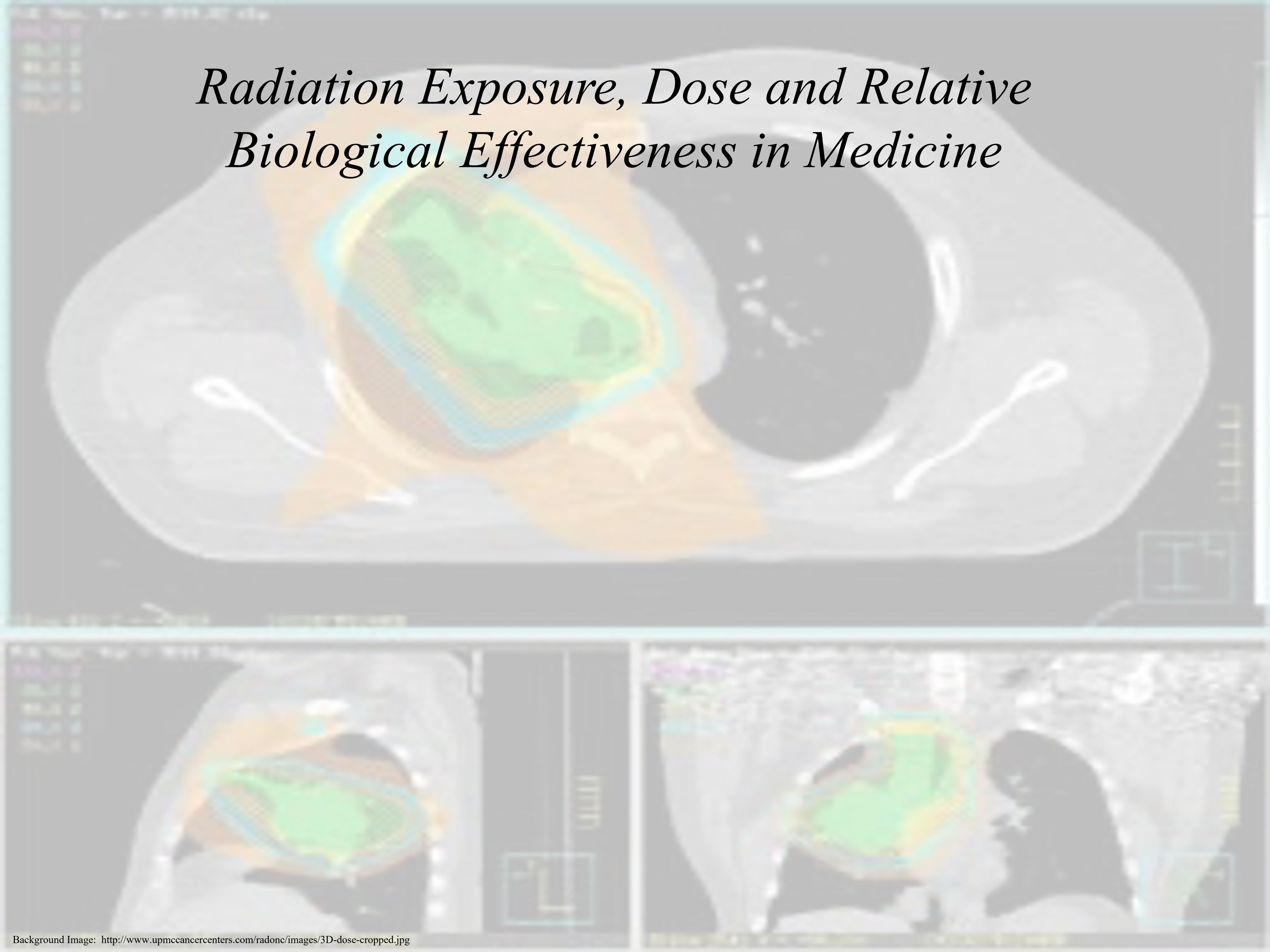
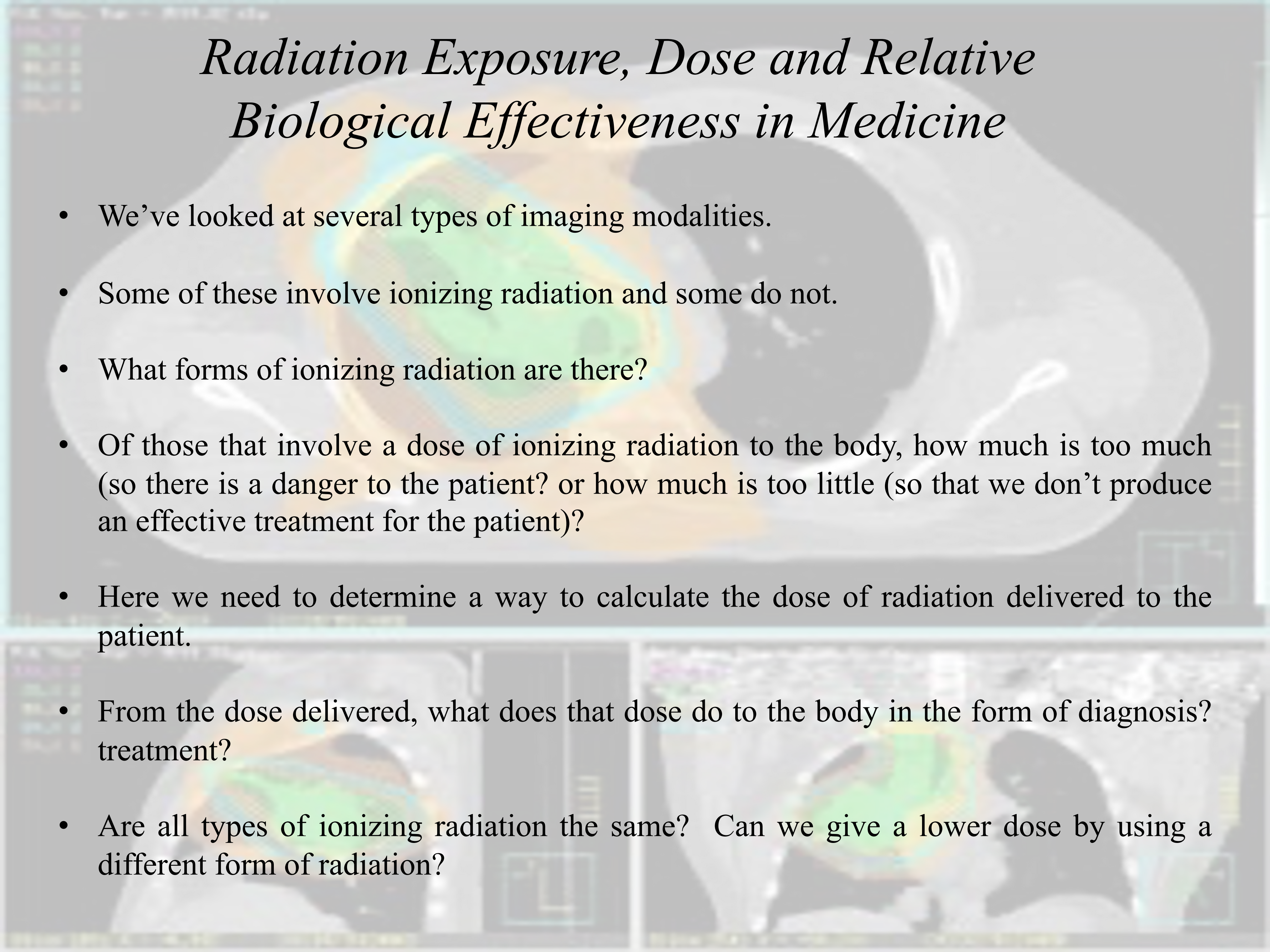
# *Radiation Exposure, Dose and Relative Biological Effectiveness in Medicine*



Background Image: http://www.upmccancercenters.com/radonc/images/3D-dose-cropped.jpg

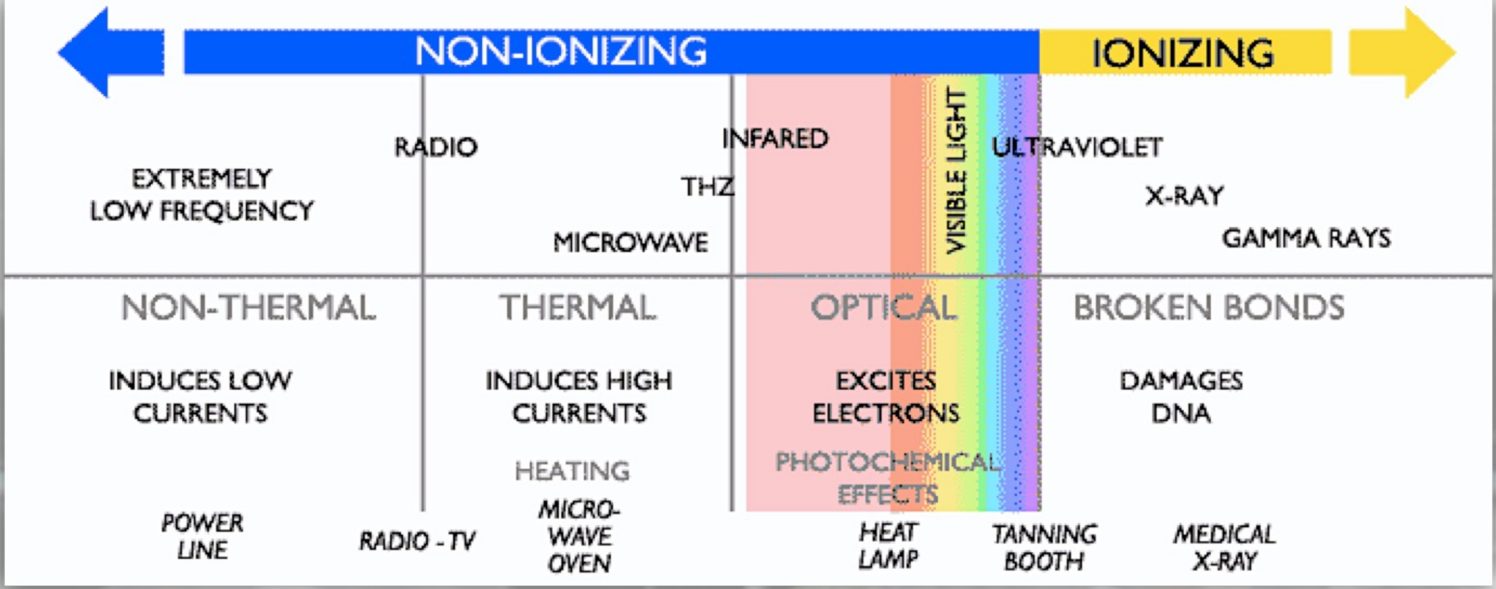
# *Radiation Exposure, Dose and Relative Biological Effectiveness in Medicine*



- We’ve looked at several types of imaging modalities.
- Some of these involve ionizing radiation and some do not.
- What forms of ionizing radiation are there?
- Of those that involve a dose of ionizing radiation to the body, how much is too much (so there is a danger to the patient? or how much is too little (so that we don’t produce an effective treatment for the patient)?
- Here we need to determine a way to calculate the dose of radiation delivered to the patient.
- From the dose delivered, what does that dose do to the body in the form of diagnosis? treatment?
- Are all types of ionizing radiation the same? Can we give a lower dose by using a different form of radiation?

