Chapter 6 A Single Dose of Radiation

What happens to molecules

Radiation comes, either as a stream of energetic charged particles, or as a flux of electromagnetic radiation, that is neutral photons.[25] But radiation cannot have any effect on materials, including living tissue, unless some of its energy is absorbed. This absorbed energy is not spread out uniformly through the irradiated region, but occurs as a series of collisions or events, as they are called. If the absorbed energy is high, the number of events is increased but the character of each event remains the same. In a typical event an individual atom or molecule receives enough energy to be broken up, occasionally sending off a secondary charged electron or photon, perhaps with enough energy to cause a few further events on its own account.

In a beam of charged particle radiation each incident charge generates its own string of independent events called a track. Along a track events are separated by a fraction of a micron – the density of events depends on the speed and magnitude of the charge, and also on the density of the material, but not much on its composition. As it makes its track the charge may be scattered sideways a little as a result of the events, as well as gradually losing energy with each successive event. The more energetic it is initially, the further it goes, until finally it stops at the end of its range. The rate at which it loses energy along its track is called its *linear energy transfer* (LET) – this is simply a matter of the density of events.

Photons on the other hand do not create long tracks but give isolated events, more thinly spread out, often with emission of an energetic electron or secondary photon. As a result photons in a beam have an exponential distribution of penetration described by an average range, quite unlike the rather sharply defined

[25] Leaving aside neutron radiation, which is less common in the environment.

length distribution of charged particle tracks. This average range is strongly dependent on the material composition – in fact on the atomic number Z of its atoms. In particular, for high Z atoms like lead, the absorption is high and the range short. It is not just that there are more electrons in a high Z atom, each electron is more tightly bound and the effect per electron is greater. This is why lead is used to shield X-rays in places where radiation is used, including medical and dental facilities.

These collisions or events involve either an atom as a whole or a single electron in an atom – the nuclei of the material play almost no part and are unaffected. Generally the impact of ionising radiation on material is rather indiscriminate. This may be explained in terms of an energy hierarchy:

1/40 eV random thermal energy	<<	1/10 eV biological activation energy	<<	10–100 eV collision event energy	<<	1,000,000 eV incident radiation energy

The energy absorbed in a collision or event is in the range of a few electron volts[26], say 10–100 eV. Such energies are very small compared with the energy of the incident radiation, but much larger than the delicate activation energies of the biological molecules essential to life, which are on the scale of 1/10 eV. These in turn are robust compared with the random thermal energies with which molecules hit one another, simply because they are warm, 1/40 eV. This hierarchy means that the energy dumped in an event is too small to disrupt any nucleus but any molecule hit in an event suffers major damage – there is no fine tuning. Different types of ionising radiation affect the spatial distance between events, but often have less influence on the energy of each event. Equally, any kind of molecule may be hit and become the site of an event. This is the sense in which the damage caused by radiation exposure is indiscriminate.

[26] This does not include the energy given to a secondary electron, if any.

In the immediate aftermath of the passage of the radiation, distinct destruction sites of molecular debris are left where the events occurred. Very quickly the highly reactive pieces of broken molecules, called hot chemical radicals, disrupt other molecules that may have been undamaged in the initial event. This is the chemical stage of the story in which radiation and radioactivity play no part. In organic matter the presence of oxygen can prolong the destructive activity of these radicals, and so too can water molecules (H_2O) through the production of OH radicals. Anti-oxidants are biological molecules that have the opposite effect by mopping up and neutralising radicals. But, this rampage soon stops leaving relatively quiescent chemical debris.

What happens to cells

If the material is living tissue, any molecule affected by an event may have lost its ability to fulfil its biological function in a cell. Much the same kind of damage can be caused by agents other than ionising radiation – for example, by an exceptional random collision with another molecule, or by chemical action, in particular oxidation. What may be different about the effect of ionising radiation is the number of such damaged molecules within a small region. But the next stage of the story is biological in any case, whether the initial cause was radiation or chemical attack.

Living tissue is composed of cells, the units of life. These cells have a large range of size, shape and structure according to their function. However, in each case there is a cell skin that encloses both the active proteins and the genetic records that are encoded in DNA. These records, held in the nucleus of the cell, determine the production of the cell's proteins, and thence its function and reproductive cycle. The complete DNA record in a cell also contains the information for all of the other cells.

If a protein molecule is damaged and ceases to function, its role is usually taken over by others that remain intact. Such damaged molecules are then naturally replaced along with the undamaged ones in the next cycle of cell regeneration without harmful effect.

The only way that errors (whether caused by radiation or chemical attack) can get copied to later generations of cells is through damage to the DNA record. If the DNA is altered, its copies in subsequent generations of cells may be altered too. However, that is too simplistic as it turns out, for there are several ways in which such errors in the DNA get progressively weeded out.

Evidence at high dose

Before following this biological story further, we look at some actual evidence that shows the effect of radiation on animals and humans. Do they show a dose-damage curve similar to the ones for other stresses that we looked at? Does the curve have the characteristic sigmoid shape (Figure 7b) suggesting some kind of protective repair mechanism? Or is it described by the straight line of the LNT hypothesis (Figure 7a)?

Figure 9 shows data on mortality due to acute doses of radiation with different intensities. Data on laboratory rats given a single exposure of X-rays to the whole body are sketched in Figure 9a. The curve follows the familiar non-linear S-shape that we have come to expect. A dose of about 7,000 millisievert is sufficient to cause the death of 50% of rats, but with half that dose less than 1% die. If LNT were correct, the curve would be replaced by the heavy dashed line and 25% of the rats would be expected to die from this halved dose. The experiment can be repeated with many rats so that uncertainties are small. Evidently the response is non-linear, at these high doses at least.

