Chapter

The Secondary Photoelectron Effect: Gamma Ray Ionisation Enhancement in Tissues from High Atomic Number Elements

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Abstract

The absorption of gamma rays is roughly proportional to the fifth power of the atomic number of an element. This immediately raises the issue of tissue ionisation enhancement effects from photoelectron production by elements of high atomic number incorporated into living tissue. The issue was raised in the 1950s in relation to calcium in the bone but has received little attention since then. New results, derived from mathematical modelling carried out at the University of Ulster, of photoemission from nanoparticles of gold and uranium are presented. These show that significant ionisation enhancement effects can occur when incorporated particles of high atomic number are exposed to natural background gamma radiation, effects which increase sharply at the lower energy end of the spectrum, around 150 keV. The effects must also occur for molecular species. The general problem is discussed, with reference to the literature, and approximate enhancement factors are derived for the effect. The implications for the evolutionary selection of elements by life are explored.

Keywords: gamma rays, ionisation, biological effectiveness, absorbed dose, radioprotection, photoelectron, secondary photoelectric effect, evolution

1. Introduction

Gamma is a high photon energy electromagnetic radiation which is absorbed by material with a number of different physical consequences. Its absorption results in the generation of fast electron tracks capable of breaking chemical bonds in living tissue with the generation of reactive ionic species and free radicals. These energetic fragments can then, themselves, migrate away from the ionisation track to react with other stable molecules and ions. The overall processes result in damage to living cells, either by direct interaction with a molecule or by indirect effects from the ionised or reactive species, and this can result either in cell death or in downstream genetic and genomic effects which are harmful to the health of the exposed individual. The mechanisms of genetic and genomic biological damage which follow from gamma ray exposure and X-ray exposures are described in the literature and are accepted by all the radiation risk agencies [1–3]. In this chapter, I will write *gamma ray*, but it is to be assumed that the processes I discuss apply to X-radiation also.

It is generally accepted now that the biological effects of exposure are a consequence of either direct damage to cellular DNA or due to induction of instability in cellular DNA through a mechanism involving the detection of ionisation, expressed as an increased concentration of reactive oxygen species (ROS), generated by gamma ray interaction with water. Either way, the essential biological effective target for gamma ray (and indeed all ionising radiation) absorption is not primarily water but is the cellular DNA. Historically, the method developed for assessing exposure after 1950 involved defining quantities based on the absorption of energy per unit mass of material exposed to these high-energy photon radiations. Since the detection and quantification of gamma radiation (and X-rays) became most easily based on the ionisation of gases (Geiger Muller counters, proportional counters and ionisation chambers and, later, scintillation counters), it was a simple step to quantify absorption by living tissue in the same way. Thus, for ionising radiation, the quantity *absorbed dose* became the prime measure of risk. Since it became clear that for heavily ionising radiations, alpha and neutron radiations which have higher ionisation per unit track length, there must be allowance made, the later quantity, *equivalent dose*, was introduced whereby a weighting factor was added, based on the ionisation density or linear energy transfer of the radiation. However, for the purposes of this brief chapter, the concern is with *absorbed dose* and its calculation for the purposes of radiation protection.

Clearly, from the outline above, it is the ionisation density at the DNA which is the key factor defining radiation risk. But *absorbed dose* does not measure this. In the way it has come to be employed by the radiation risk agencies; it is a measure of mean ionisation density over significant masses of tissues and kilograms, modelled as water. The issue of anisotropy of ionisation density for *internal* radiation exposures to alpha and beta particles from incorporated radionuclides has been addressed elsewhere [4].

The calculation of absorbed dose assumes that the tissue in which the energy is dissipated is water or its tissue-equivalent substitute. Since all photon energy absorption from *external* exposure is converted ultimately to energetic electron tracks in tissue, either in the initial instance or as a result of the reabsorption of photons from other secondary sources (e.g. Compton, Bremsstrahlung), the averaging of these tracks over all tissue may seem reasonable as an approximation. But what this does (and this is the issue explored here) is it fails entirely to address or incorporate increases in absorption of photon radiations by elements of higher atomic number Z than water or tissue-equivalent material which is largely absorbed by the highest Z element in it, namely, oxygen (Z = 8). This would not matter much if any elements of higher Z were uniformly distributed in the tissue: in such a case, since gamma and X-ray absorption increases very quickly with atomic number, the overall absorption might be slightly increased, but where an incorporated elevated Z element is chemically bound to DNA, the transfer of energy into the DNA becomes very much greater than that which is assumed by conventional dosimetry. A similar enhancement of local dose occurs near high-Z nanoparticles incorporated into tissue. This is an interesting and important area of concern which has implications both for radiation safety and for the development of cancer therapy. Apart from some early work on the enhanced photoelectron density near the bone, it seems to have been entirely overlooked. The issue is also an important one for radiation protection in the nuclear industry and the military, especially in the case of uranium particle contamination, perhaps the reason why little research has been carried out on the subject. There are also other areas of interest, implications for medical prostheses and even for arguments about the development of living systems generally.

2. The absorption of gamma radiation by matter and the secondary photoelectron effect

Gamma radiation and matter interact mainly by three different mechanisms, Compton scattering, pair production and the photoelectric effect. The different contributions of these to absorption depend on the absorbing material, principally its atomic number Z and the quantum energy **E** of the incident photon, proportional to frequency **E** = **hυ**.

In the photoelectric effect, incident photon energy causes the emission of an electron from the absorbing element. The electron has the energy of the absorbed photon minus the binding energy of the electron. For gamma radiation the binding energies are second order, and the emission electron carries almost all the initial gamma energy. Electrons may also lose energy in secondary processes occurring within the atom. For energies below 1 MeV, the photoelectric effect largely predominates. **Figure 1** illustrates the effects by incident gamma energy.

Thus, for energies below 1 MeV, the photoelectric effect predominates. The cross section for the photoelectric effect is approximately proportional to the atomic number Z to the power of five and to the incident photon energy to the power of −7/2 [5]. The sharp dependence of photoelectron generation on Z immediately raises interest in the resulting wide variation in absorption of gamma rays by high atomic number atoms and molecules in tissue. This concern is related to the range of the photoelectrons and their deposition of ionisation effects close to the atom. For low-energy photoelectrons generated by low-energy gamma and X-ray photons, the effects will be increasingly local to the atom, and if the atom is local to DNA, there will be an enhancement of radiobiological effectiveness of the absorbed energy. This may be termed the secondary photoelectron effect. The SPE will also occur in the vicinity of internal particles of high-Z elements and in the vicinity of metal prosthetic structures.

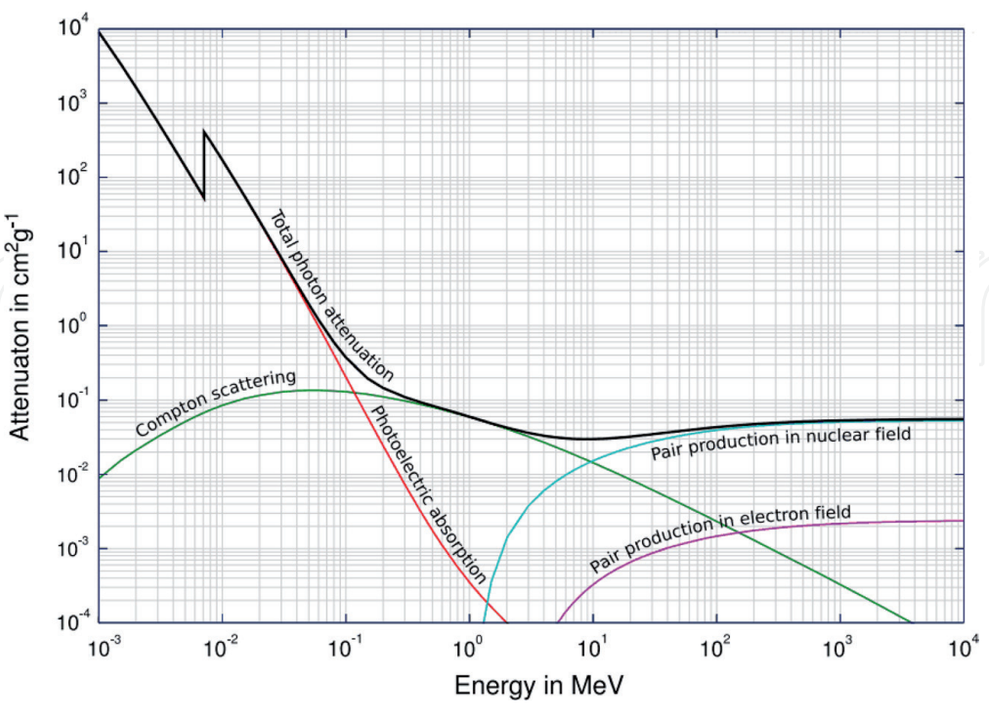

Figure 1.
Relative contributions of the main different types of energy conversion in materials following the absorption of gamma ray photons. The specific curves differ considerably for different elements, driven by the electronic structure of the element. Note that the attenuation coefficient is normally given in $cm^2\ g^{-1}$ and thus incorporates the density of the element.