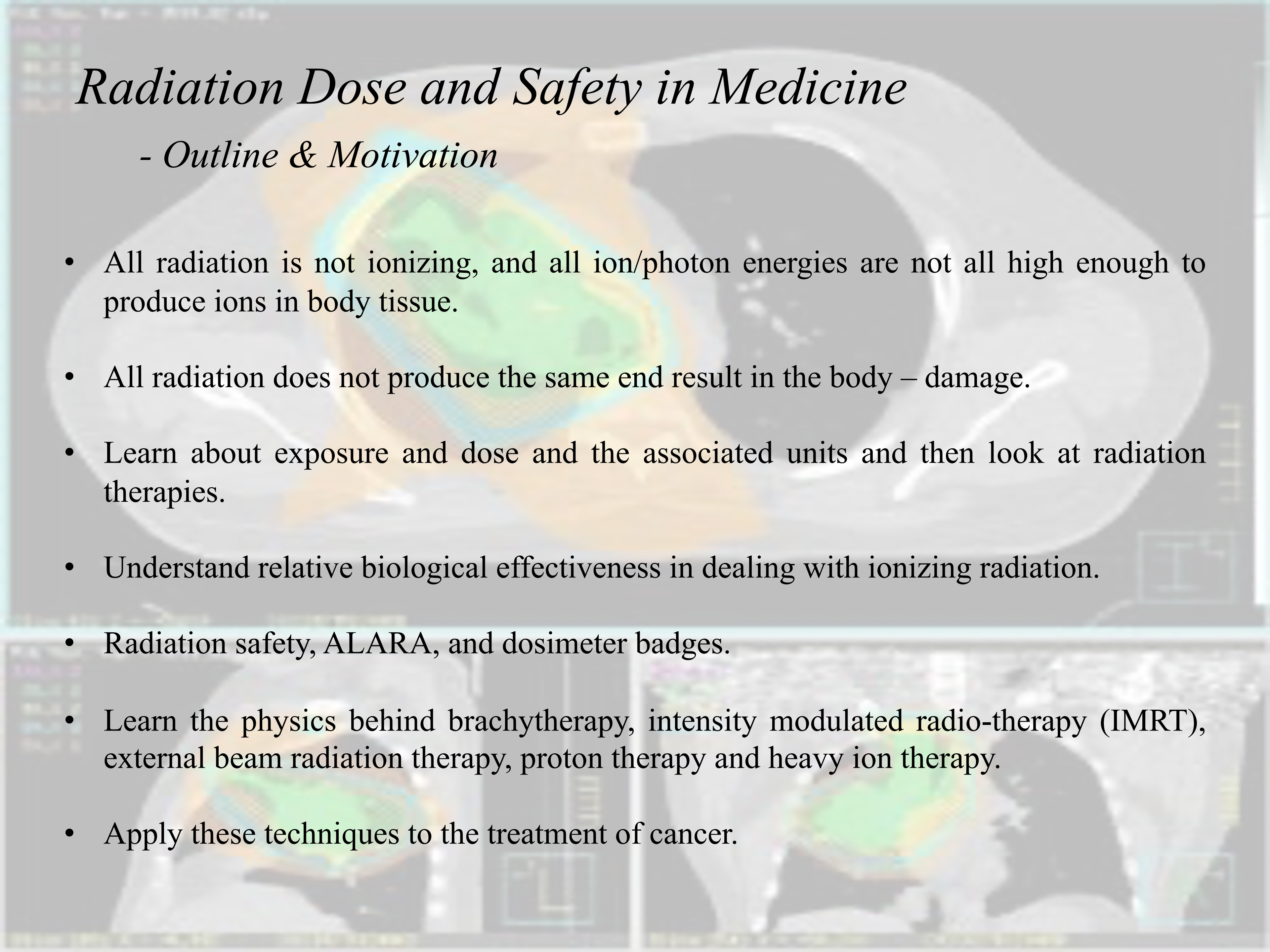
# *Radiation*

## *- ionizing vs. non-ionizing*



http://www.radiologyandphysicalmedicine.com/non-ionizing-radiation-applications-in-medicine/

What’s the difference between the two types of radiation?



# *Radiation Dose and Safety in Medicine*

## *- Outline & Motivation*

- All radiation is not ionizing, and all ion/photon energies are not all high enough to produce ions in body tissue.

- All radiation does not produce the same end result in the body – damage.

- Learn about exposure and dose and the associated units and then look at radiation therapies.

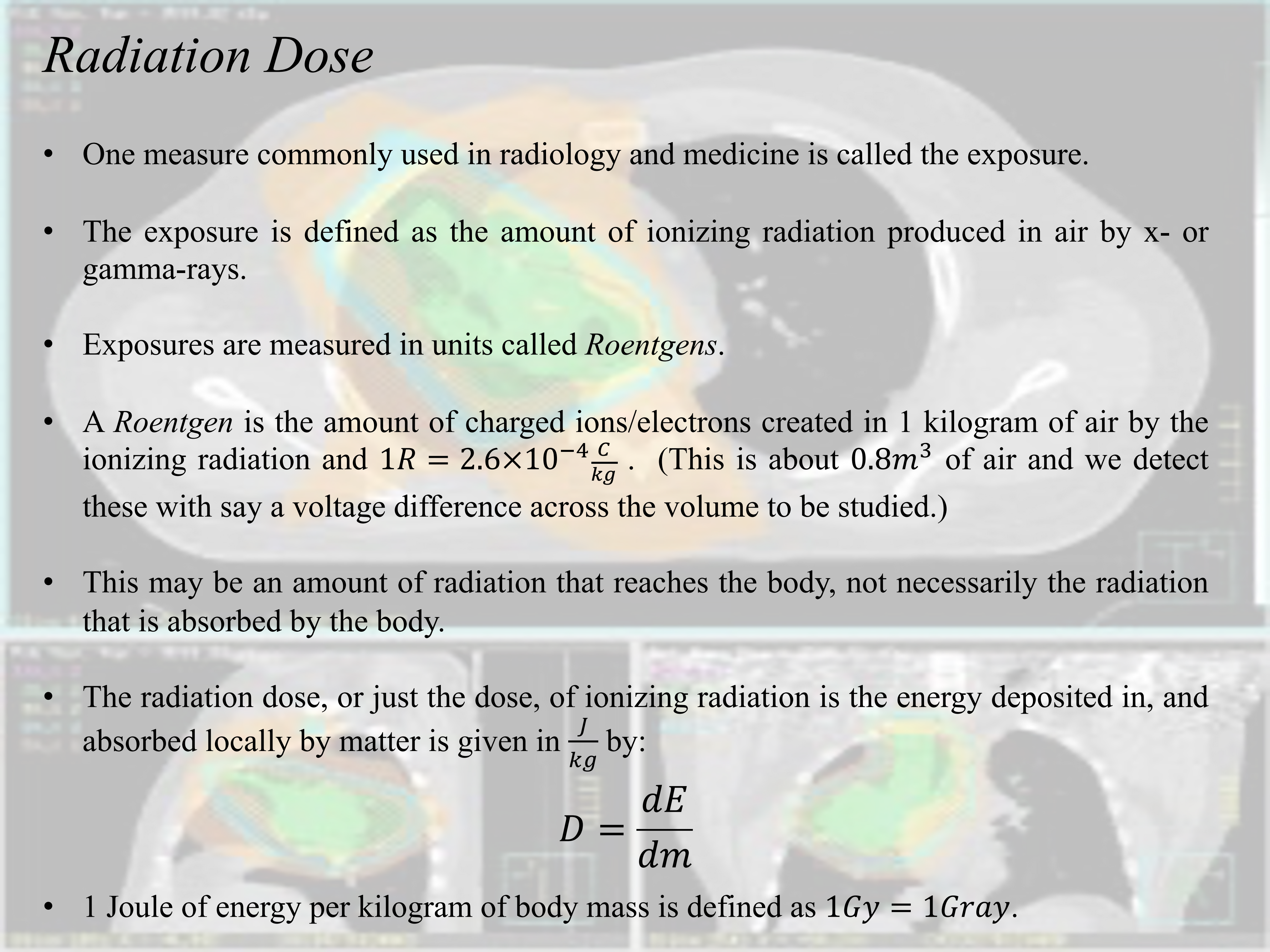
- Understand relative biological effectiveness in dealing with ionizing radiation.

- Radiation safety, ALARA, and dosimeter badges.

- Learn the physics behind brachytherapy, intensity modulated radio-therapy (IMRT), external beam radiation therapy, proton therapy and heavy ion therapy.

- Apply these techniques to the treatment of cancer.

# *Radiation Dose*

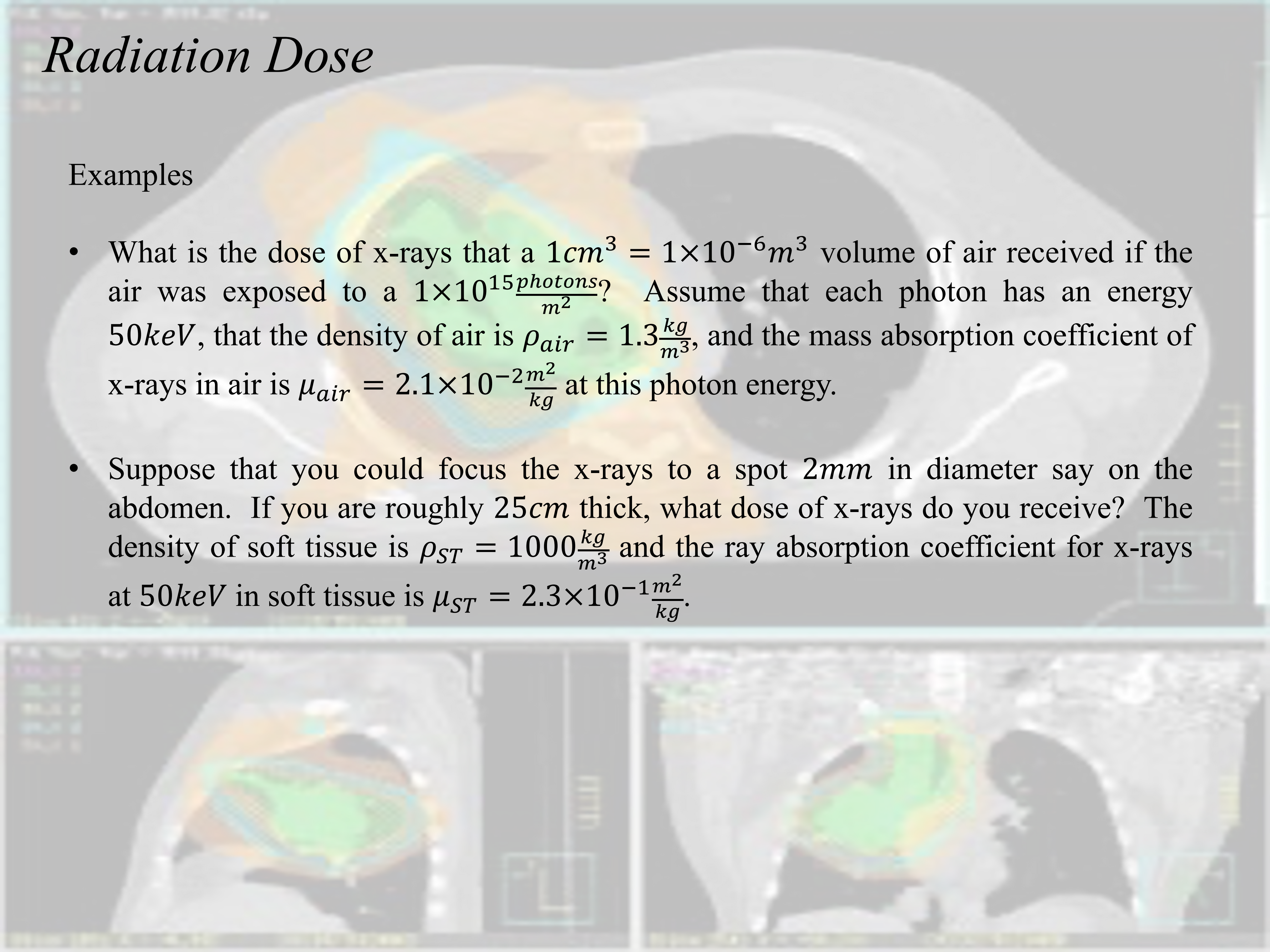


- One measure commonly used in radiology and medicine is called the exposure.
- The exposure is defined as the amount of ionizing radiation produced in air by x- or gamma-rays.
- Exposures are measured in units called *Roentgens*.
- A *Roentgen* is the amount of charged ions/electrons created in 1 kilogram of air by the ionizing radiation and $1R = 2.6\times10^{-4}\frac{C}{kg}$ . (This is about $0.8m^3$ of air and we detect these with say a voltage difference across the volume to be studied.)
- This may be an amount of radiation that reaches the body, not necessarily the radiation that is absorbed by the body.
- The radiation dose, or just the dose, of ionizing radiation is the energy deposited in, and absorbed locally by matter is given in $\frac{J}{kg}$ by:

$$D = \frac{dE}{dm}$$

- 1 Joule of energy per kilogram of body mass is defined as $1Gy = 1Gray$.