But how different are humans from rats? At the Chernobyl accident there were 237 workers who were exposed to intense radiation in the early stages of fighting the fire. Of these, 28 died of acute radiation sickness in the following few weeks. The mortality of these workers is shown in four bands of radiation dose by the crosses in Figure 9b. The width of each cross indicates the range of dose for that band; the vertical height represents the statistical uncertainty in the measured mortality

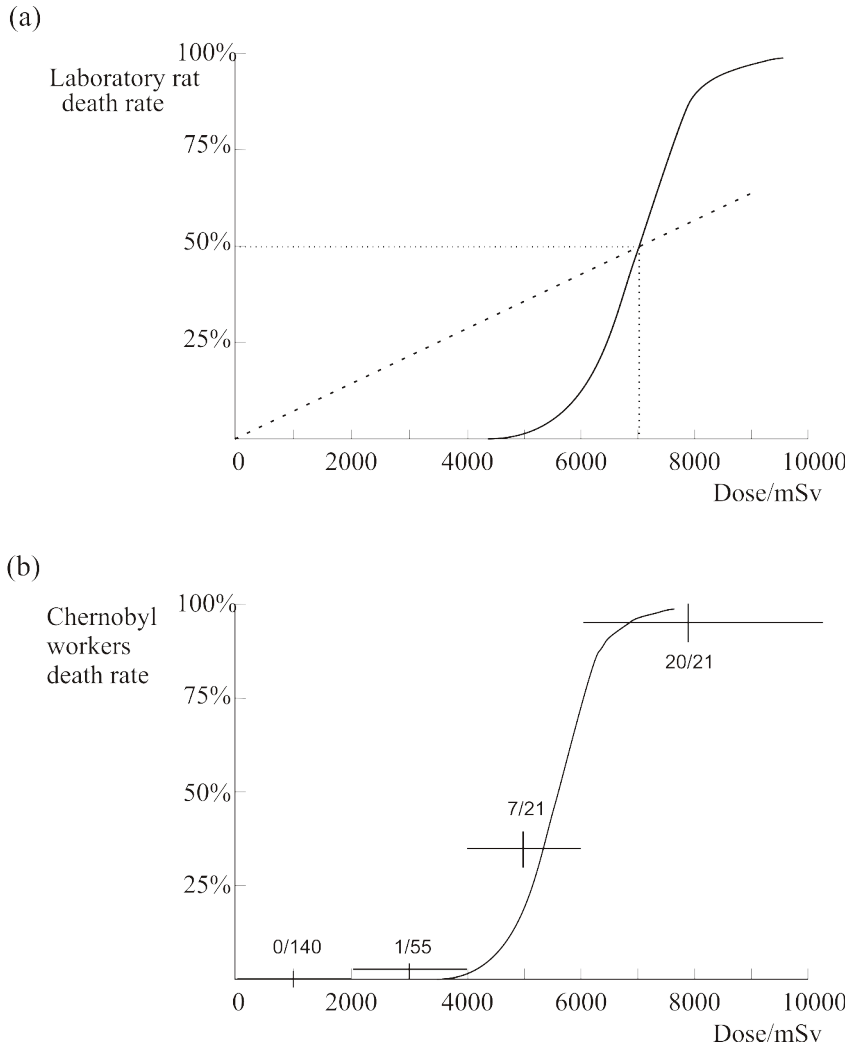

Figure 9 (a) The observed mortality of laboratory rats for different radiation doses (solid curve) compared with LNT (dashed line). The vertical and horizontal dotted lines are solely to guide the eye. (After Henriksen and Maillie [16].) (b) The mortality of Chernobyl workers (crosses) in four dose bands compared with the mortality of the rats, as in (a) but scaled to a slightly lower dose.

given the small number of workers.[27] So in the highest band 20 out of 21 died, in the next band 7 out of 21, in the third band 1 out of 55, and in the lowest band out of 140 all survived. Also shown is the S-shaped curve found for the rats, scaled to give 50% human mortality at 5,500 millisievert instead of 7,000 millisievert.

The Chernobyl data and this curve match well, given the uncertainty reflected in the size of the crosses. Of course the human experiment may not be repeated accurately with many subjects like the rat experiment. Even so, the conclusion is clearly that the dose-mortality curve for humans at high doses is not described by LNT but follows a typical non-linear S shape.

Repair mechanisms

The discussion in Chapter 5 would suggest that this non-linearity arises from one or more repair mechanisms. Discovering these has been a matter for biological study with cells in the laboratory and with further experiments on animals. We start by thinking about what kind of protection biology might have developed.

Imagine a similar situation in a non-scientific context – a business liable to random attack from fire or robbery. Good management would implement some defensive procedures. The first of these could be to equip all areas with fire extinguishers and an alarm system that is activated by any intruder or fire outbreak. Next multiple copies of all working documents should be made so that, if one copy is lost or damaged, others would survive. Then a rapid reaction unit capable of quickly repairing simple damage to master records. Another line would be a continuous programmed replacement of all elements of the structure. Finally a regime of cleanliness to remove all unwanted material as quickly as possible. Interestingly, it seems that cellular biology has developed elements of defence along similar lines.

[27] These are standard statistical errors so that the probability that the true result falls within the range shown is 63%.