E (keV)	Oxygen (8)	Water	Muscle (striated)
10	2.950E−4	2.515E−4	2.536E−4
50	4.992E−3	4.320E−3	4.356E−3
100	1.647E−2	1.431E−2	1.443E−2
150	3.325E−2	2.817E−2	2.841E−2
500	2.018E−1	1.766E−1	1.781E−1

Table 1.
Continuous slowing down range r_0 in g cm^{-2} for electrons of different energies in oxygen, water and muscle tissue [6].

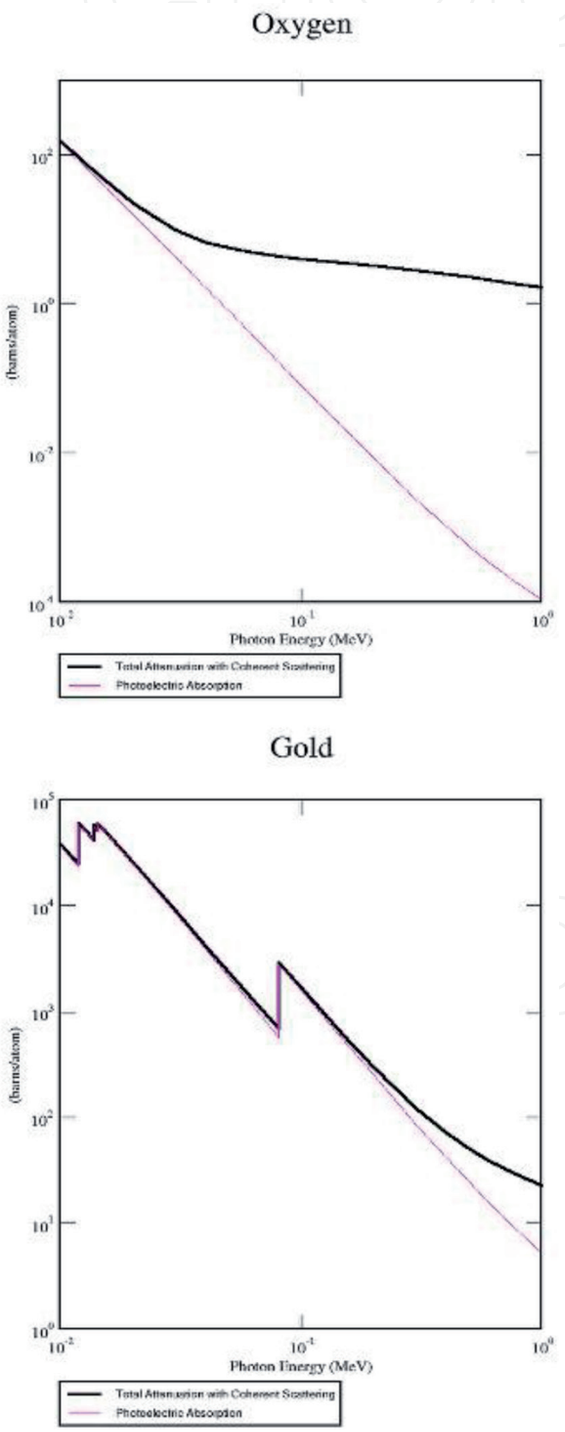

Figure 2.
Gamma ray absorption cross sections for oxygen (Z = 8) and gold (Z = 79).

The starting point for examining this issue is the electron range in tissue by electron energy. This can be calculated on the basis of the continuous slowing down approximation (CSDA), and results for the lower energies for muscle tissue are given in **Table 1** [6]. In the lower-energy regions, the ranges of electrons in tissue are shown in **Figure 2**.

For electrons of energy <500 eV, the range in tissue is in the order of 1–10 nm [7]. This is of the order of the dimensions of the DNA molecule.

3. Absorption of photons by chemical elements

The photoionisation cross sections with photon energy of low Z (oxygen 8) and high Z (Gold 79) are shown in **Figure 2**. From **Table 1** we can see that oxygen may be used to approximate tissue absorption. In the low-energy region around 100 keV, it is clear from **Figure 2** that the absorption (and thus photoelectron production) of gold is several orders of magnitude greater than tissue. **Table 2** gives the photoionisation cross sections for a section of elements of interest [8].

If the absorption of gamma ray photons by chemical elements varies so widely, with such an increased cross section for the higher Z elements, it seems clear that the incorporation of high-Z elements in living tissue would be essentially harmful. There is evidence from evolution to support this idea, and this will be discussed below. Apart from contamination issues due to anthropogenic sources and the question of medical procedures, the problem arises because of the continuous irradiation of living creatures by natural background radiation (NBR). The gamma

Z	Element	10 keV	50 keV	100 keV	150 keV
1	Hydrogen	4.5E−3	1.8E−5	1.6E−6	4.1E−7
6	Carbon	4.1E+1	2.0E−1	2.0E−2	5.4E−3
8	Oxygen	1.5E+2	8.1E−1	8.2E−2	2.2E−2
11	Sodium	5.7E+2	3.6E00	3.7E−1	1.0E−1
15	Phosphorus	2.0E+3	1.5E+1	1.6E00	4.4E−1
16	Sulphur	2.6E+3	1.9E+1	2.2E00	5.9E−1
17	Chlorine	3.3E+3	2.5E+1	2.8E00	7.8E−1
19	Potassium	4.1E+3	3.3E+1	3.7E00	1.0E00
20	Calcium	6.2E+3	5.2E+1	5.9E00	1.7E00
26	Iron	1.6E+4	1.6E+2	1.9E+1	5.4E00
53	Iodine	3.4E+4	2.5E+3	3.6E+2	1.1E+2
74	Tungsten	2.8E+4	1.6E+3	1.3E+3	4.3E+2
78	Platinum	3.5E+4	2.0E+3	1.5E+3	5.1E+2
79	Gold	3.7E+4	2.1E+3	1.6E+3	5.4E+2
80	Mercury	3.9E+4	2.3E+3	1.7E+3	5.7E+2
82	Lead	4.3E+4	2.5E+3	1.8E+3	6.2E+2
92	Uranium	6.9E+4	4.0E+3	6.4E+2	9.4E+2

Table 2.
Photoionisation cross sections for a selection of elements of interest at different incident energies in the natural background low-energy region (barns) (Hartree-Fock approximation) [8].

spectrum of NBR increases rapidly to lower energies, roughly as the −7/2 power of the energy. From **Table 2**, it is clear that the absorption of photon energy in the NBR region (50 keV) from iodine is about 3000 times that from oxygen or water/tissue. It has been suggested that this may explain the radiosensitivity of the thyroid gland [9]. It should be noted in passing that the absorption coefficients at the energies tabulated do not generally reflect the overall absorption differences between the low-Z and high-Z elements over the whole-energy spectrum because of discontinuities in the absorption by the d- and f-orbital electrons in the heavier elements like gold and uranium. These discontinuities for gold are clear in **Figure 2**. For gold, the enhancement factor relative to water at the four energies tabulated (10, 50, 100 and 150 keV) are 246, 2592, 19,500 and 24,545. Similar variations in enhanced photon cross section are apparent for uranium which has 45,000 times the photoelectron cross section at 150 keV than the oxygen in water.

It is clear from this approach that the determining absorption of living tissue is defined not by water but by the higher Z elements present. This is starkly true for iron and iodine which must form centres for photon absorption and photoelectron production. It may therefore be plausible to argue that this is why that the main cancers associated with external radiation exposures are leukaemia and thyroid cancer.

4. The gamma energy spectrum of natural background radiation

Since secondary photoelectrons will be generated from all exposures to gamma radiation and since the local ionisation density near the absorbing atom, particle or metal prosthesis is the quantity of interest, it is clear that the energy spectrum of gamma NBR is an important component of any assessment. External gamma radiation degrades in energy as it passes through tissue as a result of the various processes which occur. Energy is lost by Compton scattering resulting in the production of a Compton photon of lower energy than the initial energy. Electrons generated by the photoelectric effect lose energy through collisions and the generation of Bremsstrahlung photons of low energy and so forth. Thus, the further the initial photon travels in tissue, the greater the number of low-energy photons there are in the medium. The natural background radiation spectrum in Burnham-on-Sea, Somerset, UK, is reproduced in **Figure 3**.