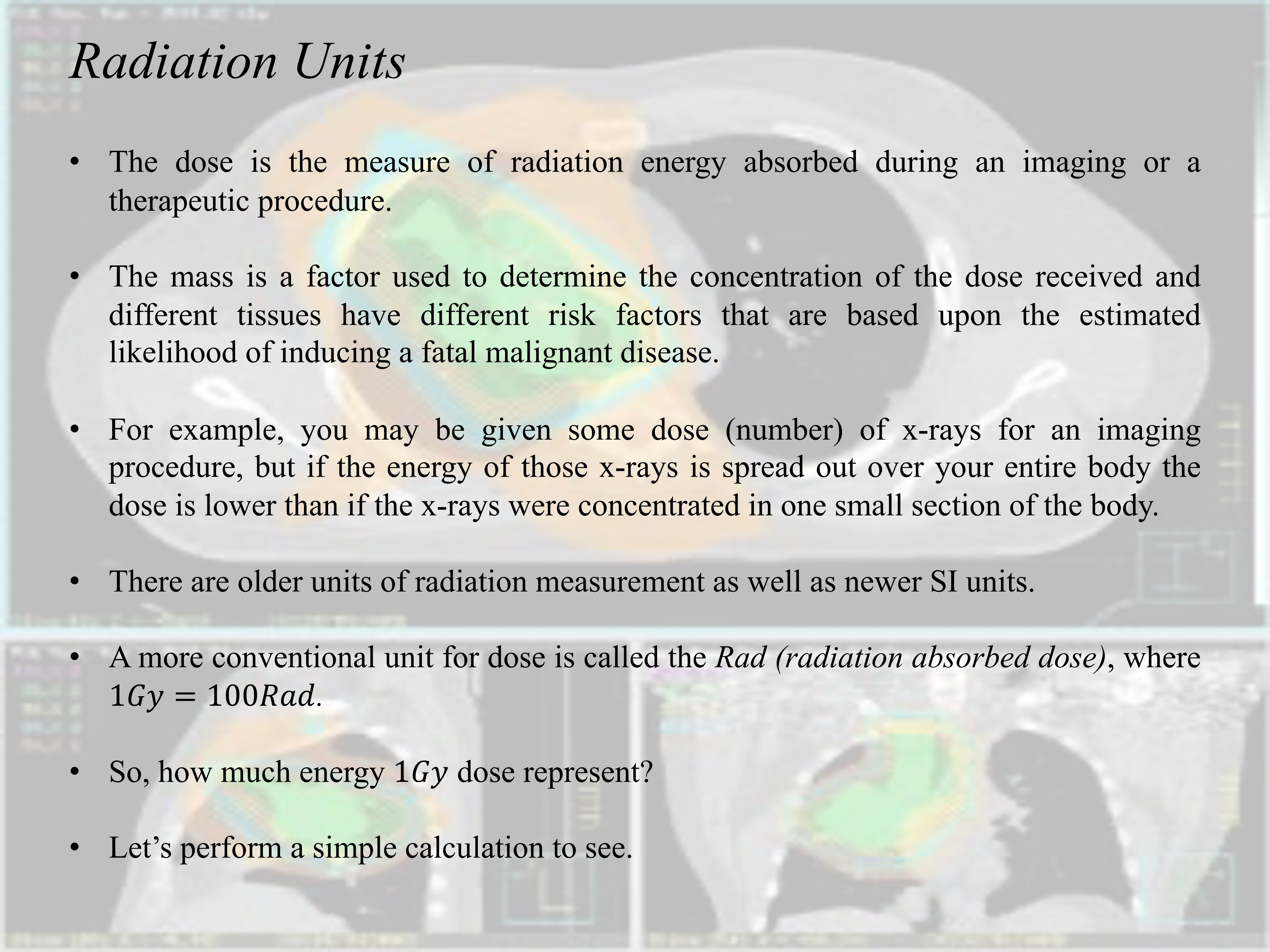
# *Radiation Dose*



Examples

- What is the dose of x-rays that a $1cm^3 = 1\times10^{-6}m^3$ volume of air received if the air was exposed to a $1\times10^{15}\frac{photons}{m^2}$? Assume that each photon has an energy $50keV$, that the density of air is $\rho_{air} = 1.3\frac{kg}{m^3}$, and the mass absorption coefficient of x-rays in air is $\mu_{air} = 2.1\times10^{-2}\frac{m^2}{kg}$ at this photon energy.

- Suppose that you could focus the x-rays to a spot $2mm$ in diameter say on the abdomen. If you are roughly $25cm$ thick, what dose of x-rays do you receive? The density of soft tissue is $\rho_{ST} = 1000\frac{kg}{m^3}$ and the ray absorption coefficient for x-rays at $50keV$ in soft tissue is $\mu_{ST} = 2.3\times10^{-1}\frac{m^2}{kg}$.



# *Radiation Units*

- The dose is the measure of radiation energy absorbed during an imaging or a therapeutic procedure.

- The mass is a factor used to determine the concentration of the dose received and different tissues have different risk factors that are based upon the estimated likelihood of inducing a fatal malignant disease.

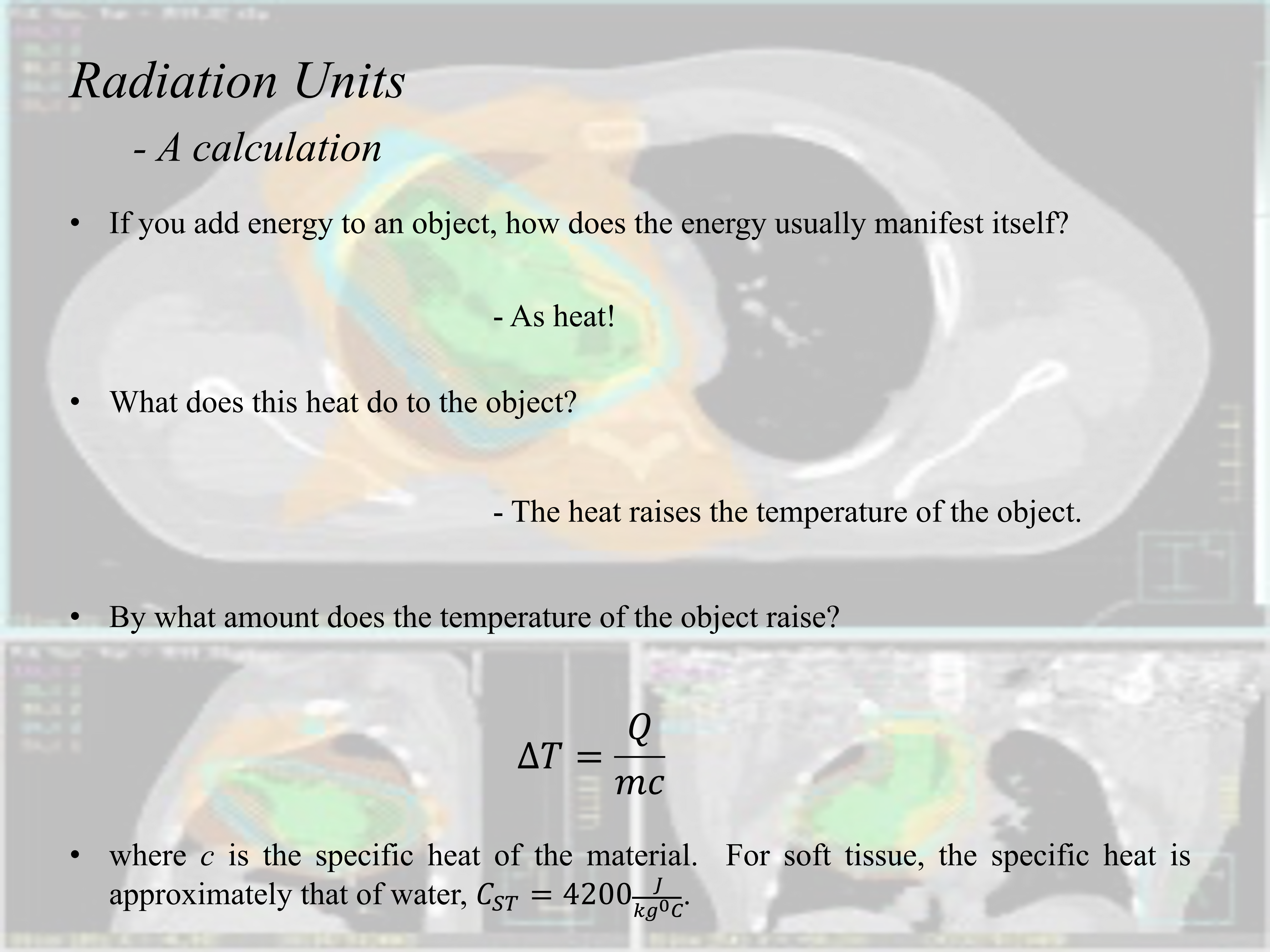
- For example, you may be given some dose (number) of x-rays for an imaging procedure, but if the energy of those x-rays is spread out over your entire body the dose is lower than if the x-rays were concentrated in one small section of the body.

- There are older units of radiation measurement as well as newer SI units.

- A more conventional unit for dose is called the *Rad (radiation absorbed dose)*, where $1Gy = 100Rad$.

- So, how much energy $1Gy$ dose represent?

- Let’s perform a simple calculation to see.



# *Radiation Units*

## *- A calculation*

- If you add energy to an object, how does the energy usually manifest itself?

- As heat!

- What does this heat do to the object?

- The heat raises the temperature of the object.

- By what amount does the temperature of the object raise?

$$\Delta T = \frac{Q}{mc}$$

- where *c* is the specific heat of the material. For soft tissue, the specific heat is approximately that of water, $C_{ST} = 4200\frac{J}{kg^0C}$.

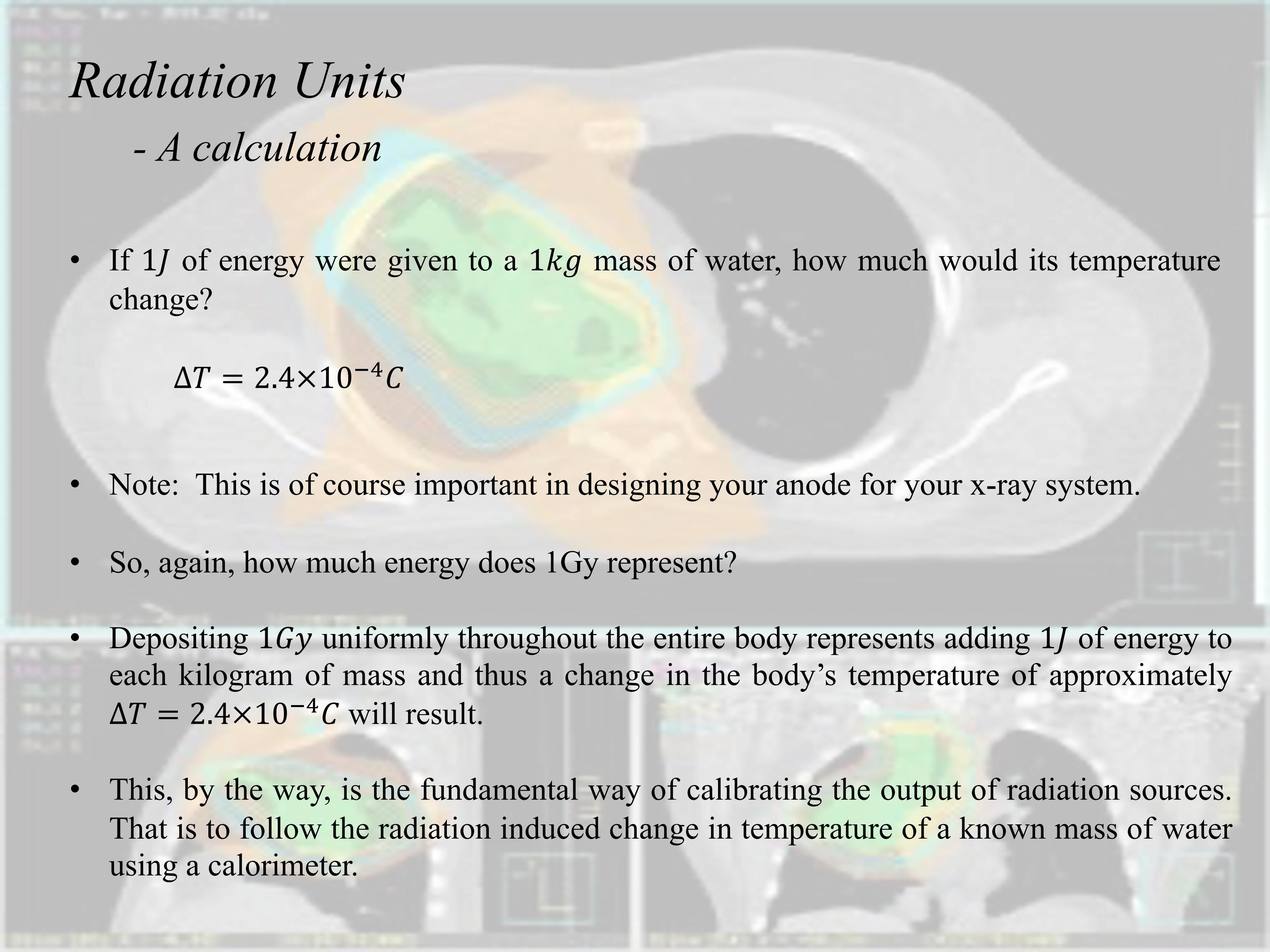
# *Radiation Units*

## *- A calculation*

- If $1J$ of energy were given to a $1kg$ mass of water, how much would its temperature change?