The equivalent of the fire extinguishers is the promotion of anti-oxidant molecules in cells, capable of quenching the radicals produced by radiation at the early or chemical stage of radiation damage. These can cope also with the early effects of any oxidative attack, so no special provision is needed for radiation. The alarm system is provided by inter-cellular signalling such that cells cooperate and warn other cells whenever an attack is detected. Protection by copying takes place at two levels. Within each cell there are multiple copies of many functional proteins. The effectiveness of this is shown by the observation that, in the early stages of a cell's life cycle when the number of copies is smallest, its sensitivity to radiation is greatest. But there are no spare copies in each cell of the DNA with its genetic information. However, the cells themselves are copied and the DNA in each cell contains the complete record for the whole organism, not just its own part. Each cell contains enzymes that repair single breaks in DNA strands – these enzymes are the rapid reaction unit in our analogy. Because DNA has the special double strand helix, a molecule that suffers a single strand break (SSB) remains connected and can be mended without error. Test tube experiments show that these enzymes can repair most single breaks within a few hours. Double strand breaks (DSBs) are less frequent. When they occur they can still be repaired but may be mis-repaired. A further level of protection is needed to cope with these.

Copies of whole cells are produced dynamically by the process of cell division and programmed replacement. While functioning cells divide to create new ones, existing cells are regularly scrapped. Cells may die of their own accord, they may be encouraged to die by inter-cellular signalling or they may be attacked. Anyway these mechanisms provide discrimination in favour of cells recognised as native over those that have changed or are foreign. This organised cleansing process is called apoptosis. The disposal of dead cells and other debris is undertaken by cells called macrophages.

So there are levels of protection within a cell, and should they fail there are active renewal mechanisms to replace whole cells. The details are not important in this brief sketch – the point is that these mechanisms exist and are effective. They were not developed specifically to cope with the detritus left by a dose of ionising radiation – they are mostly employed to cope with chemical attack and random breakages. They are active on various timescales from hours to a few weeks, depending on the particular organ and the age of the individual. Important to the working of these defence mechanisms is the fact that cells communicate – the inter-cell signalling. The word gets around that this cell has been damaged or that another needs to be scrapped. The immunological process then sees to it that such cells do not survive.

This type of behaviour by cells is not unlike the way in which people behave in crowds. Social groups that survive do so by selection and by robust rejection of those that do not belong. Often this is not a pleasant process and includes all manner of discrimination – it can even become self-destructive with witch hunts and other types of social self-harm.

The scientific study of this sociology of cells and its response to ionising radiation is the subject of radiobiology. This is studied in the laboratory with cells in solution, and also in experiments with laboratory animals similar to man, such as rats and mice. We shall focus on what can be learnt from human data, because it is slightly easier to follow and also because that is what we are really concerned about. We will see how the data confirm the picture that the radiobiologists find in their laboratory work.

According to this picture the repair and protection mechanisms that cope well with low doses are overwhelmed at higher doses, and this naturally gives rise to the sigmoid curve. Following a high dose, cell division is suspended or delayed and more cells die than are created. Some organs in the body have a particularly rapid turnover of cell population under normal circumstances – for example, the digestive tract. As a result these are the first to fail following a very high acute dose. The symptoms of acute

radiation sickness are vomiting, diarrhoea, dehydration and death in a few days, or weeks at the outside. This was the experience of those who died from a high dose at Chernobyl (Figure 9b). Cancer is not involved in these cases.

These observations are for high doses. How effective are these repair mechanisms for lower acute doses? Then the repair and cell replacement mechanisms operate, but an occasional DNA error survives.

Low and intermediate doses

The effect of lesser doses of ionising radiation may be an increase in the observed incidence of various cancers that become evident long after the exposure. These cancers vary in mortality. The cause in an individual case cannot be determined, but statistically, incidence can often be related to smoking, diet or radiation – or be apparently without cause, that is spontaneous. In all cases the origin is understood as a chemical attack of some kind on the DNA. Even when a significant radiation exposure has been experienced, the cancer rate due to other causes is still much larger (with the exception of thyroid cancer). The contribution of ionising radiation may then be impossible to measure with any confidence unless data are available for very large populations in receipt of significant doses of radiation.

Let us take a fictitious example to illustrate the point. Suppose that there are two groups, each of 10,000 people. In the first group the chance of dying of cancer in 50 years is 10%, but in the second it is 10.5% because this group has received a certain dose of radiation. If the test were repeated many times the average number of cancer deaths in the two groups would be 1,000 and 1,050. However, if data are available for only one such test, the number in the first group would fluctuate statistically, being greater than 1,030 for 18% of such tests and greater than 1,060 for 2.5% of them.[28] Similarly the number of deaths

[28] These variations are reliable statistical results, independent of this problem.

counted in the second group would be less than 1,020 for 18% of tests and less than 990 in 25% of tests. So comparing the number of deaths in one such test would be quite inconclusive, simply because of the statistical uncertainty. If the number of people in each group was 10 times larger or the radiation dose (or its effect) was much greater, the test might provide meaningful evidence. Then to reach a firm conclusion the radiation dose for each group member must be measured and checks applied to ensure that other causes of cancer are not confusing the situation – these are called confounding effects.

There are relatively few such sources of data and these have received a great deal of attention from researchers. The basic data have been discussed between laboratories from all over the world and the results may be found on the Web. The largest source is the medical records of the human survivors of Hiroshima and Nagasaki. Then there is the Chernobyl accident, and we have looked at the high dose data from there already. Another large source of internationally compiled data is concerned with the incidence of lung cancer and its correlation with the radiation environment in which people live. There are the health records of those who have worked with radioactive material over the decades, including medical radiologists. Then there are the people who painted the dials of watches and other instruments with luminous paint in the decades up to 1950. They absorbed quantities of radium that remained with them as an internal source of alpha radiation. Finally there are data for patients who have received radiation in the course of medical diagnostic imaging, or, more significantly, in radiotherapy treatment. We look at these in this chapter and the next.