Note the sharp increase in the number of photons at low energy: the cut-off is a result of absorption by the shielding of the thallium-doped sodium iodide scintillation detector. The degradation of photon energy inside the human body can be examined by placing an insulated scintillation detector inside a water-filled container and comparing the spectrum with that obtained in air. The spectrum obtained in this way, which compares well with that employed by Pattison et al. (who attempted to model the photoelectron effects in uranium particles [10]), is shown in **Figure 4**. The cut-off at low energy 15 cm inside the water jacket is due to the absorption of the low-energy short-range photons. By subtraction it is possible to show that the number of photons of low energy increases inside the water sphere of 30 cm diameter (used to approximate the body). Thus, the dispersion curve shifts to lower energy. The enhancement of photon numbers by energy is shown in **Figure 5**.

What is clear from these results is that NBR delivers mainly low-energy photons. It turns out that 60% of in-air NBR photons have energy below 150 keV and the peak in photon numbers increases to low energy below 50 keV. Photoelectrons of this energy have a mean CSDA range (**Table 1**) which is comparable with the dimensions of a single cell or cell nucleus. Therefore, a high-Z atom in a cell will be continuously amplifying NBR in proportion to the photoionisation cross section

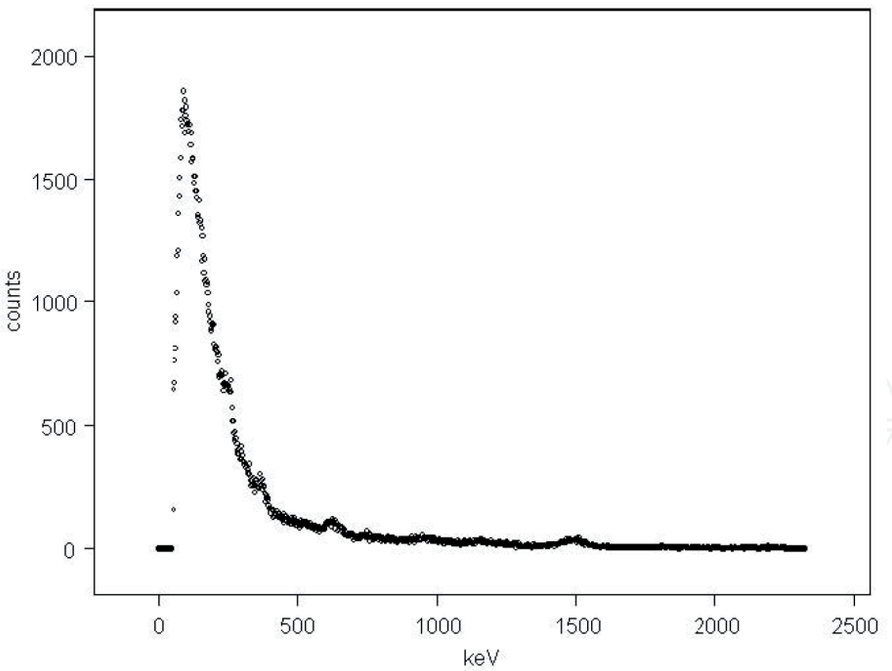

Figure 3.
Gamma ray spectrum obtained on beach at Burnham-on-Sea using a 2-in. NaI (Tl) Scionix detector. Note rollover at about 60 keV.

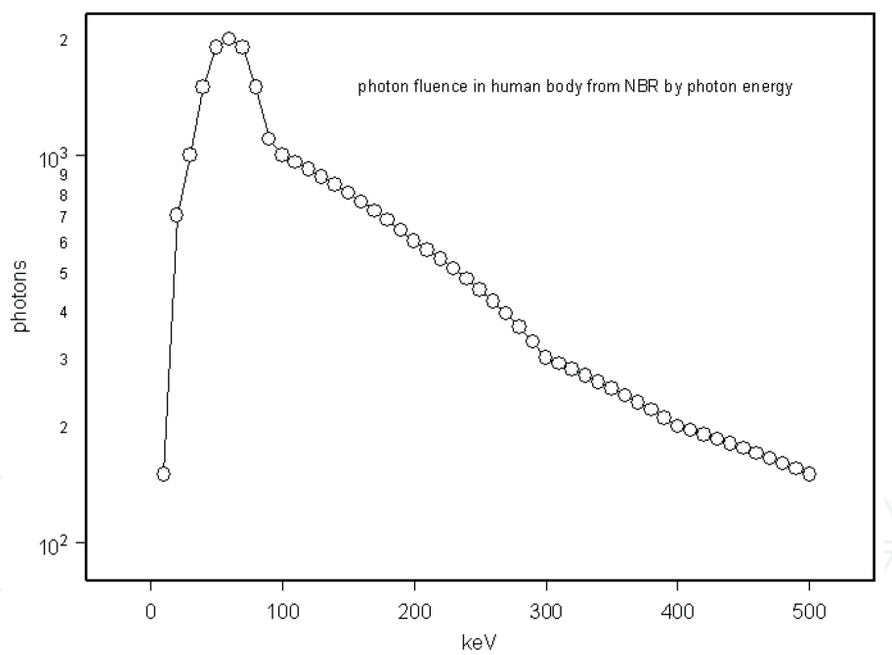

Figure 4.
*Energy dispersion in the low-energy region 0–500 keV of the natural background gamma photons at 15 cm depth inside a human body. Based on Pattison et al., **Figure 3** and unpublished work using a gamma probe packed with bags of water. Shielding effects on the primary in-air dispersion below 100 keV are uncertain, and the energy dispersion of photons inside the body is very uncertain.*

shown in **Table 2** and delivering enhanced ionisation to that cell or cell nucleus relative to that calculated using the concept of absorbed dose which is based on the assumption that the absorber is effectively water (i.e. oxygen). Further, the biological effectiveness of NBR, its damage to tissues, will be defined by the highest Z atoms in the tissue. This will also be true for other exposures, for X-rays, medical examinations and exposures to anthropogenic sources, indeed the entire range of exposures which are regulated by the law on the basis of the current risk models.

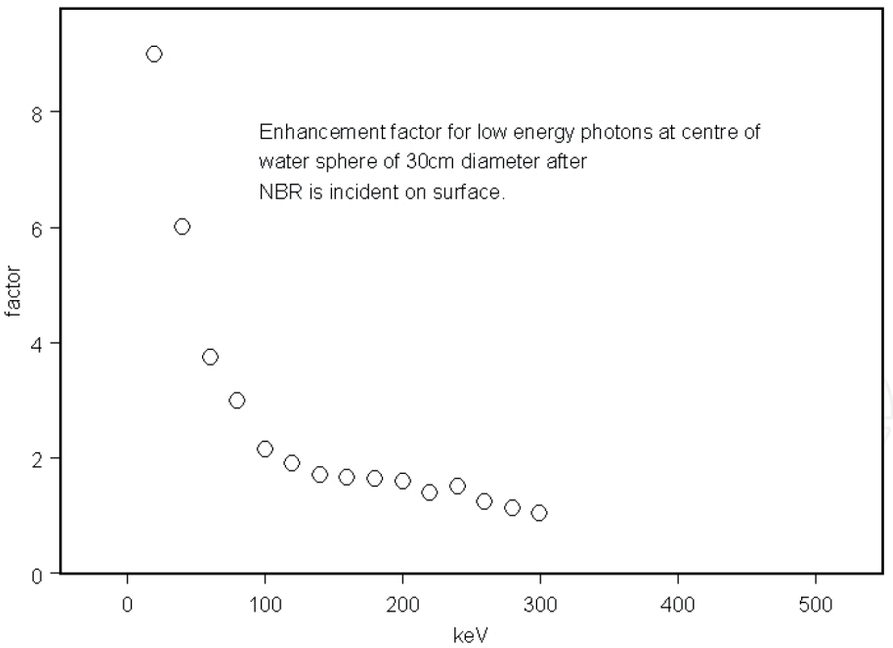

Figure 5.
Enhancement of photon energy at different energies on passage through 15 cm water. Internal photon fluence divided by external photon fluence. Unpublished measurements.

It will be the location in the body of a high-Z atom or particle relative to the target DNA which will be the determinator of biological risk. This is a phantom radioactivity: the atom is radioactive by virtue of its high atomic number and its amplification of NBR gamma radiation through photoelectron emission.