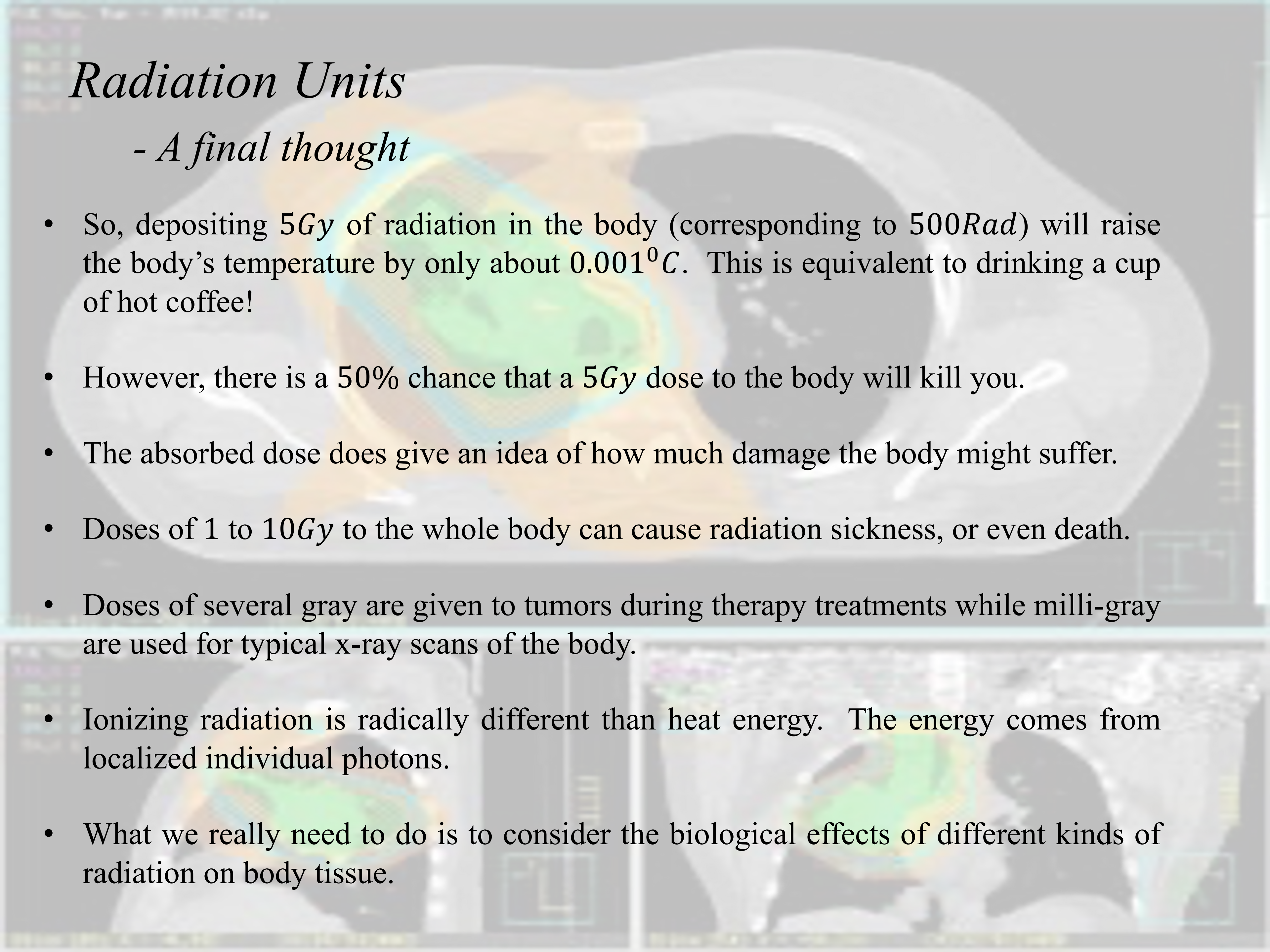
$$\Delta T = 2.4\times10^{-4}C$$

- Note: This is of course important in designing your anode for your x-ray system.
- So, again, how much energy does 1Gy represent?
- Depositing $1Gy$ uniformly throughout the entire body represents adding $1J$ of energy to each kilogram of mass and thus a change in the body's temperature of approximately $\Delta T = 2.4\times10^{-4}C$ will result.
- This, by the way, is the fundamental way of calibrating the output of radiation sources. That is to follow the radiation induced change in temperature of a known mass of water using a calorimeter.



# Radiation Units

## - A final thought



- So, depositing $5Gy$ of radiation in the body (corresponding to $500Rad$) will raise the body's temperature by only about $0.001^0C$. This is equivalent to drinking a cup of hot coffee!

- However, there is a $50\%$ chance that a $5Gy$ dose to the body will kill you.

- The absorbed dose does give an idea of how much damage the body might suffer.

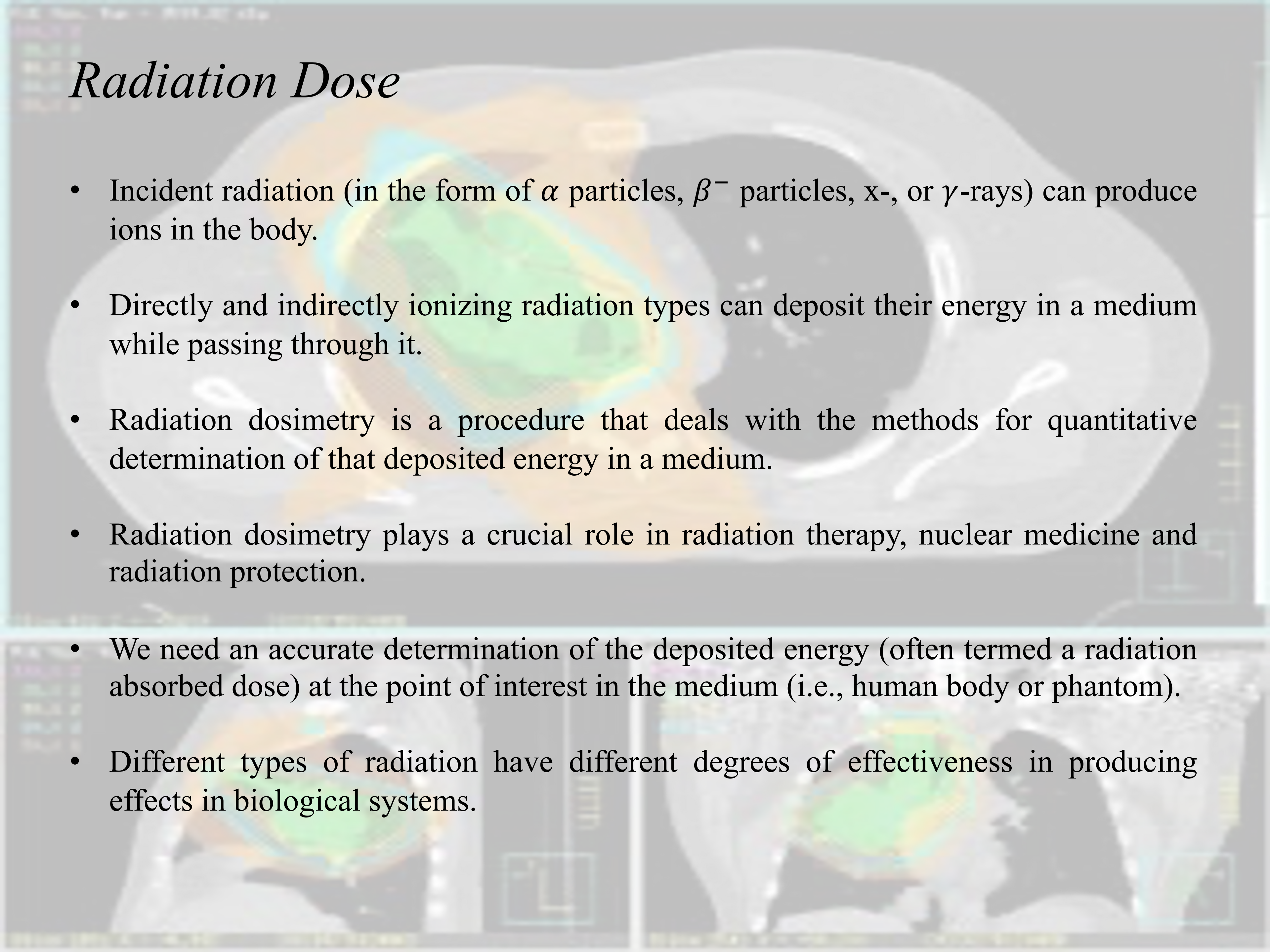
- Doses of 1 to $10Gy$ to the whole body can cause radiation sickness, or even death.

- Doses of several gray are given to tumors during therapy treatments while milli-gray are used for typical x-ray scans of the body.

- Ionizing radiation is radically different than heat energy. The energy comes from localized individual photons.

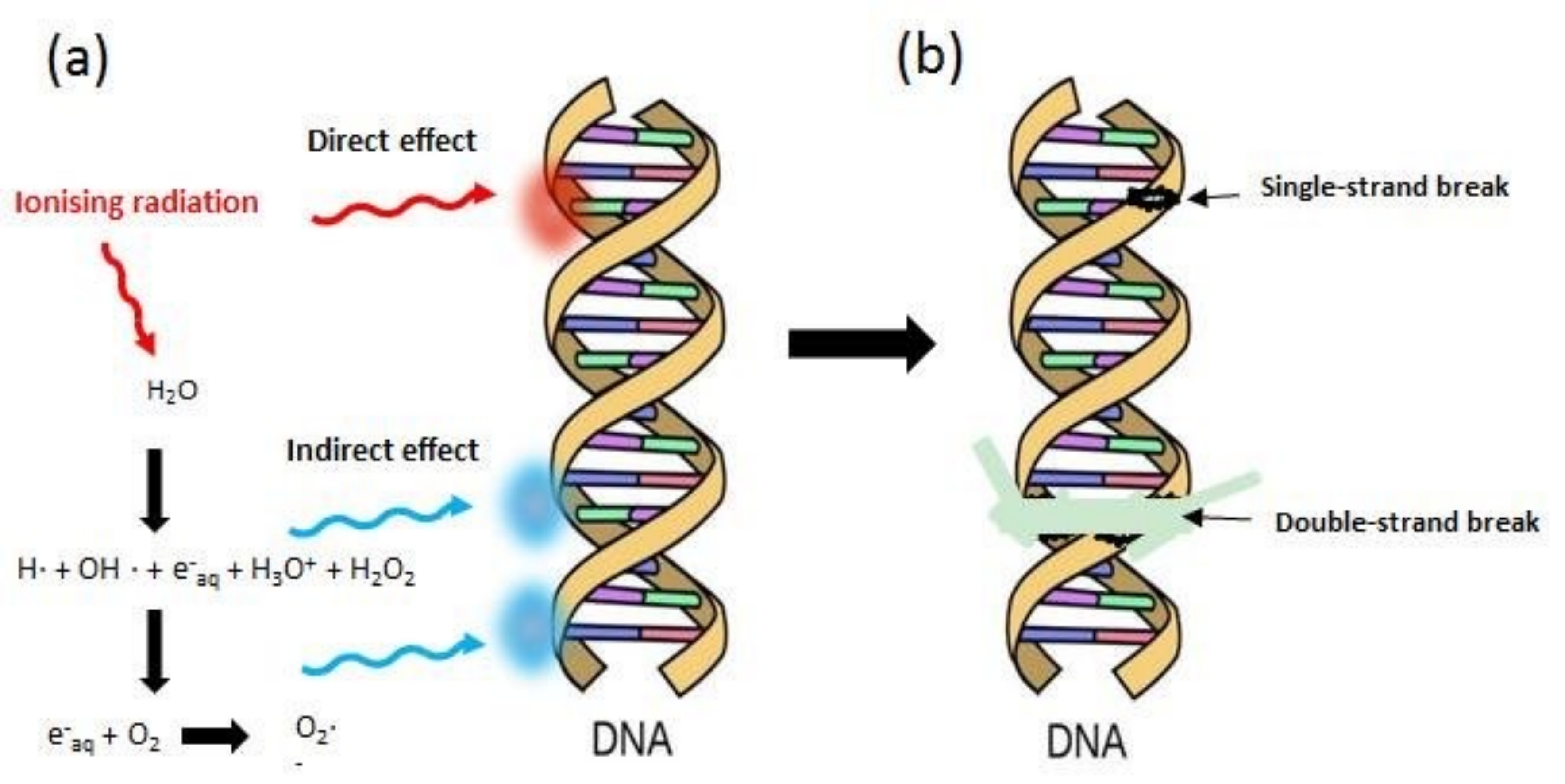
- What we really need to do is to consider the biological effects of different kinds of radiation on body tissue.

