. So the question is how do we quantify the effects of ionizing radiation? And here the literature is, at first glance, quite confusing because there are three terms of radiation dose that are being used. First we have the absorbed dose. The absorbed dose is essentially very simple. It's the energy deposited by the radiation per unit mass of material. So it is essentially the energy per mass. It's joules per kilogram is the unit, and here the unit Gray was introduced, Gy. That's the absorbed dose. So the absorbed dose here is given by the number of photons times their energy. Each photon carries a certain energy. If you have a 1,000 photons of them, we deposit more energy per mass than if we have only 100 photons. So D is proportional to the photon energy times the number of photons. So, in other words, the absorbed dose depends on the intensity of the incident x-ray and the duration of exposure. There is no per time here, it's per mass. The next term is the equivalent dose, H.

Notes

Summary

8m 57s

How are the effects of ionizing radiation quantified ?

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Absorbed dose D:
energy deposited by ionizing radiation per unit mass of material:

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Equivalent dose *H*:
= D corrected for effectiveness of radiation to produce biological damage
(w_R = radiation weighting factor)

$H = Dw_R$
Units: [Sievert[Sv] = 1J/kg]

Absorbed dose D depends on

1. Intensity of incident x-ray
2. Duration of exposure

$\mathbf{w_R}$ = 1 (x-rays, β particles)
[20: for α particles]

Bio-imaging:
Equivalent dose H = Absorbed dose D

3-17

And it is essentially equal to the absorbed dose, but then it's corrected for the possibility of the type of radiation that is being used to produce biological damage. Not all types of radioactivity produce the same kind of-- can produce damage to biological tissue. So mathematically, *H* is again given by the absorbed dose, *D* times WR. This is a tissue weighting factor. Now the units to distinguish this are given in sievert, in SI units, still as joules per kilogram because the tissue weighting factor is dimensionless. And the good news is, for biomedical imaging, we have a tissue weighting factor of 1 for x-rays and β particles. Those are the majority of ionizing radiation that is being used, primarily x-rays for our course. And it is 24 ***α*** particles, but we are not considering imaging with ***α*** particles. So we do not consider that, so the good news is equivalent dose is equal to absorbed dose for biomedical imaging. That is the relationship that we have for the types of x-rays that we use. And finally there's the third term, that's the effective dose, and this is essentially taking into account, once we have the equivalent dose of our radiation, in our case is equal to the absorbed dose.

Notes

Summary

10m 22s

How are the effects of ionizing radiation quantified ?

Three forms of radiation dose

Absorbed dose D:
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Units: [Gray[Gy]=1J/kg]

Equivalent dose *H*:
= D corrected for effectiveness of radiation to produce biological damage
(w_R = radiation weighting factor)

$H = Dw_R$

Units: [Sievert[Sv] = 1J/kg]

Effective dose *E* :
H corrected for sensitivity of tissue T
(w_T = tissue weighting factor)

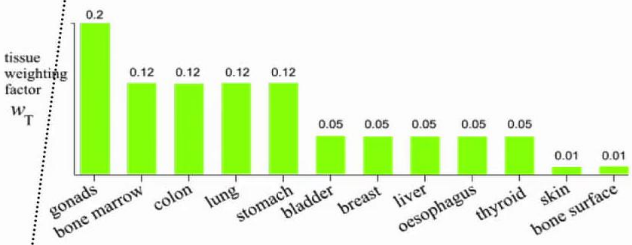
$$E(\mathrm{Sv}) = \sum w_T H_T(\mathrm{Sv})$$

Absorbed dose D depends on

1. Intensity of incident x-ray
2. Duration of exposure

$\mathbf{w_R}$ = 1 (x-rays, β particles)
[20: for α particles]

Bio-imaging:
Equivalent dose H = Absorbed dose D



3-17

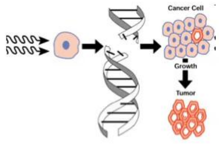
We have to correct this for the sensitivity of the tissue to the radiation. So we'll introduce here now a tissue weighting factor, and so the equivalent dose-- it's given in sievert-- is equal to the sum of the equivalent doses *H* here for the given tissue, so how much is this tissue in sievert exposed to the radiation, and then we multiply it by a weighting factor WT. We'll have to do it over all the tissues to get the total equivalent dose. So we'll take this for all types of tissues, and here is a list of different tissues. The tissue weighting factor, WT, for different tissues. And actually we find for the gonads, it's very high. For skin and bone surface, it's very low, and we have a number of organs where it's 0.05 and 0.12. Again, there are not huge differences but there are differences in terms of the sensitivity of the tissue T-- different tissues relative to the x-rays they're being exposed to.

Notes

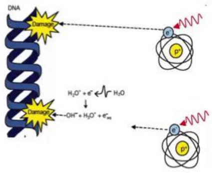
Summary

11m 51s

Credits



Development of cancer
http://www.vmcli.com/veterinary-medical-center-long-island-introduction-to-radiation-safety.html



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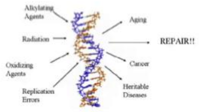
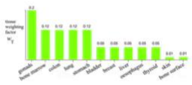


Chemical damage to DNA bases
http://dnamismatch.com/dna-mismatch/chemical-damage-to-dna-bases/



Tissue/organ sensitivity
http://nuclearsafety.gc.ca/eng/resources/radiation/introduction-to-radiation/radiation-doses.cfm

Notes

Summary

13m 04s