5. Internal particles

The radiobiological issue of photoelectron emission by internal high atomic number particles was raised in 2005 by Busby in connection with depleted uranium weapons which create respirable submicron particles on impact [11]. Research in Iraq, where DU weapons were deployed in 1991 and later in 2003, were shown to have caused high levels of congenital effects and cancer in a number of studies both of civilians in Iraq and of military veterans [12–14]. The concerns about the genotoxicity of DU particles led to research by a number of groups in the early 2000s. The laboratory researches demonstrated that both uranium and uranium particles were capable of causing measurable genetic effects, chromosome breakages and so forth [15–17]. In one study with mice, both embedded uranium and tungsten particles caused local cancer effects [18]. These findings have been reviewed in Busby [19, 20] and will not be rehearsed here. What will be presented here are some results from nanoparticle mathematical modelling studies carried out at the University of Ulster between 2009 and 2012 which looked at photoelectron production from water, gold and uranium spheres [21, 22].

5.1 The University of Ulster studies

Photoelectron emission from nanoparticles of water, gold and uranium was investigated by Elsaessar, Busby and Howard from 2009 to 2012. Preliminary results were presented at a conference [21], and the studies contributed to a PhD thesis [22]. The CERN FLUKA code was employed. The beam geometry is shown in **Figure 6**, and in **Figure 7** results are given for 10 nm particles of water, gold and uranium. Referring

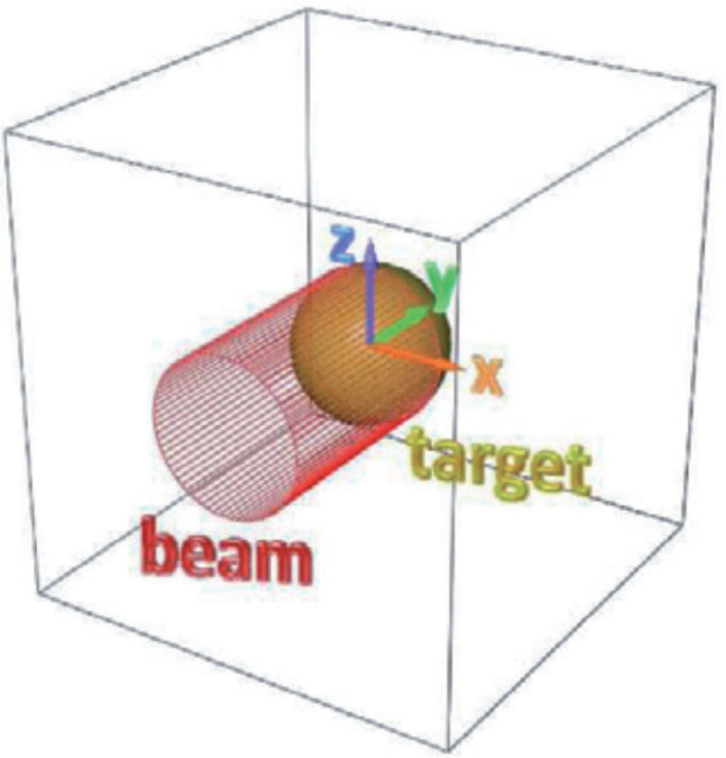

Figure 6.
Beam and target geometry for FLUKA calculations. A photon beam of cross-sectional diameter equal to that of a particle of water, gold (Z = 79) and uranium (Z = 92) [21, 22].

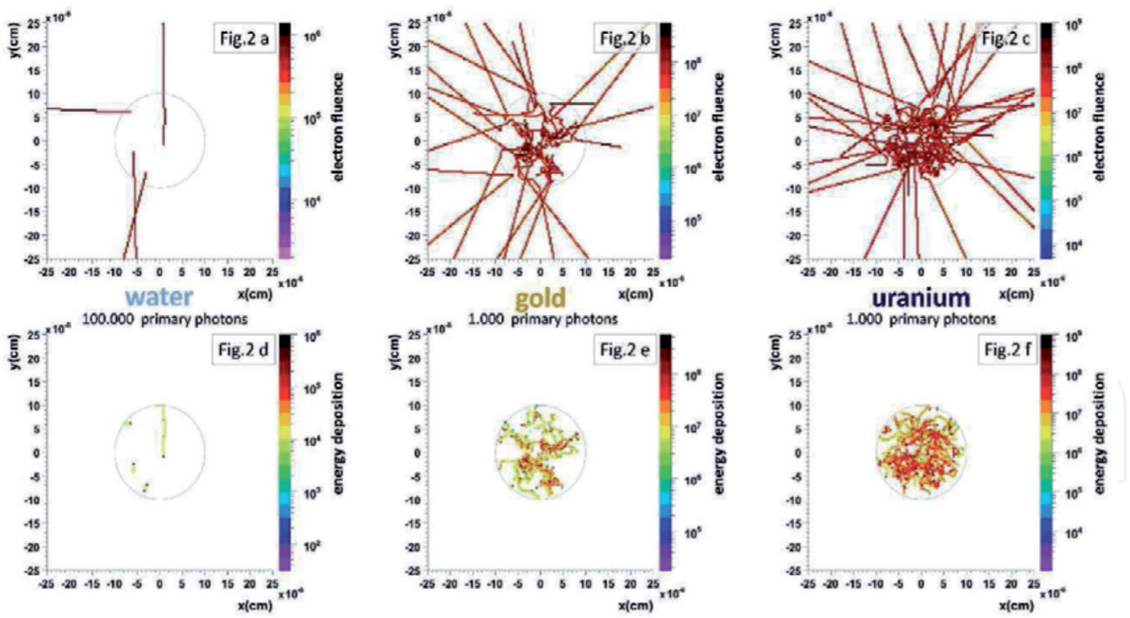

Figure 7.
*Secondary escaping photoelectron production (seen in two dimensions following incident 100 keV photon beam into 10 nm particles of water (Z = 7.5) [**Figure 2a** and **d**], gold (Z = 79) [**Figure 2b** and **e**] and uranium (Z = 92) [**Figure 2c** and **f**]). Below: corresponding energy deposition. Monte Carlo calculation with 1000 incident photons for gold and uranium but 100,000 for water [21, 22]. Individual figure numbers are from [21].*

to the numbering in **Figure 7**, which is from the conference presentation [21], the top row of **Figure 2a–c** shows photoelectron tracks induced by an incident photon beam of 150 keV involving 1000 photons in the cases of 10 nm diameter gold and uranium particles, whilst for the water particle, the number of photons was 10,000. Thus, it is clear that the photoelectron tracks of various energies (lengths) induced

in the particles of the high atomic number elements gold and uranium are orders of magnitude greater than those in water. The emission of secondary photoelectron tracks from the three materials is roughly in agreement with a fourth or fifth power law. **Figure 2d–f** shows the energy deposition in the particles on a coloured scale given also in the picture. It is immediately clear from **Figure 7** how the internal particles of high-Z elements result in increased absorption of background radiation and its re-emission by photoelectrons and associated enhanced biological damage relative to the absorption by tissue (water). Due to self-absorption of the induced photoelectrons, the danger exists mainly from smaller particles. Results for different sizes of particles of gold and three different photon energies are shown in **Figure 8**. This shows the variation secondary photoelectron production with photon energy (100 keV, 250 keV, 500 keV and 1 MeV) in a gold target. Photon penetration depth decreases as energy decreases, but the number of electrons escaping the target increases.

To examine the deposition of photoelectron energy into the tissue surrounding the particles examined in the analysis presented in **Figures 7** and **8**, particles were modelled surrounded by water spheres, and the deposition of energy into the