Survivors of Hiroshima and Nagasaki

The data that have been studied most are the health records of the survivors of Hiroshima and Nagasaki – the number of individuals is large, they have been studied for over 50 years, and the individual doses cover a wide range with an average 160 millisievert, a significant intermediate exposure.

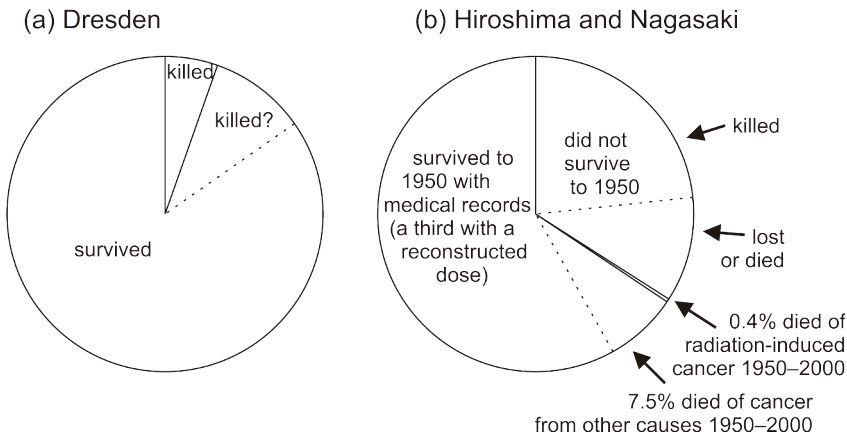

Figure 10 Pie charts of the mortality of the bombings of (a) Dresden and (b) Hiroshima and Nagasaki. The numbers killed immediately are not well known but the history of those who survived to 1950 is well documented.

At the time of the bombing the population of the cities was 429,000. It has been estimated that in the explosion, the fire and the early effects of radiation more than 103,000 died. Naturally, early information is lacking but the data become more reliable from 1950 after which the medical records of 283,000 individual survivors have been followed. This leaves 43,000, either dead, unaccounted for or lost in the period between 1945 and 1950. Figure 10b shows the situation graphically. At Hiroshima and Nagasaki the chance of not surviving until 1950 was about a third. This is compared with about 10% or more at Dresden, Figure 10a. How many inhabitants of the Japanese cities in 1945 succumbed to radiation-induced cancer in the period 1950–2000? Such a question could not be answered in earlier decades and therefore an extremely cautious view was taken. Today, no such provisional caution needs to be applied, because the question can be answered. The detailed numbers are given below but may be summarised. The chance of surviving to 1950 and then dying of cancer between 1950 and 2000 was 7.9%. As will be seen later, the chance of surviving and then dying of radiation-induced cancer during this period was only 0.4%. This is much less than

might have been expected, and so we should look in some detail at how it is derived.

Of course no resident of these cities was wearing a radiation monitor on the day the bombs were dropped, but it has been possible to estimate the individual radiation exposure for 86,955 of the survivors.[29] This has been done in three different ways, allowing cross checks to be made.

The first estimate comes from a knowledge of exactly where the individual was relative to the centre of the detonation and calculating the radiation flux received, taking into account the absorption of intervening material. The second method uses the incidence of chromosome damage, which retains a long memory of radiation dose. This method, called FISH (fluorescence in situ hybridisation), is found to be non-linear, itself showing a failure of LNT [17]. The third comes from measuring the radiation damage recorded in the teeth and bones of each survivor using electron spin resonance (ESR) [18]. This determines the density of unpaired electrons – in such solids these remain a frozen record of ionising radiation exposure even after several years. Individual doses have been re-analysed using these methods on more than one occasion, most recently in 2002.

The subsequent medical records of the survivors with reconstructed dose have been compared with those of a control group of 25,580 people who lived in Japan outside the bombed cities and received no radiation. Data on the mortality from leukaemia and solid cancers have been compiled for both sets. Data on other causes of death, and also the effect on pregnancies and other sensitive conditions, have been compiled, but here we concentrate on the cancers. The reason for this choice is that a statistically significant radiation-induced effect is seen for these

[29] The proportion of post-1950 radiation-induced cancer deaths is assumed to be the same for all the survivors as that for those with a reconstructed dose. The figures are 0.5% and 0.1% for solid cancers and leukaemia, and these are then multiplied by 0.6, the probability of survival to 1950.

cancers, whereas the increase in the incidence of other conditions is reported to be smaller and less certain.[30]

Radiation-induced cancers

Table 4 Data from Preston et al [19, Table 7] on the number of deaths from leukaemia between 1950 and 2000 among the survivors of Hiroshima and Nagasaki with measured doses, compared with the number expected using data for the inhabitants of nearby cities.

Dose range millisievert	Number of survivors	Survivor deaths actual	expected	Extra risk per 1000
<5	37,407	92	84.9	–0.1 to 0.5
5 to 100	30,387	69	72.1	–0.4 to 0.2
100 to 200	5,841	14	14.5	–0.7 to 0.6
200 to 500	6,304	27	15.6	1.0 to 2.6
500 to 1,000	3,963	30	9.5	3.8 to 6.6
1,000 to 2,000	1,972	39	4.9	14 to 20
>2,000	737	25	1.6	25 to 39
All	86,955	296	203	0.9 to 1.3

[30] Shimizu et al [20] have shown that there have been between 140 and 280 deaths (up to 1990) from other diseases that are statistically related to radiation. They report no evidence for any radiation effect below 500 millisievert.