# *Radiation Dose*



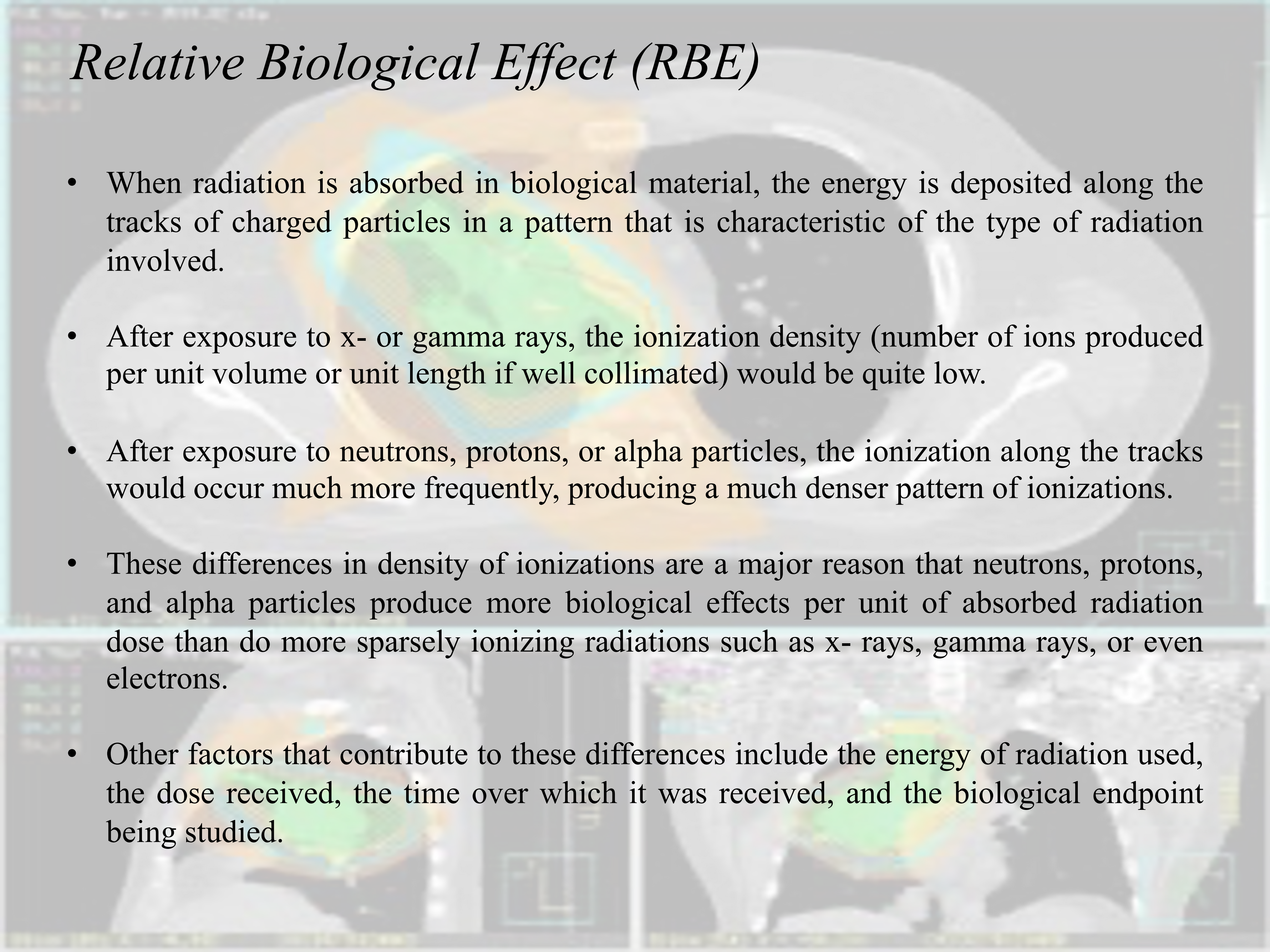
- Incident radiation (in the form of $\alpha$ particles, $\beta^-$ particles, x-, or $\gamma$-rays) can produce ions in the body.
- Directly and indirectly ionizing radiation types can deposit their energy in a medium while passing through it.
- Radiation dosimetry is a procedure that deals with the methods for quantitative determination of that deposited energy in a medium.
- Radiation dosimetry plays a crucial role in radiation therapy, nuclear medicine and radiation protection.
- We need an accurate determination of the deposited energy (often termed a radiation absorbed dose) at the point of interest in the medium (i.e., human body or phantom).
- Different types of radiation have different degrees of effectiveness in producing effects in biological systems.

# *Radiation Dose*



Milborne, Ben & Arafat, Abul & Layfield, Rob & Thompson, Alexander & Ahmed, Ifty. (2020). The Use of Biomaterials in Internal Radiation Therapy. Recent Progress in Materials. 2. 1-34. 10.21926/rpm.2002012.

# *Relative Biological Effect (RBE)*



- When radiation is absorbed in biological material, the energy is deposited along the tracks of charged particles in a pattern that is characteristic of the type of radiation involved.

- After exposure to x- or gamma rays, the ionization density (number of ions produced per unit volume or unit length if well collimated) would be quite low.

- After exposure to neutrons, protons, or alpha particles, the ionization along the tracks would occur much more frequently, producing a much denser pattern of ionizations.

- These differences in density of ionizations are a major reason that neutrons, protons, and alpha particles produce more biological effects per unit of absorbed radiation dose than do more sparsely ionizing radiations such as x- rays, gamma rays, or even electrons.

- Other factors that contribute to these differences include the energy of radiation used, the dose received, the time over which it was received, and the biological endpoint being studied.

# *Relative Biological Effect (RBE)*

- Many scientific investigations have been conducted to study the differing effectiveness of radiations under different experimental conditions.

- Analysis of the Relative Biological Effectiveness, RBE, is a useful way to compare the results observed in these studies.

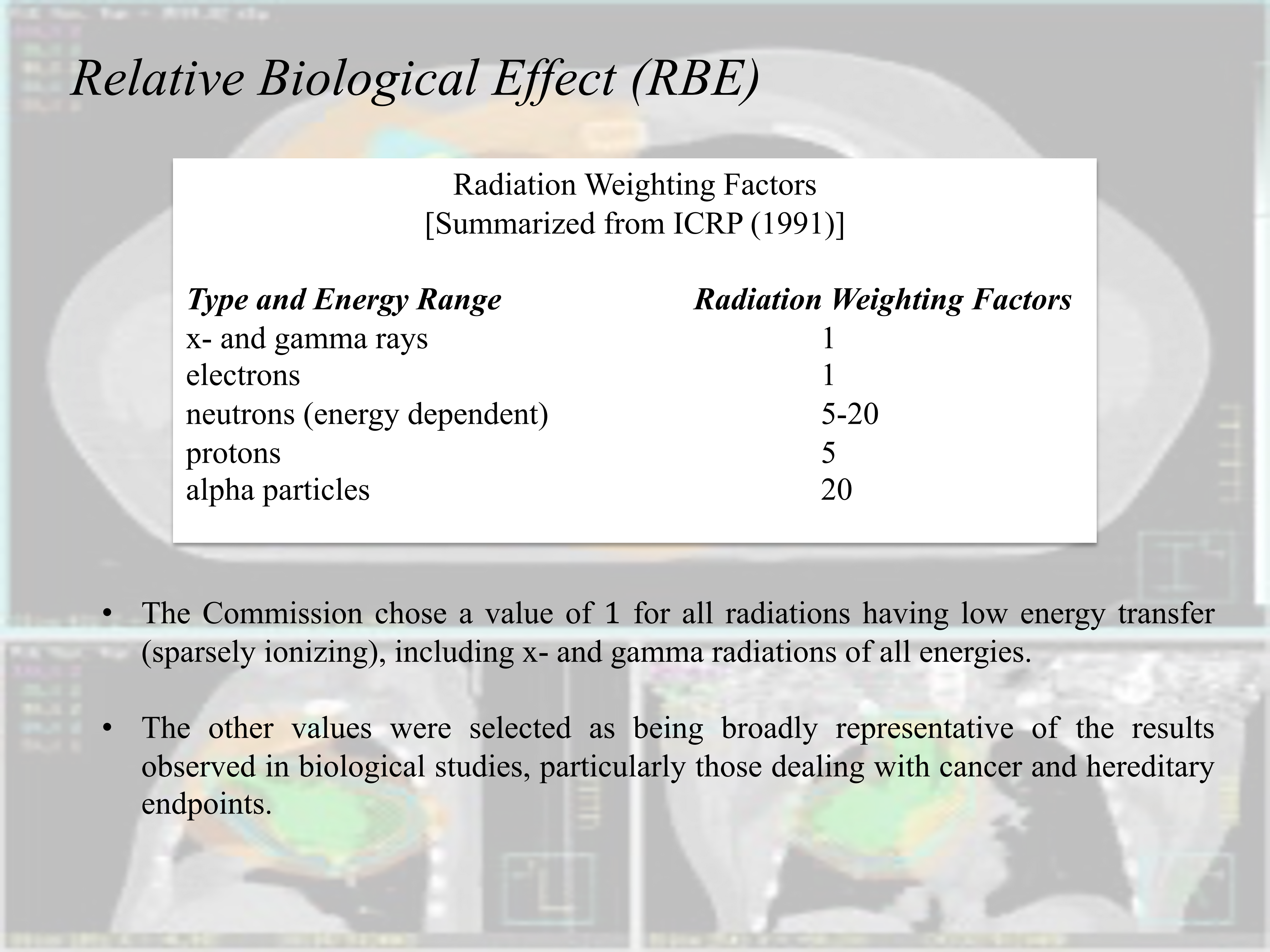
- The relative biological effectiveness for a given test radiation, is calculated as the dose of a reference radiation, usually x-rays, required to produce the same biological effect with a dose, $D_T$, of another radiation.

$$RBE = \frac{\text{Dose of reference radiation required to produce a response}}{\text{Dose of radiation used to produce same response}} = \frac{D_{reference}}{D_T}$$

- Suppose that it takes $200mGy$ of x-rays but only $20mGy$ of neutrons to produce the same biological effect, the RBE would be 10 ($= \frac{200}{20}$) using x-rays as the reference radiation.

- For radiation protection purposes, the International Commission on Radiological Protection, ICRP, has described the effectiveness of radiations of differing qualities by a series of Quality Factors (ICRP 1977) and more recently by a series of Radiation Weighting Factors (ICRP 1991).

# *Relative Biological Effect (RBE)*



Radiation Weighting Factors
[Summarized from ICRP (1991)]

| ***Type and Energy Range*** | ***Radiation Weighting Factors*** |
|---|---|
| x- and gamma rays | 1 |
| electrons | 1 |
| neutrons (energy dependent) | 5-20 |
| protons | 5 |
| alpha particles | 20 |

- The Commission chose a value of 1 for all radiations having low energy transfer (sparsely ionizing), including x- and gamma radiations of all energies.

- The other values were selected as being broadly representative of the results observed in biological studies, particularly those dealing with cancer and hereditary endpoints.

# *Relative Biological Effect (RBE)*

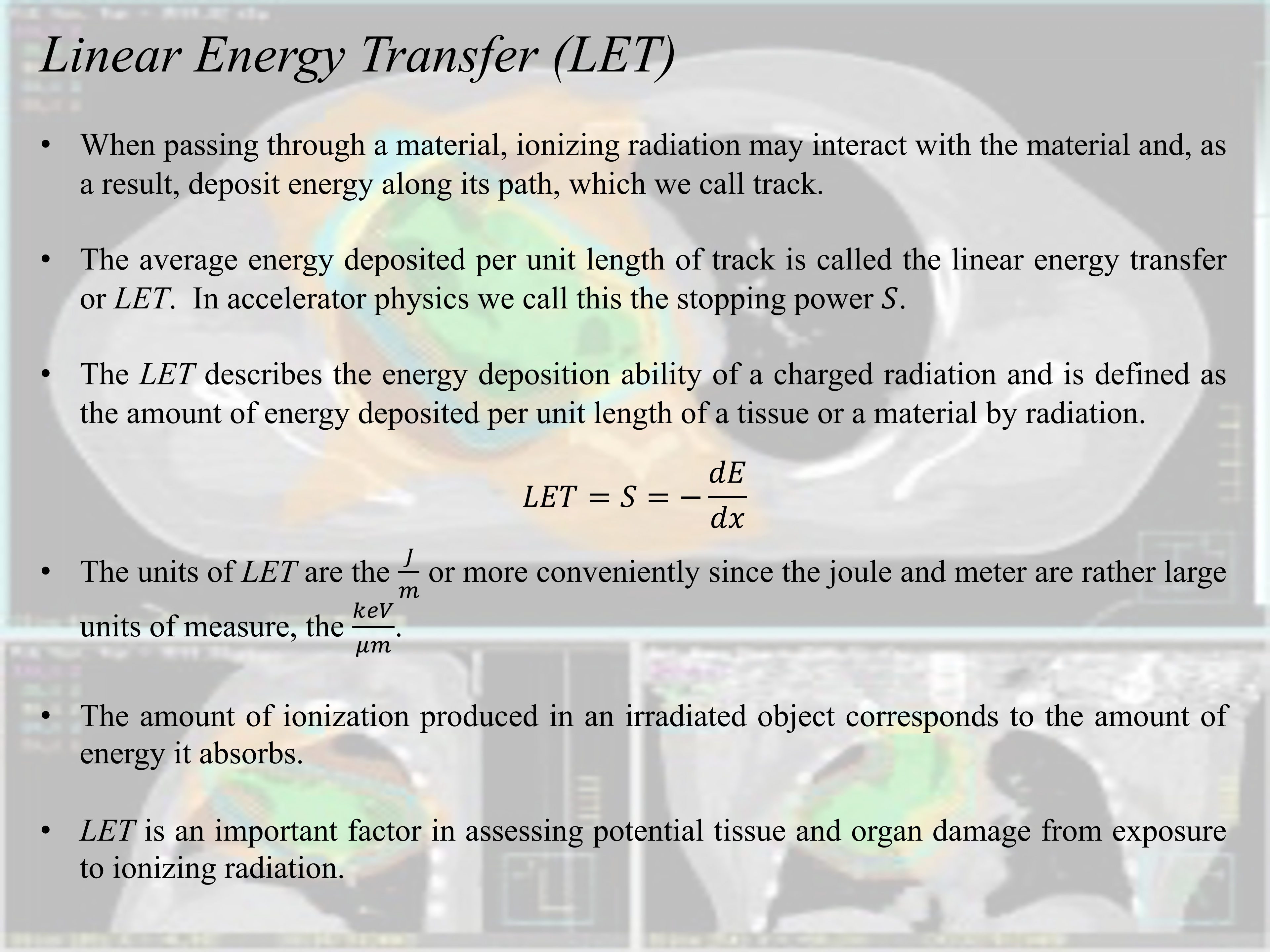
- X-rays and gamma rays interacting with materials give rise to fast electrons (with unit charge). The primary interactions of x-rays are will separated in space (they have a low *LET*) and are said to be sparsely ionizing. These electrons can indirectly damage DNA and we take their RBE to be 1.