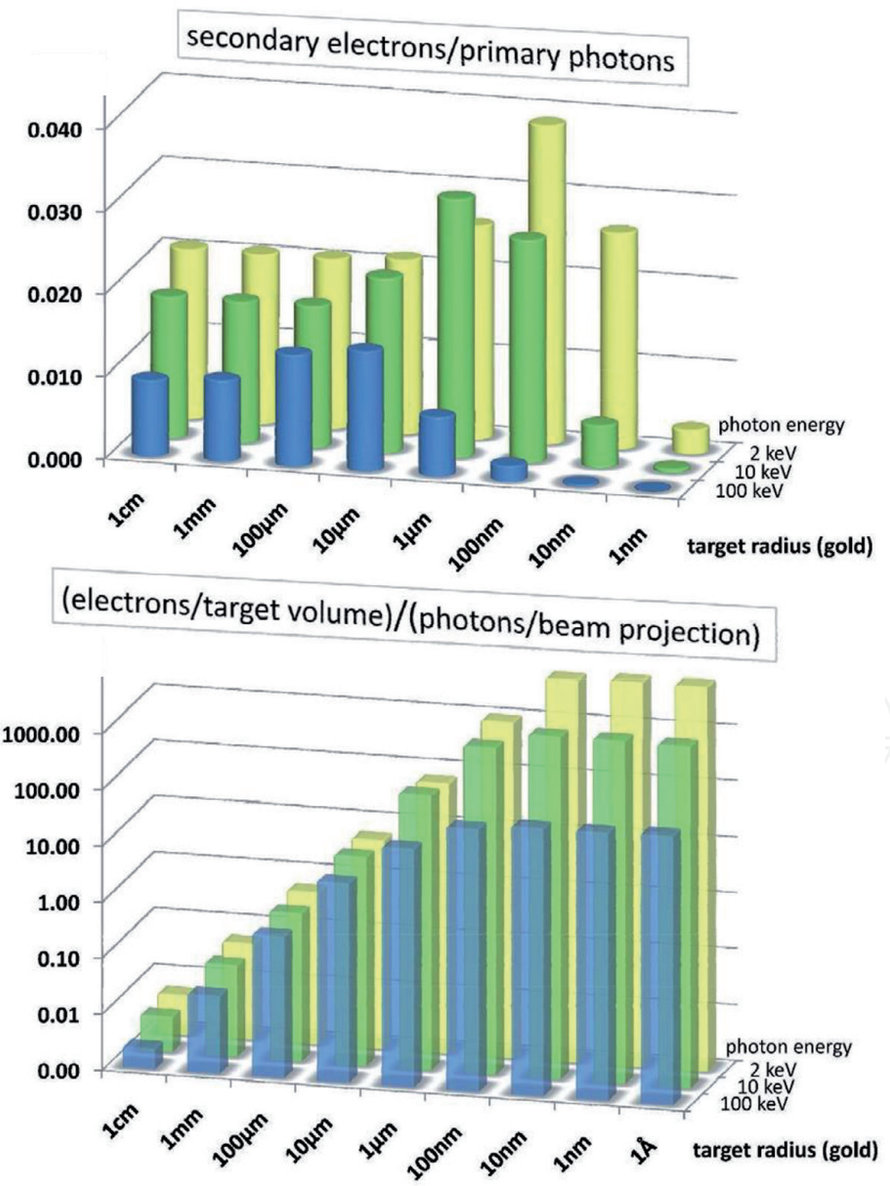

Figure 8.
Upper: secondary electrons/primary photons in gold particles of different diameters and photon energies 2, 10 and 100 keV. Lower: electrons per target volume/photons per beam projection for gold particles of different diameters and photon energies of 2, 10 and 100 keV [21, 22].

spheres was obtained. In **Figure 9**, results for different photon energies of 100, 250, 500 and 1000 keV are presented. As the photon energy was decreased, the penetration also decreased, as expected, but the photoelectron density in the local volume near the particle increased. This is not unexpected since the photoelectron range would be shorter with the low-energy photoelectrons.

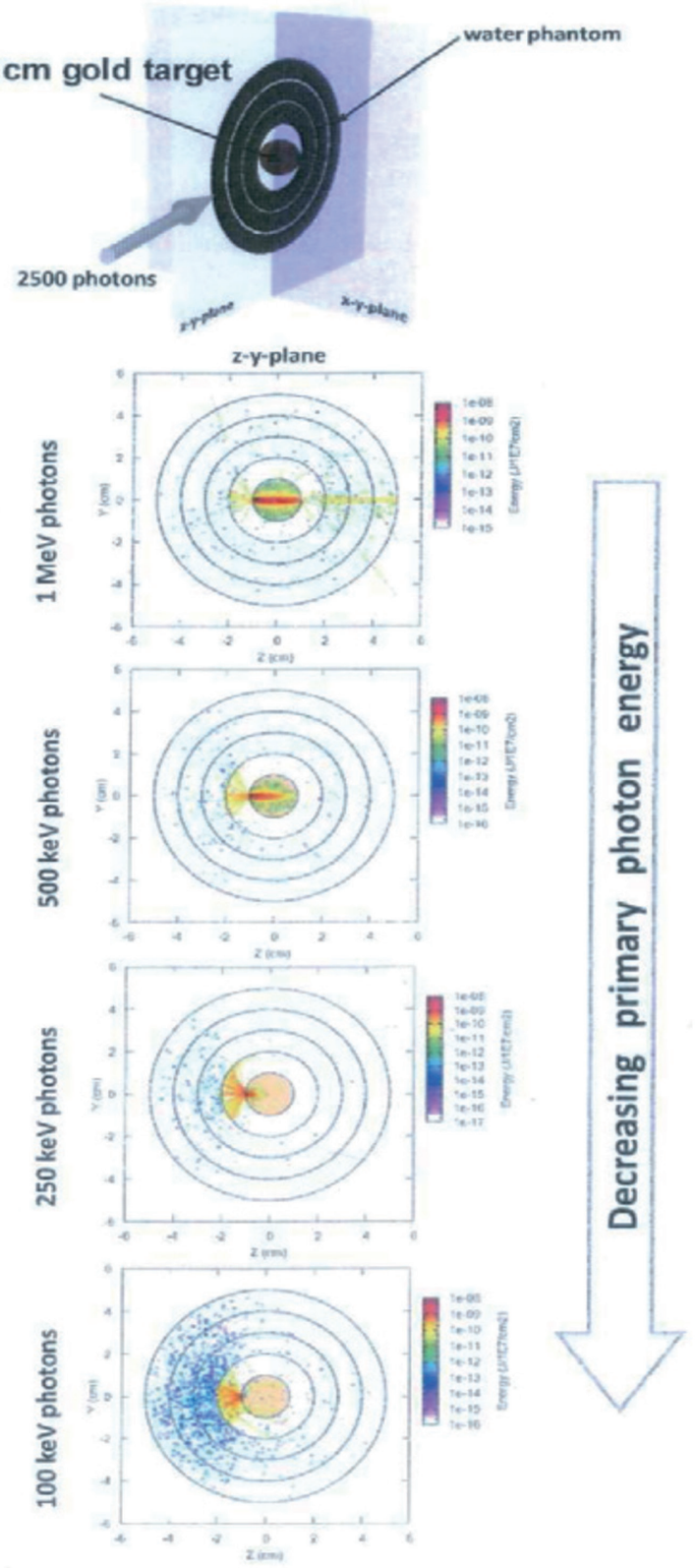

Figure 9.
The variation of secondary photoelectron production with photon energy (100 keV, 250 keV, 500 keV and 1 MeV) in a gold target. Photon penetration depth decreases as energy decreases, but the number of electrons escaping the target increases [21].

The Ulster results can be used to obtain enhancement factors for photoelectron production from 10 nm diameter gold and uranium particles relative to a water particle of the same size. This enhancement factor is compared with a fourth-power law comparison in **Table 3** [19].

The range of the photoelectrons increases as the photon energy increases, but the number of photons increases at low energy for natural background radiation as has been discussed above. The trade-off is shown in **Figure 10**. Dose enhancement (energy per unit mass) falls off rapidly with distance from the high-Z particle but is significant in the micron region. Results for a 400 nm uranium particle are given in **Figure 11** [19].

Figure 11 shows enhancement of dose close to a 400 nm uranium particle embedded in tissue and exposed to natural background radiation. For the method of obtaining this, see [19].

5.2 Other modelling studies of the secondary photoelectron effect

Because of the use in the battlefield of uranium weapons and the fact that there are other sources of uranium particles (which will be discussed below), there is considerable financial and military investment in showing that these photoelectron effects are not biologically important. The author was a member of the UK Ministry of Defence Depleted Uranium Oversight Board [23] from 2001 to 2005 and also the UK Committee Examining Radiation Risks from Internal Emitters (CERRIE) [24]. He also gave evidence to the Royal Society Committee on Depleted Uranium in 2001. In 2009 a paper describing the secondary photoelectron effect entitled "Phantom Radioactivity of Uranium" was sent by him to the chair of the Royal Society Committee which had published reports on the issue in 2001 and 2002. These reports argued that DU could have no adverse health effects as the absorbed doses from the particles were too low [25]. At the suggestion of the chair, Brian Spratt, the photoelectron paper was submitted to the *Journal of the Royal Society Interface* and sent for peer review. The three reviewers all advised that the idea was important and should be published. Despite this, the editor of the journal, William Bonfield, rejected the paper because of "lack of space". Nevertheless, the idea was next presented in a German conference [9] and was covered by the New Scientist in an article in 2009 [26]. Shortly after this a Monte Carlo study appeared in the same journal that had refused to publish the original idea, the *Journal of the Royal Society Interface*, by Pattison et al. arguing that there was no enhancement of dose by uranium particles [10]. A year later, another Monte Carlo study was published by Eakins et al. of the UK National Radiological Protection Board [27]. Both studies were badly flawed for various reasons which will be briefly summarised.