Table 4 shows the data for leukaemia deaths among survivors with reconstructed dose. Each row describes a band or range of radiation dose, and in each case the mortality is compared with what would be expected using the death rate among the control sample. In total 296 survivors died of leukaemia in the 50-year period while only 203 would be expected in the absence of radiation. So approximately 93 extra deaths in the population of 86,955 are attributable statistically to radiation-induced leukaemia, although of course it is not possible to say which ones were spontaneous and which radiation-induced. The data in each dose band are summarised in the final column, which shows the number of extra deaths in 50 years per 1,000 people – this is given as a range described by the statistical error.[31] To put such numbers in perspective, if the chance of dying of radiation-induced leukaemia in 50 years is 1 in 1,000, then average life expectancy is reduced by 2 weeks. The data in the rows of the table for any dose less than 200 millisievert are consistent with no risk, and also with a reduction in life expectancy of less than 2 weeks. For the 15% of the survivors who received more than 200 millisievert, a definite risk is measured. Above 1,000 millisievert (3% of the survivors) the risk is greater than 21 per 1,000, a reduction in life expectancy of about a year. In summary, out of the 296 survivors who died of leukaemia over 50 years, some 203 would have died in this way in the absence of radiation. And the incidence of radiation-induced leukaemia is smaller than the incidence of natural leukaemia, even when those who received higher doses are included.

Table 5 shows similar data to Table 4 but for survivor deaths due to cancers other than leukaemia. The total number of these fatalities was 10,127, much greater than for leukaemia. The majority occurred naturally or were related to diet or smoking. This background count is shown as 9,647, the number of expected deaths, based on the control sample. The difference, 480 deaths, is the number probably caused by the radiation. This

[31] The measured risk in parts per 1,000 is given with a one standard deviation range. This means that the actual risk has a chance of 2-to-1 of being within the quoted range.

is half of 1% of the survivors and 5% of those who died of cancer unrelated to radiation. The table shows that the evidence for a radiation-related effect is confined to those with a dose above 100 millisievert. Below this dose the number of deaths was 7,657 compared with an expected 7,595 – the difference of 62 is too small to have meaning statistically and is consistent with no effect due to radiation.

Table 5 Mortality from solid cancers between 1950 and 2000 among the survivors of Hiroshima and Nagasaki with measured doses, from Preston et al [19, Table 3].

Dose range (millisievert)	Survivors	Survivor deaths		Extra risk per 1,000
		actual	expected	
<5	38,507	4,270	4,282	–2.0 to 1.4
5 to 100	29,960	3,387	3,313	0.0 to 3.5
100 to 200	5,949	732	691	3.5 to 12.5
200 to 500	6,380	815	736	9 to 18
500 to 1,000	3,426	483	378	25 to 37
1,000 to 2,000	1,764	326	191	63 to 83
>2,000	625	114	56	72 to 108
All	86,611	10,127	9,647	5.0 to 5.2

In conclusion, these data show that there is an effective threshold at 100 millisievert for an acute dose. We can think of this threshold level as distinguishing the intermediate dose range, where there is an effect, from the low dose range where the effect is too small to be measurable. The threshold might be as high as 200 millisievert, as given by the leukaemia data, but use of the 100 millisievert figure is more conservative. The point is that there are no data, in this or any other study, that show that there is a measurable risk of cancer for a single dose below this level. There are always uncertainties, but the margin of error in this case is about 1 in 1,000, an effect on life expectancy of 2 weeks. This level of risk is so low compared with the natural occurrence of cancer that it cannot be detected, even in this 50-year-long study of nearly 100,000 people exposed to the detonation of two nuclear bombs. Finally, the established repair mechanisms should be effective in this low range at least, so we expect there to be no risk at all, that is no loss of life expectancy, even if it could be measured.

The boundary between an intermediate and a high acute dose is at about 2,000 millisievert. Above this, early cell death becomes increasingly likely from a single dose; below it, cell death is less likely. In the intermediate range there are well established links between radiation and cancer, although, even there, radiation is usually a relatively minor cause.

Medical diagnostic scans

Ionising radiation has been used for clinical imaging in hospitals and dental surgeries for well over a century, and the doses delivered to patients in such scans are very small compared with the threshold of 100 millisievert.[32] Historically, scans using ionising radiation were based exclusively on X-rays. Beams of these photons suitable for medical imaging may be produced, either directly from beams of electrons, or from within atoms or

[32] Radiation scans are quite different to those that use MRI or ultrasound. MRI does involve nuclear spin but in an entirely passive way that has nothing to do with ionising radiation.

nuclei. X-rays do not *remember* where they came from and their effect does not depend on the source, except to the extent that it affects the energy and intensity. Traditional X-ray pictures are taken with a beam of photons generated by electrons focussed onto a small spot on a metal target such as tungsten, essentially in the way that Röntgen used when he discovered X-rays.

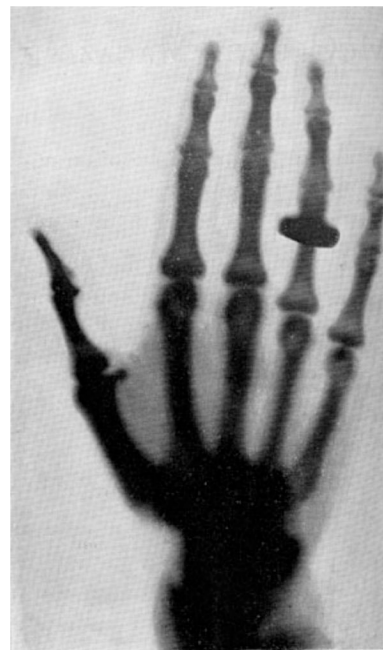

Figure 11 An X-ray image of a hand with ring (printed in McClures Magazine, April 1896).