- Beta particles (electrons) also have a fairly low LET and are sparsely ionizing. They do not travel far into a material before they lose most of their energy.

- Neutrons interact with protons in nuclei and produce recoil protons of unit charge. They are fairly densly ionizing and have a high *LET* but they don't travel far in the material. Their RBE is greater than 1. It takes a lower dose of neutrons to affect the same outcome as a dose of x-rays.

- Alpha particles have two, unit charges and are very heavy. These deposit energy in a very small distance but are very densely ionizing because of their charge. They have a high *LET* and their RBE is greater than one. It takes a much lower dose of alphas to affect the same outcome as a dose of x-rays.

- Protons are unit charge. These can travel far into the material, based on their energy, and are fairly densly ionizing. Their *LET* is rather large, and it takes a much lower dose of protons to affect the same outcome as a dose of x-rays.



# *Linear Energy Transfer (LET)*

- When passing through a material, ionizing radiation may interact with the material and, as a result, deposit energy along its path, which we call track.

- The average energy deposited per unit length of track is called the linear energy transfer or *LET*. In accelerator physics we call this the stopping power $S$.

- The *LET* describes the energy deposition ability of a charged radiation and is defined as the amount of energy deposited per unit length of a tissue or a material by radiation.

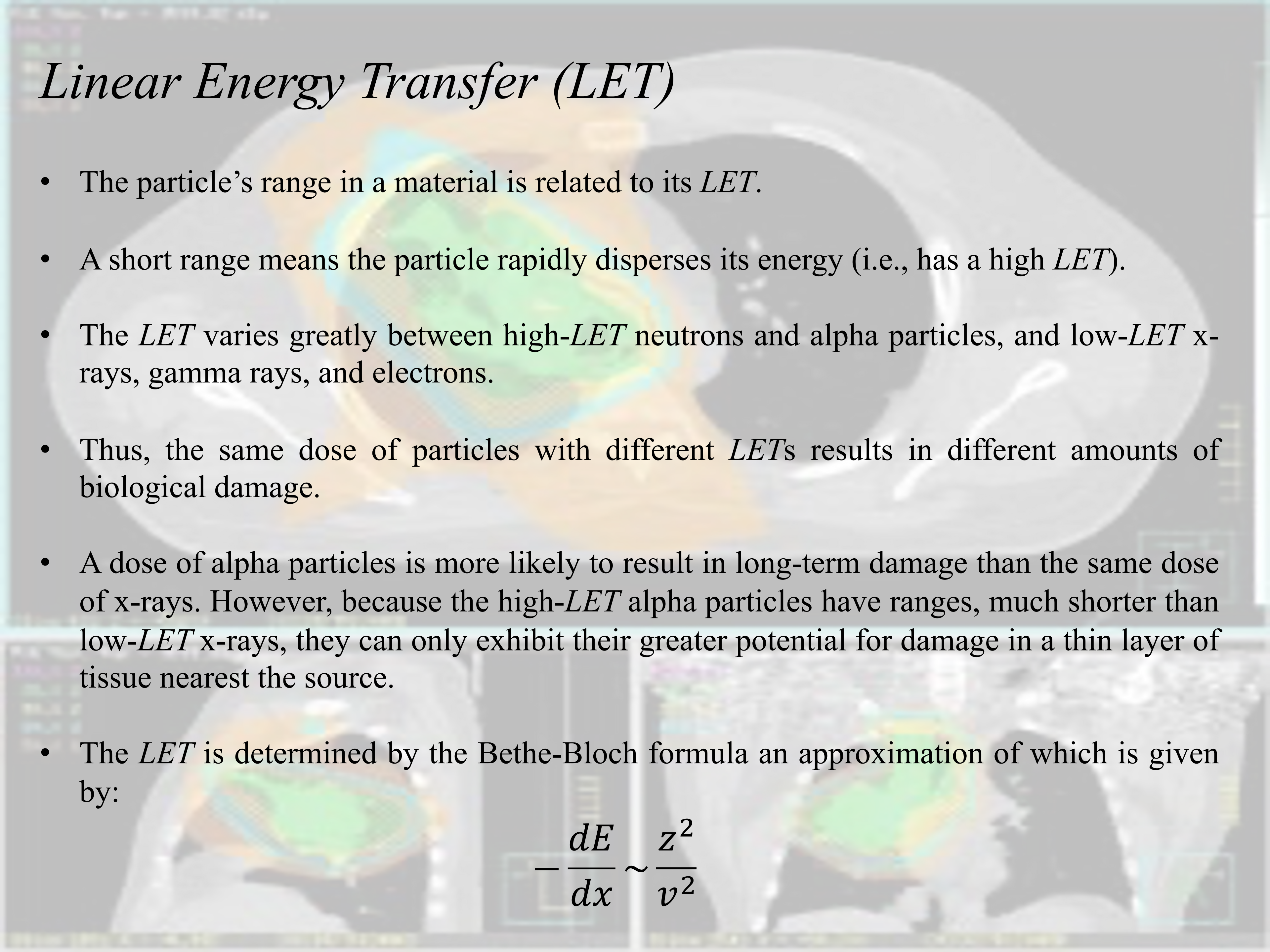
$$LET = S = -\frac{dE}{dx}$$

- The units of *LET* are the $\frac{J}{m}$ or more conveniently since the joule and meter are rather large units of measure, the $\frac{keV}{\mu m}$.

- The amount of ionization produced in an irradiated object corresponds to the amount of energy it absorbs.

- *LET* is an important factor in assessing potential tissue and organ damage from exposure to ionizing radiation.

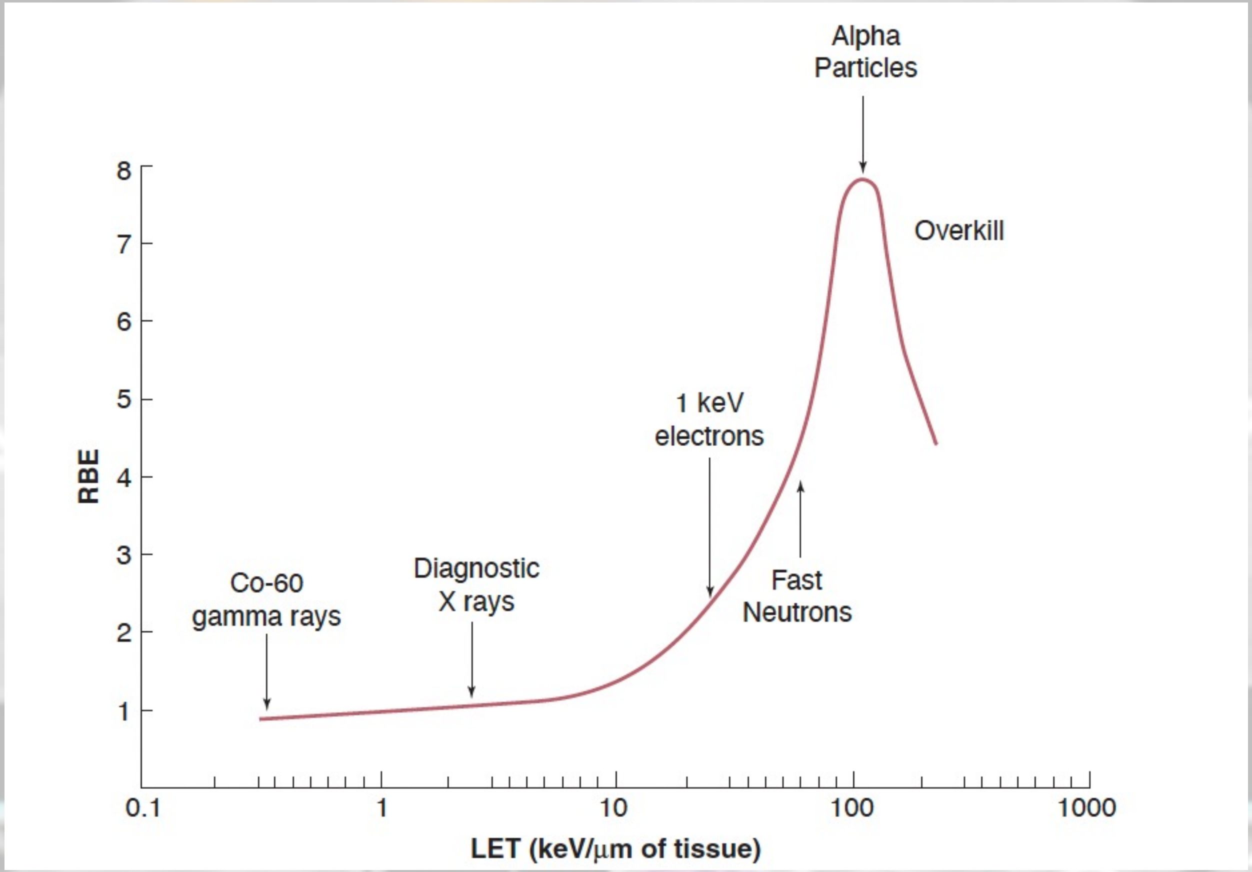
# *Linear Energy Transfer (LET)*



- The particle's range in a material is related to its *LET*.
- A short range means the particle rapidly disperses its energy (i.e., has a high *LET*).
- The *LET* varies greatly between high-*LET* neutrons and alpha particles, and low-*LET* x-rays, gamma rays, and electrons.
- Thus, the same dose of particles with different *LET*s results in different amounts of biological damage.
- A dose of alpha particles is more likely to result in long-term damage than the same dose of x-rays. However, because the high-*LET* alpha particles have ranges, much shorter than low-*LET* x-rays, they can only exhibit their greater potential for damage in a thin layer of tissue nearest the source.
- The *LET* is determined by the Bethe-Bloch formula an approximation of which is given by:

$$-\frac{dE}{dx} \sim \frac{z^2}{v^2}$$

# *Linear Energy Transfer (LET)*



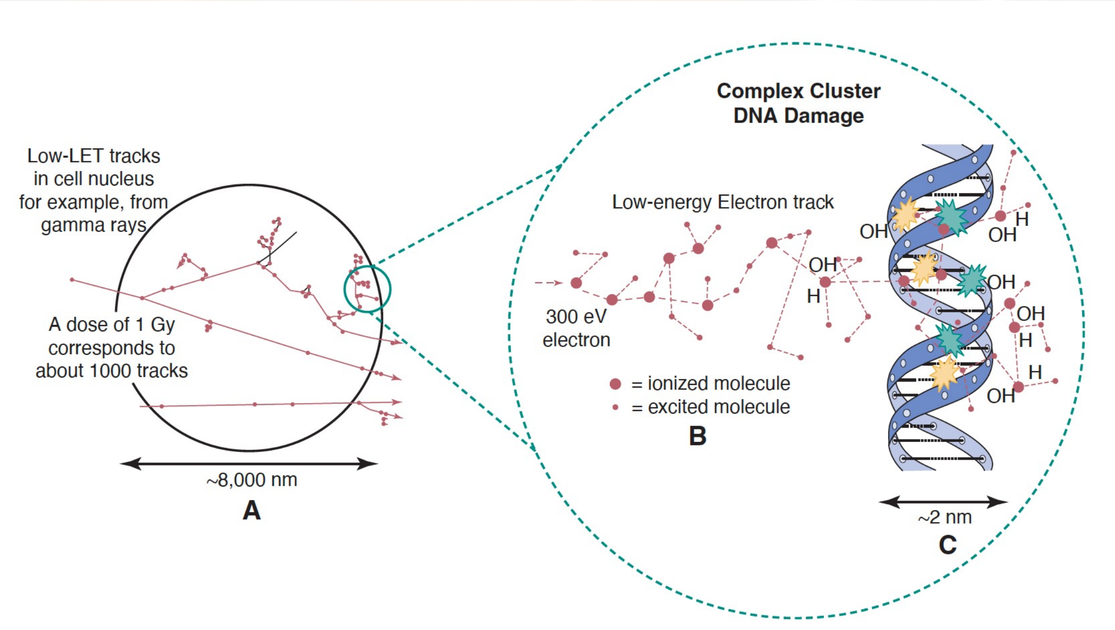
The Essential Physics of Medical Imaging, Brushberg, J.T., Seibert, J.A., Leidholdt, E.M., & Boone, J.M., Lippincott Williams & Watkins, 2012

- The RBE of a given radiation is an empirically derived value that, in general (with all other factors being held constant), increases with the *LET* of the radiation. However, beyond approximately $100\frac{keV}{\mu m}$, the radiation becomes less efficient due to overkill (i.e., the maximal potential damage has already been reached), and the increase in *LET* beyond this point results in wasted dose.