Pattison et al. carried out Monte Carlo modelling using a different code to that employed by Elsaessar, EGSnrc [10]. They modelled two sizes of cylindrical particles and hollow cylindrical particles of 10 μ diameter and length. Using input photons of 200 keV, they concluded that the enhancement of dose was significant and of the order of one to tenfold. Apart from the fact that the particles they modelled were too large to represent the respirable DU particles found in Iraq, and the input photons too energetic, the key to dismissing their approach was their finding that the dose enhancement was largest for the larger particles, the opposite result to that obtained at Ulster. This was because their method was to fix the spherical volume into which the photoelectrons were emitted and calculate energy per unit mass in the annular water shell. Clearly as the particle diameter approached the water shell diameter, the dose would become infinite, showing that the method was nonsensical, and it is hard to see how the paper passed the reviewers.

Calculation	Water Z = 7.5	Gold Z = 79	Uranium Z = 92
Elsaessar et al. [21]	1	12,900	29,200
Z^4	1	12,300	22,600

Ratio of gold and uranium photoelectron numbers to water photoelectron numbers. Also shown is the Z^4 predicted ratio [19].

Table 3.
Number of photoelectrons emitted following exposure of a 10 nm particle of water, gold and uranium to 100 keV photons.

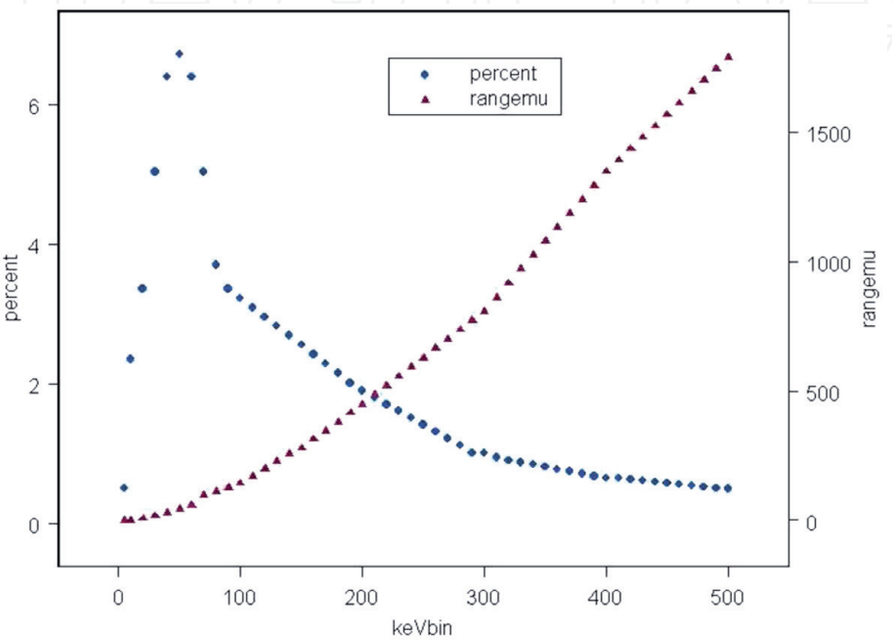

Figure 10.
Percentage of all photoelectrons with energies equal to natural background radiation photons (blue diamonds) and range in tissue in microns (red triangles) (from results presented in ***Figures 5*** *and* ***6****). Thirty percent of all NBR photons have energy <60 keV.*

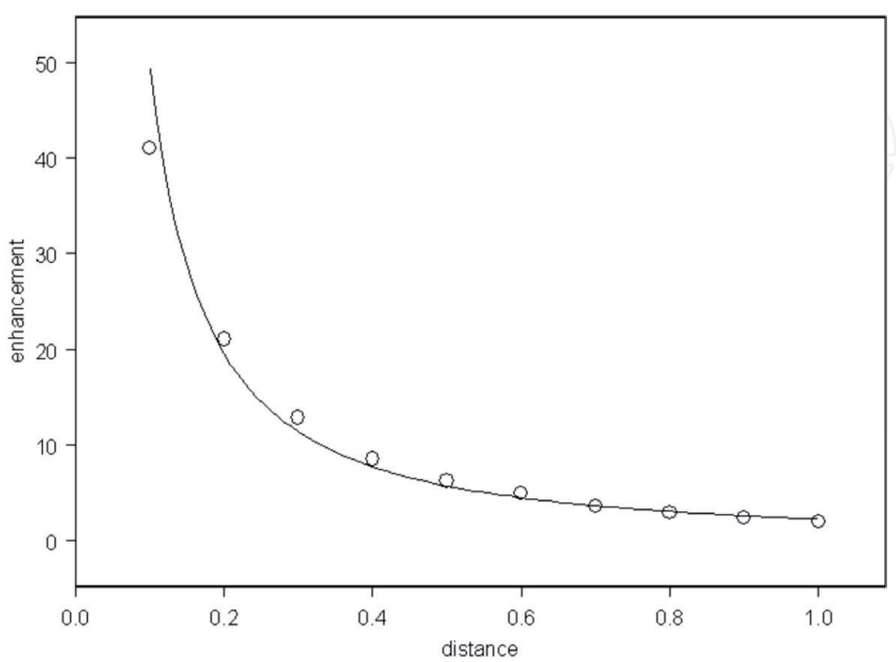

Figure 11.
Dose enhancement (energy per unit mass of tissue) by distance in nm from a 400 nm uranium particle.

Eakins et al. study was carried out by employees of the UK National Radiological Protection Board (NRPB) [27]. They used the computer code MCNP5 to model an arrangement consisting of concentric spheres with the particle at the centre and tissue shells surrounding the particle as had the Ulster modelling. However, like Pattison et al., Eakins et al. fixed the volume into which the photoelectron energy was converted into absorbed dose. The authors did, however, model a range of uranium particles, obtaining enhancements of 3-fold at 100 nm diameter and 20-fold for the 2.5 nm diameter particles. Like the Pattison et al. study, this was an absurd analysis since having a fixed volume for the dose absorption but increasing the particle size, the enhancement factor eventually becomes infinite.

6. High-Z elements and cancer radiotherapy

The augmentation of dose due to secondary photoelectron emission from high-Z elements is not a new concept; it is just that it has been ignored for the purposes of radioprotection. The idea of employing high-Z elements and their photoelectron emission to augment radiotherapy doses was advanced by Matsudeira et al. who measured the radio-enhancing effect of iodine on cell cultures [28]. Nath et al. incorporated iodine into cellular DNA with iododeoxyuridine in vitro and found a radiation enhancement of about 3-fold [29]. Herold et al. injected gold particles directly into a tumour followed by irradiation and found that the excised cells had reduced plating efficiency [30]. Mello et al. found that direct tumour injection with iodine contrast medium followed by 100 kVp X-rays completely suppressed growth of 80% of tumours in mice [31]. Norman et al. modified a CT scanner to deliver X-rays to spontaneous brain tumours in dogs after iodine injection and found a 53% longer survival [32]. Synchrotron radiation was used in combination with the tumour injected drug cisplatin to treat brain tumours in rats [33]. The issue of the mechanism of cisplatin is revisited below.

The photoelectron enhancement by high-Z nanoparticles was exploited in cancer radiotherapy by Hainfeld et al. who attempted to increase the dose delivered to tumours by injecting 1.9 nm gold nanoparticles into mice [34]. The authors also made the method the subject of a patent.

7. Radiobiological dose enhancement effects from molecular and atomic high-Z elements

It is curious that historically photoelectron emission by internal high-Z elements in living systems has received very little attention. The issue of enhanced doses near bones, due to the higher concentration of calcium in the bone, was addressed as long ago as 1949 by Spiers [35], and more recent work has also looked at photo-electron emission near the bone [36]. In 1988 Castillo reported burns and necrosis around reconstructive wires in mandibular cancer patients [37], and Regulla et al. employed a very sophisticated measuring apparatus to show a physical dose enhancement of about 100-fold and a biological enhancement into tissue of 50-fold within a range of 10μ from gold foil [38]. Despite work on enhancing radiotherapy which has been carried out, no authors appear to have related the question of photoelectron enhancement to health effects. One obvious question must be about the enhanced photoelectron doses near metal prosthetic structures containing zirconium (Z = 40). The element has a photoelectron cross section of 3.5E+3 at 150 keV compared with iron (Z = 26) at 5.4 and so would produce some 650 more photoelectrons.