Such a picture simply shows the directions in which X-rays are absorbed between this source spot and the film or detector. There are no lenses or mirrors – the image is just a shadow. Use of X-rays of medium energy picks out the high Z of calcium in bone or tooth, which absorbs strongly, in contrast to the mix of carbon, hydrogen and oxygen in normal tissue, which have low Z and are nearly transparent. A classic picture is shown in Figure 11. So that it is not faint or spotty the radiation exposure has to provide a large enough number of absorbed photons in each element or

pixel of the picture to overcome noise – that is statistical fluctuations. Even with old and inefficient equipment a dose of less than 0.02 millisievert is often sufficient for this purpose, many powers of 10 below the 100 millisievert threshold.

Many of the features that a doctor would like to find are not shown in this kind of image – for instance the pattern of blood vessels. An effective trick dating from the 1920s solves this problem by using a contrast agent – in the case of blood vessels, iodine, an element with high atomic number (Z = 53) that absorbs X-rays strongly. The patient is injected with a solution containing iodine and images are taken before and afterwards. (This is normal stable iodine, not the radioactive isotope.) The iodine makes for large differences in absorption, which picks out the blood vessels very clearly. An example of a pair of such images and their difference is shown in Figure 12. The digital subtraction provides an excellent picture of the blood vessels.

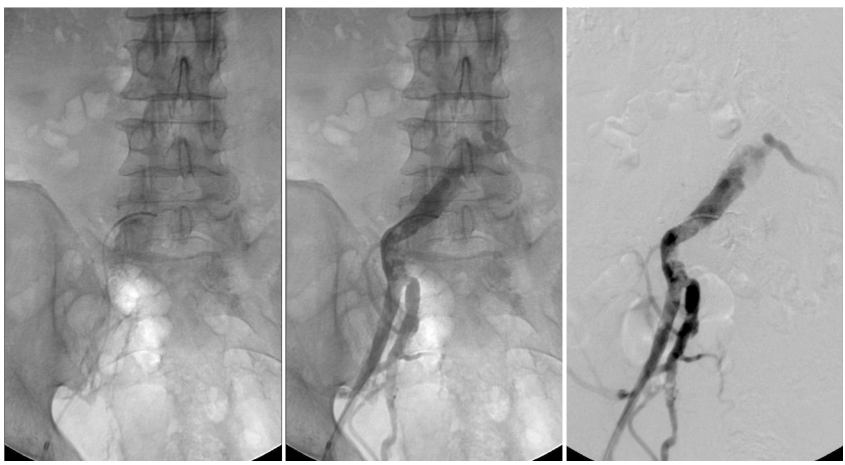

Figure 12 X-ray images of the pelvis and lower spine. On the left is an initial image; in the centre is the same region after injection of iodine as a contrast agent; on the right is an image formed by digital subtraction of the other two, clearly showing the main artery. [Images reproduced by kind permission of Medical Physics and Clinical Engineering, Oxford Radcliffe Hospitals NHS Trust.]

The same trick can be used to make images of the gut. In that case barium ($Z = 56$) is the contrast agent. Barium sulphate is a harmless chalky material, insoluble in water, that can be swallowed and quickly lines the stomach wall. Subtraction of images taken before and afterwards gives high contrast pictures of the whole digestive system.

Modern scans give rise to a higher radiation dose because they give three-dimensional information with much finer detail than is visible in Figure 11. This improved picture quality involves a much larger number of picture-elements,[33] each with a low noise requirement and therefore large number of photons. Although modern scanners make more efficient use of radiation with better detection, filtering and screening, the radiation dose may still be 1 or 2 millisievert per scan. This is larger than for a simple projective X-ray, but still quite small compared with 100 millisievert, the threshold of damage discussed earlier.

Nuclear medicine

It is possible to make images that show what tissue is doing. These are called functional images and are often clinically more interesting than simple anatomical images. Functional imaging is possible with MRI too. An example using radiation is shown in Figure 14. Typically such images incur doses in the range of 1–2 millisievert. The patient is injected with a specially prepared drug, which finds its way in the bloodstream preferentially to sites of abnormal blood vessel development or high metabolic activity, where its presence can be imaged.

This works because molecules of the injected drug are labelled with a radioactive isotope of an atom and as these decay inside the body the emitted radiation passes outside to be detected by special detectors. These can then pinpoint where the decay occurred. The resulting map of nuclear decay positions shows

[33] The picture-elements are called *pixels* and *voxels* for a two-dimensional and three-dimensional picture, respectively.

where the drug has accumulated and, therefore, where a cancerous tumour with its anomalous activity is located.

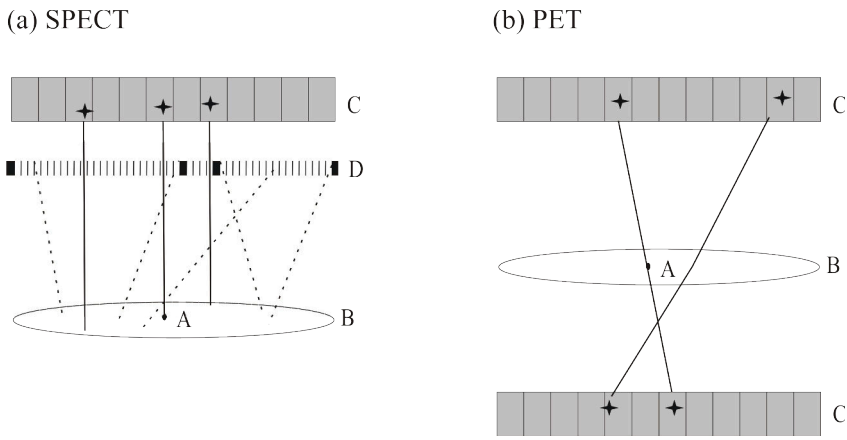

Figure 13 Illustrations of how in SPECT and PET radioactive decays at points like A in a body B emit gamma rays whose line of flight can be located through the signals, shown as stars, appearing in detectors C.