# *Linear Energy Transfer (LET)*

- Low-LET radiation like x-rays and gamma rays is considered sparsely ionizing on average; however, most of the radiation energy is deposited in small regions (on the scale of nanometers) via denser clusters of ionizations from low-energy secondary electrons.

- A segment of the electron track is illustrated utilizing a Monte Carlo simulation of clustered damage produced by ionizations and excitations along the path of a low-energy (300 eV) electron. Excitation and ionization along with secondary electrons are shown until the electron energy drops below the ionization potential of water which is about $10eV$.



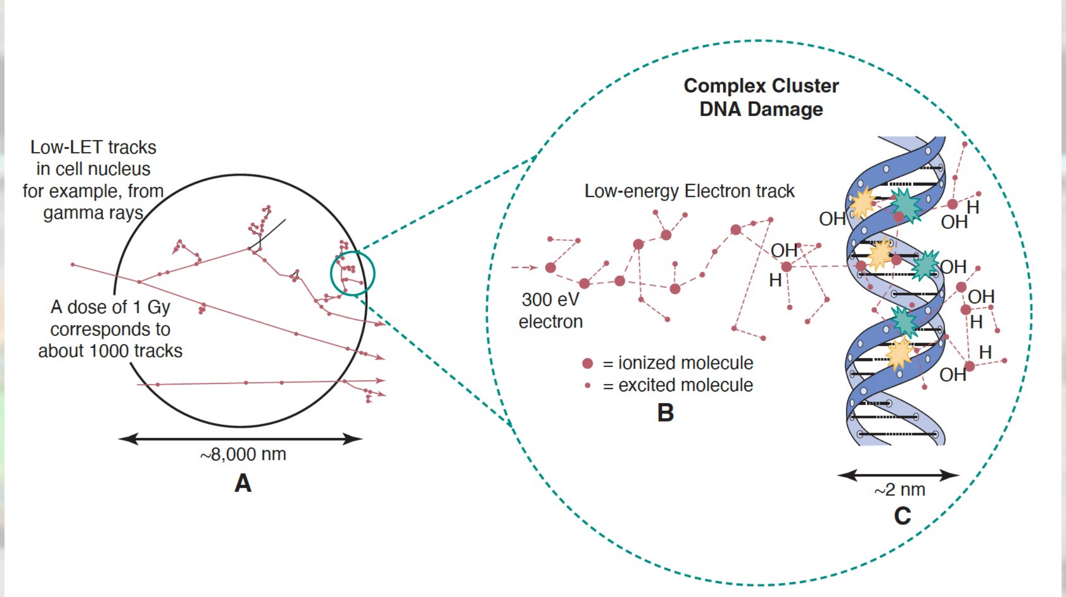
The Essential Physics of Medical Imaging, Brushberg, J.T., Seibert, J.A., Leidholdt, E.M., & Boone, J.M., Lippincott Williams & Watkins, 2012

# *Linear Energy Transfer (LET)*

- DNA double helix drawn on the same scale as the ionization track. Complex clustered damage can result from closely spaced damage to the DNA sugar-phosphate backbone and bases due to direct ionizations and diffusion of OH radicals produced by the radiolysis of water molecules in proximity (few mm) with the DNA

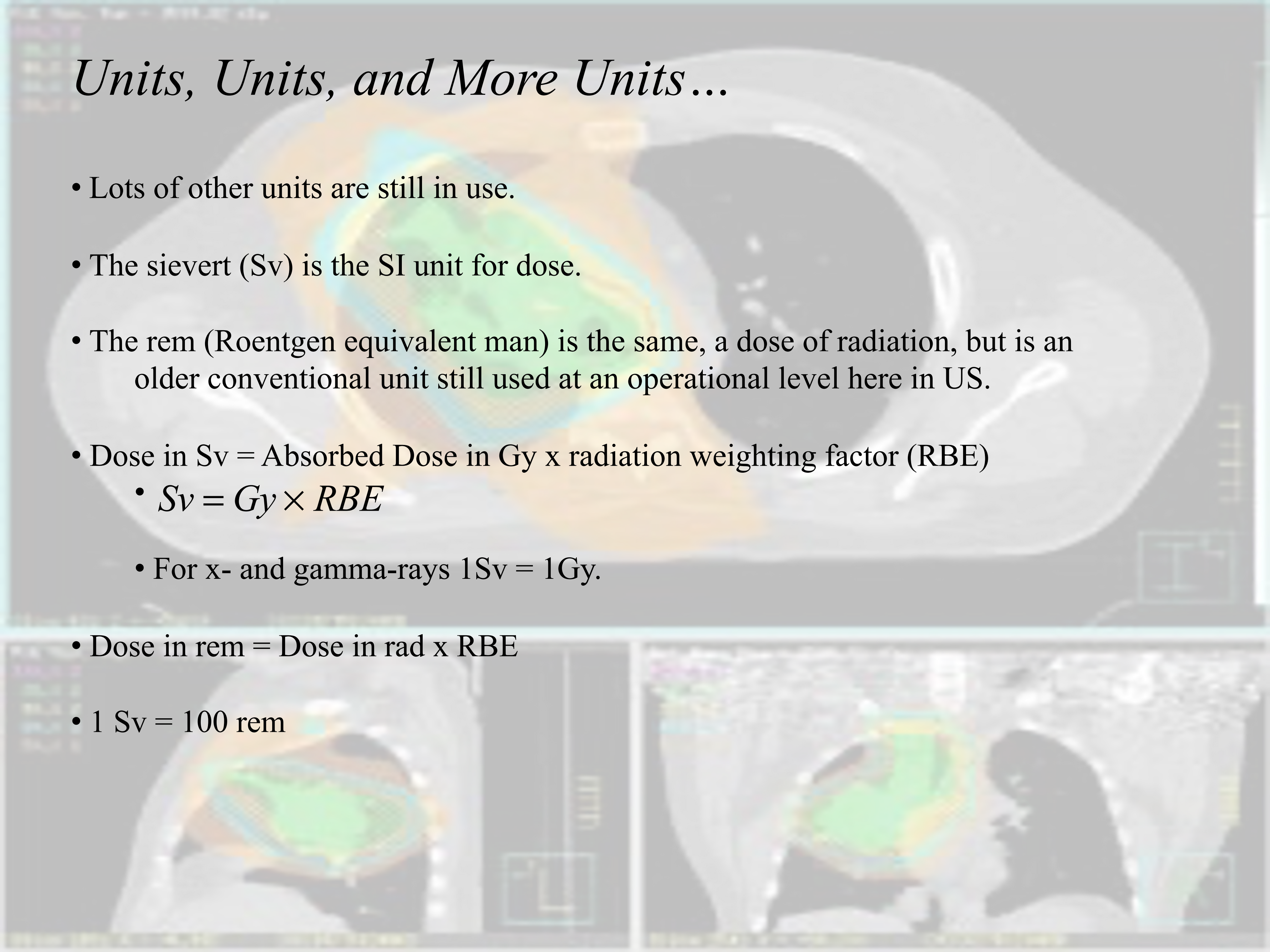
- Multiple damaged sites are shown as green and orange, and these denote DNA strand breaks, or damaged bases, respectively.

- In this example, the result is a complex double strand break, This example has three strand breaks and three damaged bases, all within ten base pairs along the DNA. This type of damage is difficult for the cell to repair and can lead to cell death.

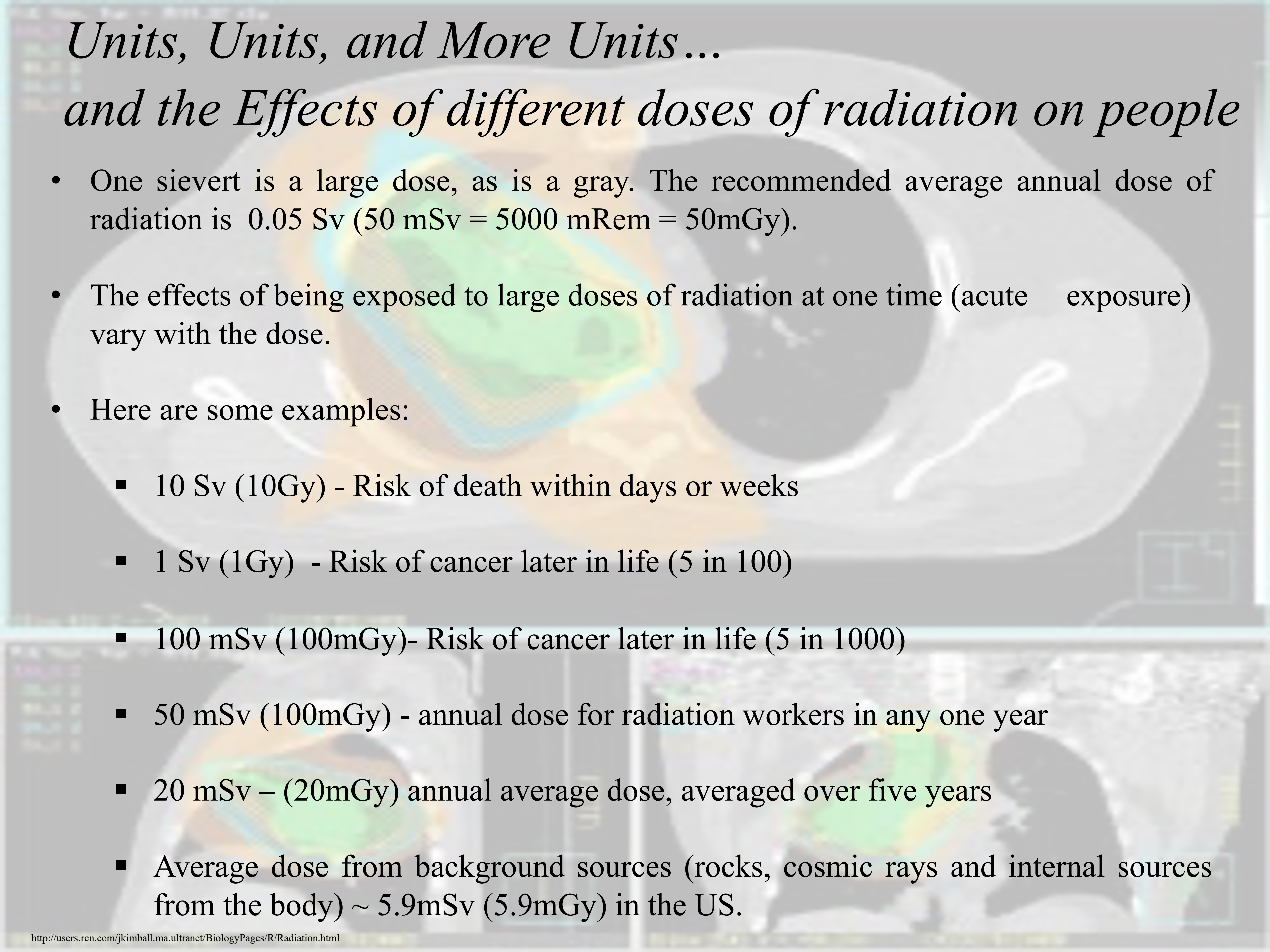


The Essential Physics of Medical Imaging, Brushberg, J.T., Seibert, J.A., Leidholdt, E.M., & Boone, J.M., Lippincott Williams & Watkins, 2012

# *Units, Units, and More Units…*



- Lots of other units are still in use.
- The sievert (Sv) is the SI unit for dose.
- The rem (Roentgen equivalent man) is the same, a dose of radiation, but is an older conventional unit still used at an operational level here in US.
- Dose in Sv = Absorbed Dose in Gy x radiation weighting factor (RBE)
  - $Sv = Gy \times RBE$
  - For x- and gamma-rays 1Sv = 1Gy.
- Dose in rem = Dose in rad x RBE
- 1 Sv = 100 rem



# *Units, Units, and More Units…*
# *and the Effects of different doses of radiation on people*

- One sievert is a large dose, as is a gray. The recommended average annual dose of radiation is 0.05 Sv (50 mSv = 5000 mRem = 50mGy).

- The effects of being exposed to large doses of radiation at one time (acute exposure) vary with the dose.