The main question that has to be focused on is the enhancement of dose to the DNA from high-Z atoms or molecules which are attached to the DNA by chemical affinity. If a high-Z atom, ion or molecule were attached to the DNA, then it is easily predicted that this would cause enhanced genetic damage, measurable as downstream effects like cancer and congenital disease but also chromosome breakages and chromosome aberrations. The obvious candidate is uranium, which as the uranyl ion has been known to bind strongly to DNA since the 1960s when it began to be employed as a chromosome stain. The genotoxic effects of uranium exposure are by now well established both in human populations and in in vitro studies [12–20]. They cannot be explained by the intrinsic alpha activity, and indeed one experiment has revealed genetic effects in the absence of alpha decays [20]. The affinity of uranyl ion for DNA has been measured, and it is significant. So uranium (Z = 92) effects are one clear piece of evidence for the effects of secondary photoelectrons. But there is another one.

8. Cisplatin

There is further evidence from the anticancer agent cisplatin, cis-diamine-dichloro-platinum (II). Cisplatin has been a chemotherapeutic agent of choice since 1978 and is given to more than half of all cancer patients. Its mode of action has been variously described as "damaging nuclear DNA and arresting cell division". A recent review states: "Almost 30 years after its clinical benefits were first recognised, studies still continue in an effort to understand exactly how cisplatin works" [39].

Cisplatin also augments radiotherapy, that is to say, the combination of cisplatin and radiotherapy results in much higher cancer therapeutic effects than either agent on its own. This is, of course, a pointer to the mechanism [33, 39]. It is suggested here, based on what has been written above, that cisplatin, a simple diamine-dichloro-square planar complex of platinum (II), merely fixes the platinum atom (Z = 78) at the centre of the nuclear DNA where the secondary photoelectron doses are sufficient to fatally damage the DNA either from natural background radiation or in the case of the radiotherapy, from the induced photoelectrons. If this is the mechanism, then two suggestions are obvious: first, uranium as uranyl acetate, for example, also will act as a chemotherapeutic agent for cancer and will augment radiotherapy in the same way. Since it is suggested that it is the high-Z aspect of cisplatin that is the reason for its action, other high-Z molecular agents could be searched for or synthesised to act as DNA-seeking chemotherapeutic agents.

9. Evolution

The question of the spectrum of elements utilised by evolution of life on earth has been generally approached from the point of view of physical chemistry and more specifically redox equilibria [40]. There may be a separate or additional explanation for the reason why elements of high atomic number (e.g. mercury, bismuth, lead, uranium) although often commonly available on earth are not used by living creatures. As has been shown, chemical elements absorb gamma and X-rays of energy below about 250 keV approximately in proportion to the fourth power of their atomic number Z, and the energy is converted mainly to photoelectrons and local Auger recoil electrons resulting from internal rearrangements in the case of high-Z elements. For elements immobilised inside living tissue, this results in higher doses to components near high-Z atoms or nanoparticles than would be experienced

by the same tissue in the absence of the contaminant. Thus, high-Z elements, inside the body, act as devices for focusing and enhancing the doses from natural background radiation and should be seen as phantom radioactivity sources.

If the phenomenon is significant, then it would seem reasonable that the contemporary spectrum of chemical elements employed by living systems will have been produced by evolutionary selection forces responding to such potentially critical damage.

It is a well-known fact that the effects of ionising radiation on living systems are mediated by genotoxicity. The damage can be seen as a consequence of both single- and double-strand breaks in DNA; the dose (D) response (E) can be written as [41]

$$E = aD + bD2 \quad (1)$$

But for the photoelectron effect being considered, dose (i.e. local dose at the DNA) can be written in terms of the atomic number Z or the elements:

$$D = \alpha Z4 \quad (2)$$

and thus

$$E = cZ4 + dZ8 \quad (3)$$

(a, b, c, α and d being arbitrary constants). For evolution it can be assumed that any stress S which prevents an individual from reproducing will represent an inhibitory effect of the survival probability of the species. S can be written in terms of the concentration C of the element in the individual and the radiation effect on the DNA from the element:

$$S = CE \quad (4)$$

$$S = C\,(cZ4 + dZ8) \quad (5)$$

Thus,

$$C = \text{Constant}/\left(cZ^4 + dZ^8\right) \quad (6)$$

If the log of the concentration of all elements found in living systems is plotted against the log of the atomic number Z, the theory predicts an approximately linear relation with slope of between −4 and −8 depending on the contributions of single- and double-strand breaks in DNA to the overall photoelectron and recoil genotoxicity. Of course, the proposed relation is for non-radioactive or weakly radioactive elements and assumes that only photoelectron and Auger effects contribute.

Figure 12 shows a log-log plot of concentration of elements vs. atomic number Z for standard man. Data were from the International Commission on Radiological Protection [42].

Results (**Figure 12**) for elements of Z > 5 seem to support the idea that the photoelectric conversion of natural background radiation has been a significant effect in evolution. The slope of the log correlation is −5.6, between −4 and −8 as predicted, suggesting that a significant component of the effect involved double-strand breaks of DNA and thus ionisation which is very local to the elements. Indeed, it is curious how very few of the elements available to life have been employed by

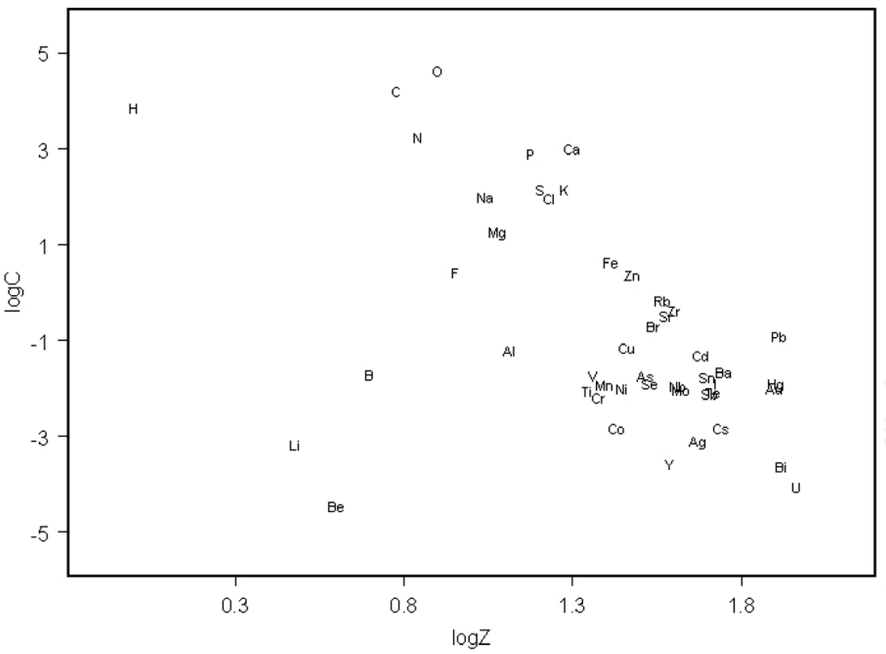

Figure 12.
Plot of log(C) vs. log(Z); investigating the relationship between concentration of elements in humans and the atomic number Z. Note H, Li, Be and B are significant outliers from a relation for which the slope of log(Z) is −5.6 (R^2 = 0.514, F-statistic = 65.23 on 1 and 41 degrees of freedom; $p < 10^{-10}$).

biological processes: evolutionary niches are generally found to be occupied but clearly not ones that involve utilising elements of high atomic number. This is not because these elements are scarce. The crustal concentrations of uranium are quite high; there is a significant quantity of uranium in seawater, yet the transfer coefficient for the gut (in mammals) ensures that the element is excluded quite efficiently. The same is true for many other high-Z elements that have been excluded from biological systems.

It is of interest that the elements lithium, beryllium and boron are significant outliers from the relation, and this needs addressing from within the general concept. One reasonable explanation is that all three elements are associated with neutron conversion effects, either the absorption of a neutron in a reaction that produces an alpha particle (boron, $^{10}B(n, \alpha)$; i.e. $^{10}B + n = {}^{7}Li + \alpha$; lithium, $^{6}Li(n, \alpha)$) or the absorption of an alpha particle in a reaction which produces a neutron (e.g. beryllium, $Be(\alpha, n)$; $^{4}He + {}^{9}Be = {}^{12}C + n$). Both alpha particles and neutrons are densely ionising and carry weightings of between 5 and 20 for radiobiological effectiveness in models which assess risk [41]. The thermal neutron cross sections of these three elements (in Barns, ^{10}Be = 3840, ^{6}Li = 9400 and ^{7}Be = 39,000) are significantly higher than other higher Z elements (^{238}U = 2.7). The neutron cross section of hydrogen is modest (0.2), but the atomic concentration of the element in water ensures significant neutron absorption and the production of energetic protons by recoil. The natural background neutron fluence at ground level, produced by cosmic rays, has been measured at 46 cm^{-2} h^{-1} equivalent to a dose of 10 nSv/h about 10% of the overall background dose [43]. Thus, the displacement of the "radiotoxicity relation" to the left by about one order of magnitude corresponds to the mean relative biological effectiveness of neutrons and alpha particles. It is therefore unsurprising that these elements are outliers in the general linear correlation of the log terms and this may be interpreted as a consequence of the existence of a natural background of these neutron radiations.