There are two methods that are widely used, called SPECT (single photon emission computed tomography) and PET (positron emission tomography). How the positions of the decaying nuclei are determined in each case is illustrated in Figure 13.

In SPECT the radioactive isotope is usually technetium-99m, which decays emitting one gamma ray of 140 keV.[34] The line of the detected radiation is fixed by the direction of the holes in a special lead collimator plate D, which blocks radiation at other angles from entering the detector C. The camera comprises the lead plate and the detector, as a unit, and during the scan this is moved along and around the patient.

[34] The *m*, appended to the isotope name, just indicates that it is an excited state.

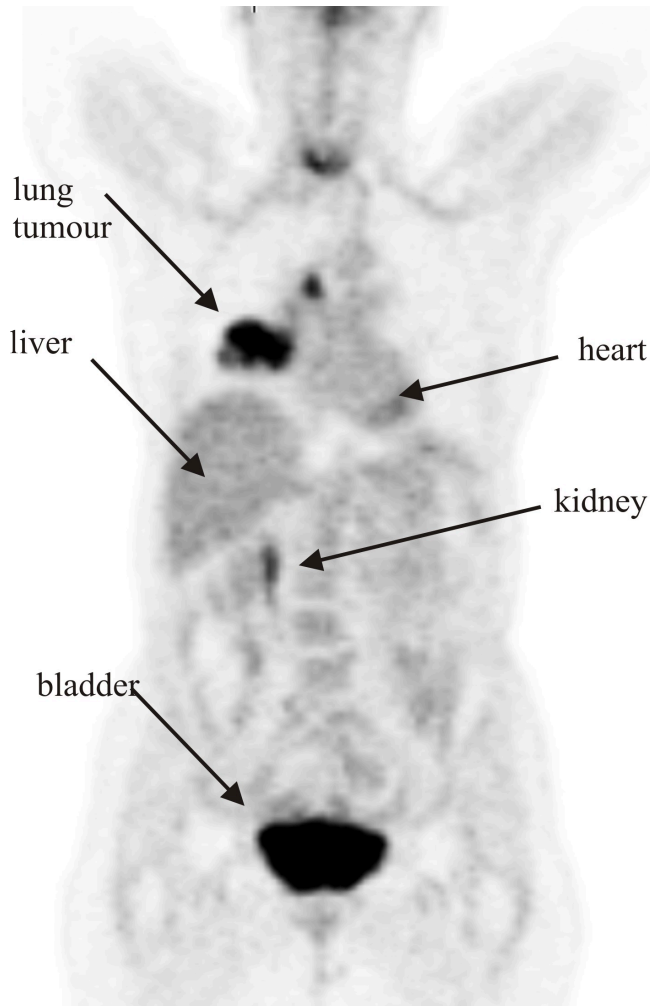

Figure 14 A PET image showing clearly the presence of a tumour on the lung. There is also an accumulation of the reagent in the bladder. [Image reproduced by kind permission of Medical Physics and Clinical Engineering, Oxford Radcliffe Hospitals NHS Trust.]

For PET the usual isotope chosen is fluorine-18, which emits a positron. This travels a millimetre or so, stops and annihilates with a simple atomic electron into *two* 511 keV gamma rays,

back-to-back in a straight line. There is no plate and the line of the radiation is fixed by the detection of two simultaneous signals.

PET gives the better quality images of the two but is more technically demanding, although in both the contrast associated with the selective concentration of the isotope can be outstanding. This concentration decreases over time by radioactive decay and by natural removal from the body by excretion. The decay half-life of technetium-99m is 6 hours; that of fluorine-18 just 2 hours. So patients receiving a SPECT scan continue to be irradiated for a longer time afterwards than those receiving PET – but there is a stronger argument in favour of PET. With SPECT most of the radiation must be absorbed in the lead sheet shown in Figure 13. In fact only a rather small fraction passes through the holes to be detected, while the rest contributes nothing. So for an image of similar quality the patient receives a greater radiation dose with SPECT than with PET. With finer holes the SPECT image is improved but the dose is higher – there is a compromise. In practice SPECT is more widely used because it is cheaper and easier than PET.

At first sight nuclear medicine may seem alarming – the patient is made radioactive! However, the radiation is specifically chosen to escape from the body with minimal absorption, therefore contributing the least dose. This is quite different to an X-ray image where the contrast arises from the absorption itself through its differences in various tissues.

The gamma rays of PET and SPECT, with energies of 511 keV and 140 keV respectively, have ranges of about 10 cm in the body. By sparing use of the isotope, the dose is kept in the range of a few millisievert, depending on the examination. Such restraint makes the images rather grainy and noisy, as shown in the example, Figure 14. Doses given in clinical practice are so far below the 100 millisievert threshold that there may be circumstances in which it would be beneficial to increase the exposure to get a clearer picture. Some authorities (Joint Report

by the French National Academies [21, 22]) think that current practice is unjustifiably cautious.

The average annual dose of ionising radiation experienced by the general public has risen slightly in recent decades because of the greater use of medical imaging with ionising radiation. This increase has been less than it would otherwise have been because of improvements in detection efficiency. Generally the benefits to health are acknowledged and are complementary to the use of MRI and ultrasound. Nowadays diagnostic images frequently use data taken by more than one method to form a fused image, combining, for example, the discrimination of PET with the precision of MRI. The risks of nuclear medicine are insignificant compared with the health benefits that are obvious to all.

People irradiated at Chernobyl

Among those irradiated at Chernobyl, two groups were particularly badly affected: those who received exceptionally high radiation doses, and those who ingested radioactive iodine and contracted thyroid cancer. Others include those who took part in the clean up, the locals who were relocated and others who lived further afield in neighbouring states and regions.