- Here are some examples:

  - 10 Sv (10Gy) - Risk of death within days or weeks
  - 1 Sv (1Gy) - Risk of cancer later in life (5 in 100)
  - 100 mSv (100mGy)- Risk of cancer later in life (5 in 1000)
  - 50 mSv (100mGy) - annual dose for radiation workers in any one year
  - 20 mSv – (20mGy) annual average dose, averaged over five years
  - Average dose from background sources (rocks, cosmic rays and internal sources from the body) ~ 5.9mSv (5.9mGy) in the US.

http://users.rcn.com/jkimball.ma.ultranet/BiologyPages/R/Radiation.html

# *Effects of different doses of radiation on people*

An Example:

Suppose that you recently had a pelvic and abdominal CT scan performed with and without contrast. Since you might be concerned about the amount of radiation you were exposed to, you called the hospital and were given the following value pertaining to your exam: $D = 21.4mGy$ for a single scan.

Should you be concerned?

Assume that the x-rays in the pelvic CT pass through skin, bone, intestines, stomach, bone and skin.

Let $E$ be the effective dose to the body from the scan and $H$ be the dose to the tissue based on the weighting factor for the radiation used. In general H is a sum as there could be many types of radiation used.

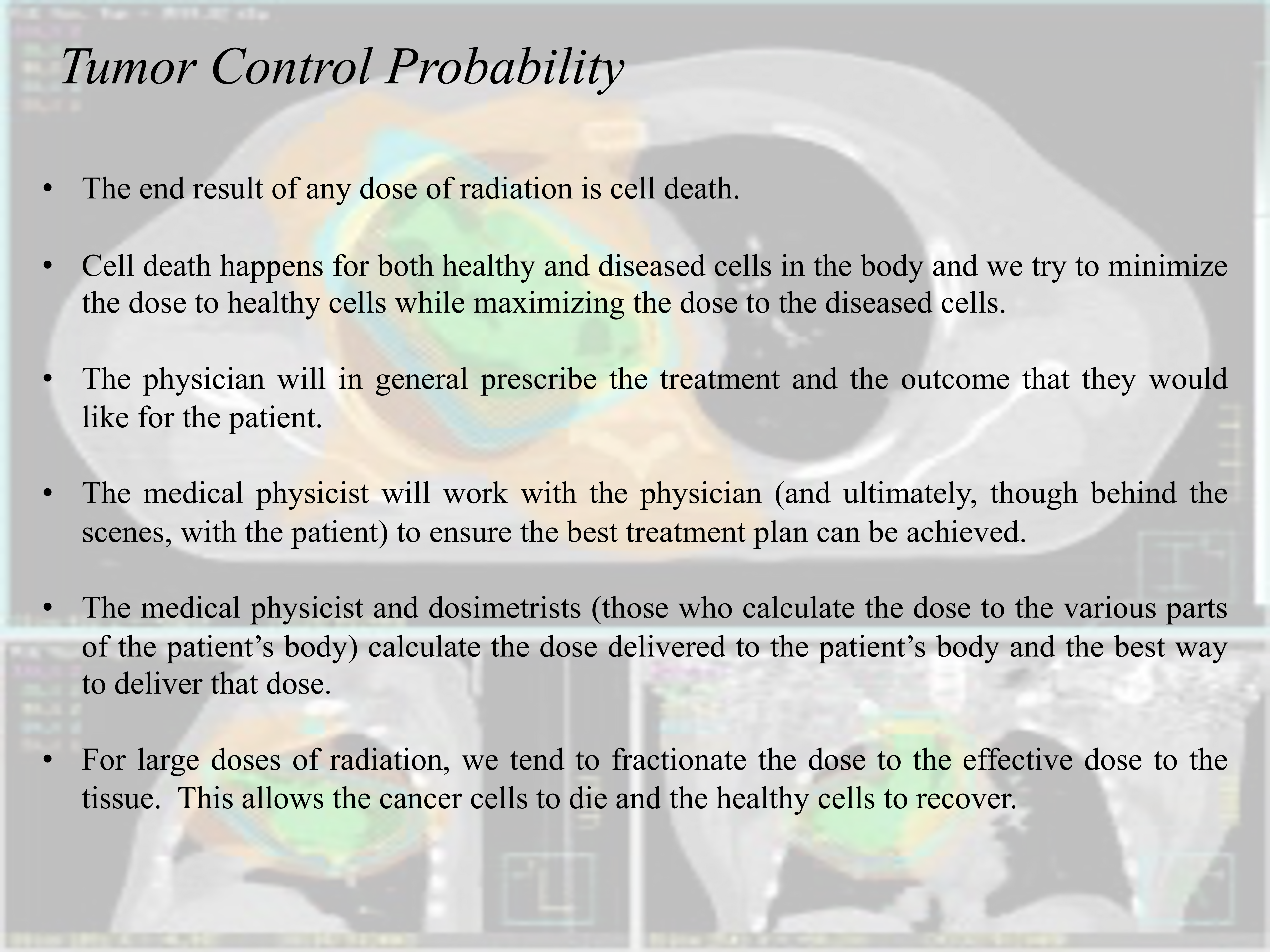
$$E = \sum_{i=1}^{N} w_i H_i$$

$$H = w_R D$$

| **Weighting factor** | **Organ/tissue** |
|---|---|
| 0.1 | Bone surface/skin |
| 0.05 | Bladder, breast, liver, esophagus, thyroid |
| 0.12 | Red bone marrow, colon, lung, stomach |
| 0.2 | Genitals |

http://www.gulflink.osd.mil/appendix_g.pdf

# *Tumor Control Probability*



- The end result of any dose of radiation is cell death.
- Cell death happens for both healthy and diseased cells in the body and we try to minimize the dose to healthy cells while maximizing the dose to the diseased cells.
- The physician will in general prescribe the treatment and the outcome that they would like for the patient.
- The medical physicist will work with the physician (and ultimately, though behind the scenes, with the patient) to ensure the best treatment plan can be achieved.
- The medical physicist and dosimetrists (those who calculate the dose to the various parts of the patient’s body) calculate the dose delivered to the patient’s body and the best way to deliver that dose.
- For large doses of radiation, we tend to fractionate the dose to the effective dose to the tissue.  This allows the cancer cells to die and the healthy cells to recover.

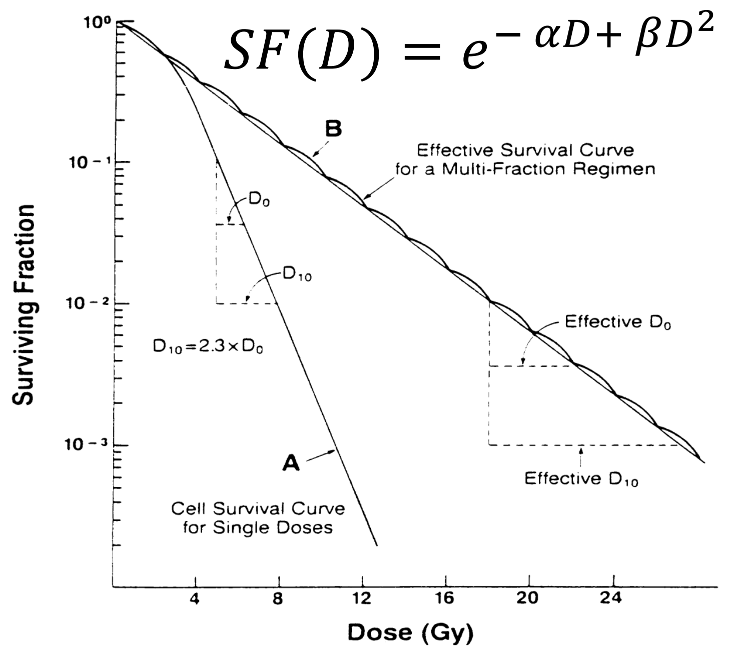
# *Tumor Control Probability*

- The surviving fraction of cells ($SF$) as a function of the dose $D$ in gray delivered.

- $\alpha$ is the coefficient of cell killing which is proportional to the dose.

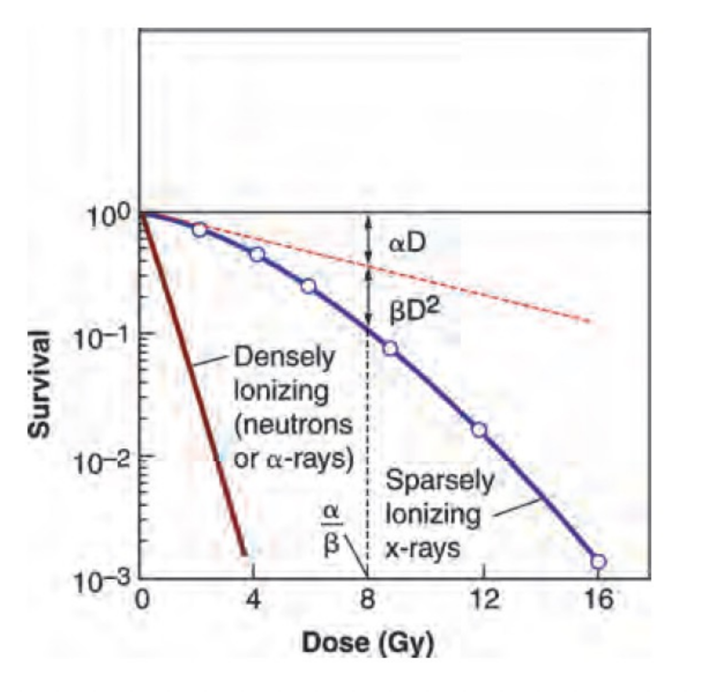
- $\beta$ is the coefficient of cell killing which is proportional to the square of the dose.

- This model, called the linear quadratic, is a mechanistic model that considers the early response to the radiation (tumor kill) and late response (healthy cell recovery) tissues.

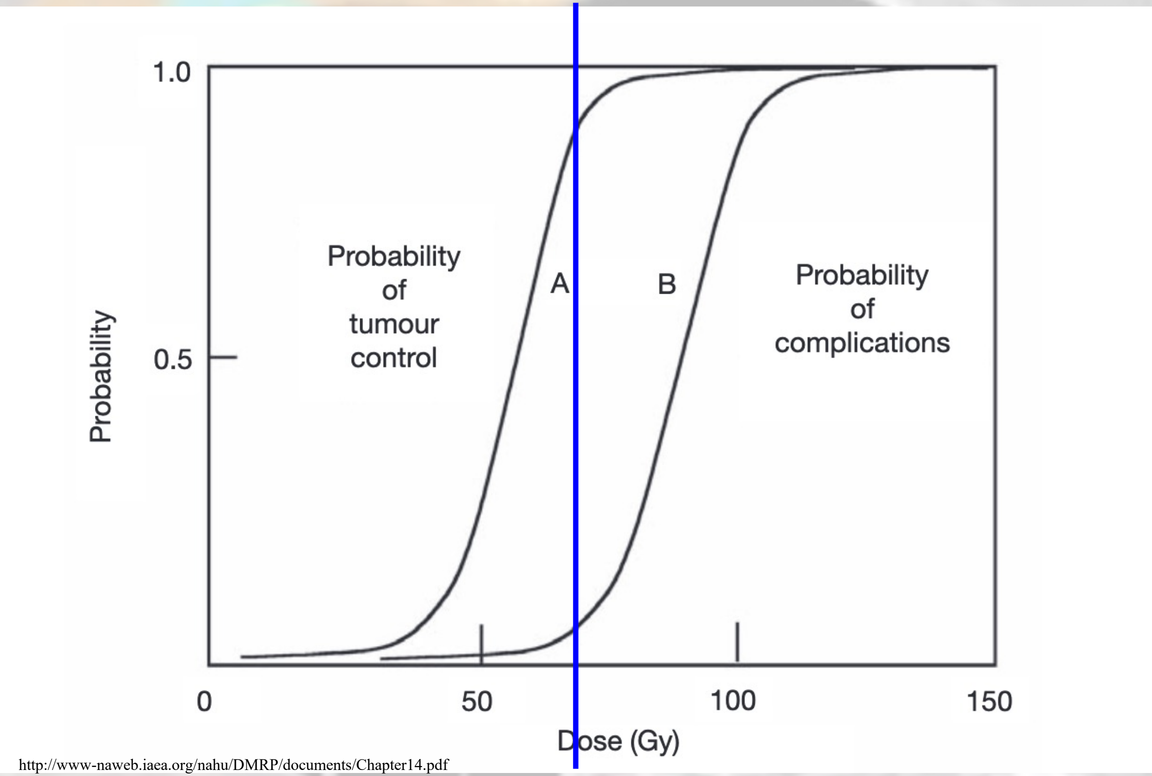


$$SF(D) = e^{-\alpha D + \beta D^2}$$

Image courtesy of Dr. Stephen Amadon, DABR



# *Tumor Control Probability*



http://www-naweb.iaea.org/nahu/DMRP/documents/Chapter14.pdf

$$TCP_{pop} = \frac{1}{\sigma_\alpha \sqrt{2\pi}} \int_0^\infty e^{-(\alpha-\alpha_0)^2/2\sigma_\alpha^2} * \prod_{i=1}^{N} \exp[-\rho_i V_i \exp(-\alpha D_i - \beta D_i^{\,2})]\, d\alpha$$

$$NTCP = \frac{1}{\sqrt{2\pi}} \int_{-\infty}^{t} e^{-x^2/2} dx$$

TCP = Tumor control Probability
NTCP = Normal Tissue Complication Probability

# *Summary*