So, in general high-Z elements are not employed by life. Why then is there the utilisation by mammals of the element iodine (Z = 53)? The iodine-containing

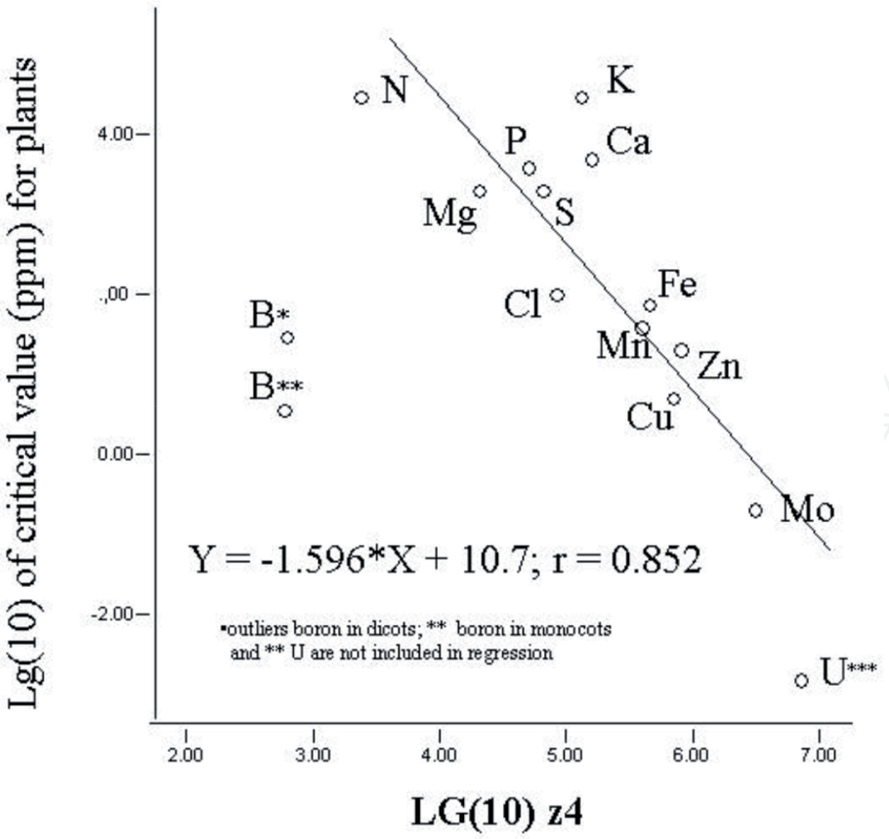

Figure 13.
Minimum concentrations of mineral elements essential for plants required for optimum growth as a function of the fourth power of the atomic number Z. The uranium data point is based upon detection of uranium in a wide range of plants [9].

systems (blood, thyroid) are those which are clinically most sensitive to radiation exposure (for reasons which are clear from the discussions above). It was suggested that the reason why iodine was employed is that the element is being exploited for its radiation detection quality and that the thyroid mediates an induced radiation damage address system through upregulation of genes associated with cellular surveillance and repair [9].

Finally, the relationships discussed here also obtain for plants. Plants are unable to move to avoid radiation exposure and might be expected to reflect responses to evolutionary stresses. The relationship between atomic number and the optimum concentration of elements for plants to thrive has been shown to conform to the same relationship [9]. The correlation is given in **Figure 13**.

10. Miscellaneous observations and suggested further research

The secondary photoelectron amplification of gamma radiation by different elements in living systems has importance in radiation dosimetry. For some inexplicable reason, elemental absorption has been entirely omitted from the calculations of absorbed dose published by radiation risk agencies like the International Commission on Radiological Protection (ICRP) which bases its recommendations of external dose limits on water- and tissue-equivalent phantoms. Furthermore, the phantom photoelectron radioactivity from this effect has considerable application to the element uranium which had been shown in a very large number of publications to have significant genotoxicity. This is particularly the case for internal uranium particles, generated from weapon use, from nuclear power station stacks, from global nuclear

atmospheric testing, from nuclear fuel reprocessing and from uranium fuel manufacture. All the official risk agencies model uranium on the basis of its very low intrinsic alpha radioactivity and conclude that it cannot pose the risk that it clearly does.

The basis for the current radiation risk model is the lifespan study of the Japanese A-Bomb survivors, the LSS. One major confounding exposure to the LSS cohorts, upon which the current risk model depends, was the post detonation black rain, which consisted of uranium particles from the weapons [44, 45]. On the basis of the arguments and evidence submitted in this chapter, the uranium particle exposures of all the different dose groups that have been used to construct a linear dose response make any attempt to use these data to define radiation risk unsafe. The unusual cancer results which emerged as soon as 1970 resulted in the researchers deciding to discard the not-in-city unexposed groups that are anomalously healthy. This was an error since these were the only groups not exposed to the black rain, although no doubt, the residual contamination will have caused inhalation exposures after they entered the cities, some months and years after the detonation. The issue was raised by Busby 2017 [45]. Studies of the LSS groups based on truly unexposed control groups in neighbouring prefectures carried out in 2009 showed that the cancer rates in all groups, especially the low-dose groups in the LSS cohorts, were significantly high [46].

What is being suggested here is that the entire understanding of gamma ray interaction with living tissue needs to be rethought. Research must be carried out to quantify the extent to which certain elements with high gamma and X-ray absorption coefficients bind to DNA and the extent to which this causes genetic and genomic damage at background levels and during radiotherapy or other external radiation situations. It is astonishing that no one has questioned the method that has been developed to assess harm from external photon radiations, the simplistic physics-based dilution of energy into water phantoms. It is not as if there was no evidence that this might be an unsafe approach. The radiosensitivity of the iodine-rich thyroid gland should have supplied clues. The mechanism of the anticancer agent cisplatin should have supplied clues.

High atomic number particles have increased in the environment in the last 50 years or more. Platinum particles emerge from catalytic converters, thorium particles emerge from gas light filaments and uranium particles are released from nuclear power stacks, reprocessing plants and many other sources. The high-Z secondary photoelectron effect is used in cancer therapy. There is a whole field of development here where anticancer agents may be synthesised to bind to DNA and carry a high-Z warhead.

Finally, it is suggested that there is a simple experiment which will demonstrate and quantify this effect. It is to contaminate a system in which genetic damage may be measured with a uranyl salt, so that the DNA is contaminated with uranium, and then to irradiate the system with different doses of X-rays or gamma rays and then measure the genetic damage. To exclude alpha particle effects, the agent cisplatin could also be employed in a similar experiment.

11. Conclusions

Although the sharp dependence of the gamma- and X-ray-induced photoelectron yield of elements on atomic number has been known for more than 100 years, the implications for radiobiology have been hardly addressed. This chapter aims to open up this issue and call for more research attention. First, it can be concluded that high-Z elements, when inside living tissue, represent a focus for absorption of photon radiation and that the resulting ionisation density close to the element

is much higher than what is calculated using conventional dosimetry such as that employed in current radiation protection, as in, e.g. [41]. This effect, the secondary photoelectron effect (SET), is most relevant to elements which also have affinity for DNA, the target for radiation-induced genotoxicity. The intrinsic radioactivity of such elements is not relevant, as can be seen by the genotoxicity and cancer therapy effect of the drug cisplatin. Results of Monte Carlo modelling carried out at the University of Ulster show that internalised high atomic number nanoparticles are likely to cause high local ionisation in living tissue. These effects are greatest for low-energy photons such as those in the natural background radiation spectrum. It is suggested that this may be one explanation for the anomalous genotoxicity of uranium particles found in many studies but hitherto dismissed as radiation effects on the basis of conventional dosimetry. Finally, an examination of the spectrum of elements employed by living systems reveals an interesting relationship which correlates the elemental composition adopted by life itself with the photoelectron cross section of the elements available to evolution. This relationship, which follows the photoelectron cross section and is highly statistically significant, suggests that living systems are exquisitely and critically sensitive to ionising radiation and have had to develop throughout evolution in such a way as to minimise the ionisation damage induced by background radiation. There are many important consequences of this approach, but the main ones are in the area of radiation risk assessment and in cancer therapy. Some approaches and experiments are suggested.

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