The fate of those 237 who received the highest doses is shown in Figure 9b on page 81. These were the firemen and other workers who fought the reactor fire in the immediate aftermath of the accident. Of these, 28 died within a few weeks with the symptoms of acute radiation sickness. In the following 18 years a further 19 died from a variety of causes – a similar number would have died in the normal course of events, although it is not possible to be sure that radiation was not the cause of death in any instance.

Thyroid cancer

Among the many radioactive fission products of uranium is iodine-131. So at the time of the Chernobyl accident the reactor contained a significant quantity, all of which vaporised readily in

the heat of the fire – iodine boils at 184°C. This radioactive iodine dispersed in the atmosphere and some was then inhaled directly by local people and farm animals, or was otherwise absorbed into the food chain, often in the form of milk or vegetables. Although the amount of iodine in the body is less than 1 part in 2 million, it accumulates quickly in the thyroid gland, whether it is radioactive or not – chemical and biological processes are quite insensitive to the nuclear properties of elements so all isotopes are treated similarly. Any radioactive iodine absorbed in the thyroid decays with a half-life of eight days and so is soon gone. However, the highly concentrated energy dose is responsible for a legacy of latent damage that may generate cancer some years later. It has long been known that if potassium iodide tablets are taken for several weeks following a radiation accident, the take-up of the radioactive form of the iodine is diluted thereby, and the radiation dose is reduced. The need to distribute iodine tablets in the event of an accident was well known early in the Cold War years and was a standard element of Civil Defence at that time – the tablets being cheap and easy to keep. The recommended dose is 130 mg per day, and half that for children. There are no side effects at these doses, whether taken as potassium iodide or potassium iodate [23], and their availability need not be controlled by medical prescription. A major release of radioactive iodine-131 into the environment occurred as a result of the nuclear accident at Windscale in 1957 [24]. However, the release was a thousand times smaller than that at Chernobyl so that more has been learnt from studying the latter.

Children are more at risk than adults as their thyroid is developing and their diet is normally rich in milk. The incidence of thyroid cancer amongst children in the neighbouring countries after Chernobyl is shown in Table 6. Not all of these 4,837 cases are radiation-induced – the incidence would have been about a tenth, but for the accident. Radiation doses to the thyroid varied from tens of millisievert to 3,000-4,000 millisievert. Most of the

sufferers have received therapy successfully[35] but there have been a number of recorded deaths – 15 cases up to 2002 [12, p.16] .

Table 6 The number of cases of thyroid cancer in the neighbourhood of Chernobyl diagnosed between 1986 and 2002 by country and age of exposure [13, Table 5].

Age at exposure	Number of cases			
	Belarus	Russia	Ukraine	Total
<14	1,711	349	1,762	3,822
15–17	299	134	582	1,015
Total	2,010	483	2,344	4,837

At Chernobyl the authorities were slow to distribute iodine tablets. The short half-life of iodine-131 suggests that, to have any effect, the tablets should be given for just a few weeks following an accident, for by then that the radioactive iodine has decayed. This may seem obvious, but a recent large-scale study of thyroid cancer at Chernobyl by Cardis [25] has shown that this is not the case! Extra normal iodine, even given much later, was found to reduce the incidence of thyroid cancer by a factor of three – presumably by boosting the development of a healthy thyroid gland with consequentially improved immunity against cancer development.[36] This is an important new observation, as noted by Boice [26]. It suggests that protection mechanisms continue to be active during the latent period, perhaps years later,

[35] Radiotherapy for thyroid cancer often employs brachytherapy (see page 114) using the very same radioactive isotope of iodine. The therapy involves maximising the uptake of radioiodine by the tumour to induce cell death rather than cancer. Alternatively external gamma ray radiotherapy may be used.

[36] The US Food and Drug Administration recommends a diet with a daily intake of 0.15 milligrams of iodine to promote a healthy thyroid, either naturally or by the addition of iodised salt to food. The concentration of iodine in such salt varies from 10 (UK) to 50 ppm (US).

between the exposure to the radiation and the appearance of the cancer. It raises the question whether the incidence of other cancers may also be reduced by general good health during latency.

A second effect found in the same study by Cardis is linked to the natural iodine content of the local diet. In the regions around Chernobyl that are poor in natural iodine, the incidence of thyroid cancer has been greater than in the regions where it is richer. It is reasonable to suppose that the take-up of the radioisotope is enhanced where the thyroid was previously starved of natural iodine. As most of the regions around Chernobyl are iodine-poor, this would have contributed to the high incidence of cancer. If a future accident occurred in a region with an adequate pre-existing level of iodine, the incidence of cancer would then be much lower than found at Chernobyl. Although the findings of Cardis [25] need confirmation, there are important implications here for public health, and the prognosis for thyroid cancer in the event of a future accident is encouraging. If thyroid health is maintained by sufficient intake of iodine under normal circumstances, the incidence of cancer might be substantially reduced, compared with Chernobyl.

Other cancers at Chernobyl

In principle the Hiroshima and Nagasaki survivor data give the cancer mortality for those suffering a given whole-body radiation dose. If the dose profile of those affected by Chernobyl were known, the number of cases of leukaemia and solid cancers expected over 50 years could be predicted without the need to assume any particular shape for the dose-damage curve, such as whether it is linear or not. However, this profile is not known at all well. The best general estimate for the accumulated doses is given in Table 7. This distinguishes the liquidators who were drafted in to clear up, those who were evacuated after a few days, those who live in the immediate zone and those who live further afield. It shows that a large number of people received a dose of less than 100 millisievert, often over a period of many years. No