



REAL-LIFE RADIOACTIVE MEN: THE ADVANTAGES AND DISADVANTAGES OF RADIATION EXPOSURE

JIM O'DOHERTY^{1,2}, * BRUNO ROJAS-FISHER³ AND SOPHIE O'DOHERTY⁴

¹ Department of Molecular Imaging, Sidra Medicine, Doha, Qatar

² Weill Cornell Medical College Qatar, Education City, Doha, Qatar

³ Joint Departments of Physics, Royal Marsden Hospital & Institute of Cancer Research, Sutton, United Kingdom

⁴ Imaging Facility, EVMC, Qatar Foundation, Doha, Qatar

Received: 9th October 2018 // Revised: 19th October 2018 // Published online: 23rd November 2018

* Corresponding author: jodoherty@sidra.org

ABSTRACT

A common perception in modern society is that exposure to any amount of radiation is a bad thing and should be avoided at all costs. In the fictional superhero genre, exposure to radiation has been used as a vehicle to enable superpowers in what were previously ordinary humans. For instance, Dr Chen Lu, a Nuclear Physicist otherwise known as Radioactive Man, exposed himself to increasing amounts of radiation until he could endure a massive barrage, and in the process turned himself into Radioactive Man. In a similar fashion, Bruce Banner was exposed to a large amount of gamma radiation, giving him the superpowers of the Incredible Hulk. Although there is an element of truth in that the body can withstand low levels of radiation without any observable effects, there are many harmful side effects of being exposed to high levels of radiation. These harmful side effects form the underlying fear of the general public's understanding of radiation exposure. This article will explore in detail the reasoning behind the principles of radiation safety, and how different types of damage are caused to the human body when exposed to radiation. Furthermore, we discuss how cellular mutations are caused, as well as the potential of organisms to develop resistance to the harmful effects of radiation and the beneficial uses of radiation in the medical field for diagnosis and cancer treatment.



PROLOGUE

Chen Lu paused as he placed his hand on the door handle. His radiation Geiger metre frantically responded as the clicking ticks blend into a single continuous noise, an indication of the danger of the contents of the laboratory, what he was about to do, and what he was about to become. He took a deep breath, opened the door and sealed his destiny...

INTRODUCTION

The application of radiation as a mysterious catalyst for the development of superpowers has captured the imagination of sci-fi enthusiasts for many generations [1]. After all, radiation is essentially invisible “rays” we can’t see, hear, smell or feel, but with unusual properties that tend to not be very well understood by non-scientists. Therefore in the world of science fiction, these properties can be held responsible for the development of any superpower that the human imagination can conjure. Although radiation is not overly dangerous in itself, the issue with radiation for us as human beings is whether it has a detrimental effect on the human body if we are exposed to it in damaging doses.

Appearing in the Marvel comic series “Journey into Mystery #93” in 1963, Dr Chen Lu is a Chinese nuclear physicist known for his research on how radioactivity could be used to trigger superpowers in humans [2]. With the support of his government, he exposes himself to low-dose radiation (over an unknown period of time) to make himself immune to the effects of radiation. Although we do not know what specific type or amount, we can speculate that it was low enough to not kill him instantaneously but ionizing enough to cause

genetic mutations. He intends to use any powers that he develops in the treatment to defeat Thor, who is responsible for stopping the Chinese army’s invasion of India. After prolonged exposure, Lu gains a number of superpowers including the ability to manipulate radiation across the electromagnetic (EM) spectrum, to emit thermal radiation or heat, to emit high-energy radiation causing symptoms of radiation sickness, to absorb radiation and convert it to energy for his own use, and accelerated healing. He wears a customized radiation suit to shield his allies so that he only exposes enemies to radiation. However for short periods of time, he can also lower the radioactivity in his body to levels that make him appear normal and thus not require the suit.

A second character with powers that stem from exposure to radiation is better known in the superhero universe than Chen Lu. For the various iterations of the Hulk (Bruce Banner) in the 1962 Marvel comic [3], 1977-1982 TV series, and the Hollywood films [4, 5], the origin story is slightly different. Nonetheless, the overall premise is that Banner is exposed to a direct blast of high-energy gamma radiation (see Figure 1). Following the exposure, when Banner gets angry he turns into the Hulk, a large green being with superhuman strength, speed, agility, powers of regeneration amongst



a host of other abilities. Insights could be made into the trigger for his transformation due to anger, which could for example be linked to a threshold in his blood chemistry, such as up-regulation of the hormones testosterone or adrenaline or a down-regulation of the stress hormone cortisol.

In this paper, motivated by the stories of Dr. Chen Lu and Dr. Bruce Banner, we will address a number of important questions in relation to radiation such as “What makes radiation dangerous?” “Can exposure to X-ray or gamma radiation, no matter how small, be damaging to our health?”, “Can we make ourselves “immune” to the effects of damaging radiation?”, “Can exposure to a huge dose of gamma radiation really give a person superhuman strength?”, and “Do mutations really occur when you are exposed to high levels of radiation?” We also consider a number of the plausible themes that have been used to allow ordinary humans to acquire superpowers following exposure to a given radiation. In addition, we explore why these narratives are interesting concepts in the field of radiation science.

WARNING – RADIATION HAZARD!

To begin answering the aforementioned questions, it is important to know why some types of radiation on the electromagnetic (EM) spectrum can be considered dangerous to human health. The broadest definition of radiation is that there are 2 types, non-ionising

and ionising radiation. Ionisation is the process by which an atom gains or loses electrons so that it can become a positively charged (by losing electrons) or negatively charged (by gaining electrons) particle. After the process the atom is referred to as an ion. Therefore, non-ionising radiation does not change the number of electrons in an atom while ionising radiation typically removes electrons from atoms.

In the human body, ionisation can directly cause damage to atoms in DNA, or indirectly by creating “free radicals” that can then damage DNA. Free radicals are highly reactive diffusible ions or molecules with unpaired electrons that interact with cellular components, and over 70% of cellular damage is caused by free radicals [6]. Ionisation results in the development of biological and physiological alterations in the molecular structures within a cell such as inability of the cell to divide correctly that may manifest themselves seconds or decades later. Consider UV radiation. It is well known to cause sunburn not long after exposure to the sun, and prolonged exposure increases the lifetime risks of developing melanoma (skin cancer) many years after the exposure [7]. High-energy radiation such as ultraviolet radiation, X-rays, and gamma rays are ionising radiation since they can cause ionisation of atoms in the human body (Figure 1). Low-energy radiation such as visible light and radio waves do not cause ionisation of atoms and are forms of non-ionising radiation. Furthermore, there is also radiation emitted as particles (rather than rays), which results from the interaction of ionising



rays radiation with matter. Examples of these are protons, neutrons and electrons, which are

even more highly biologically reactive than rays.

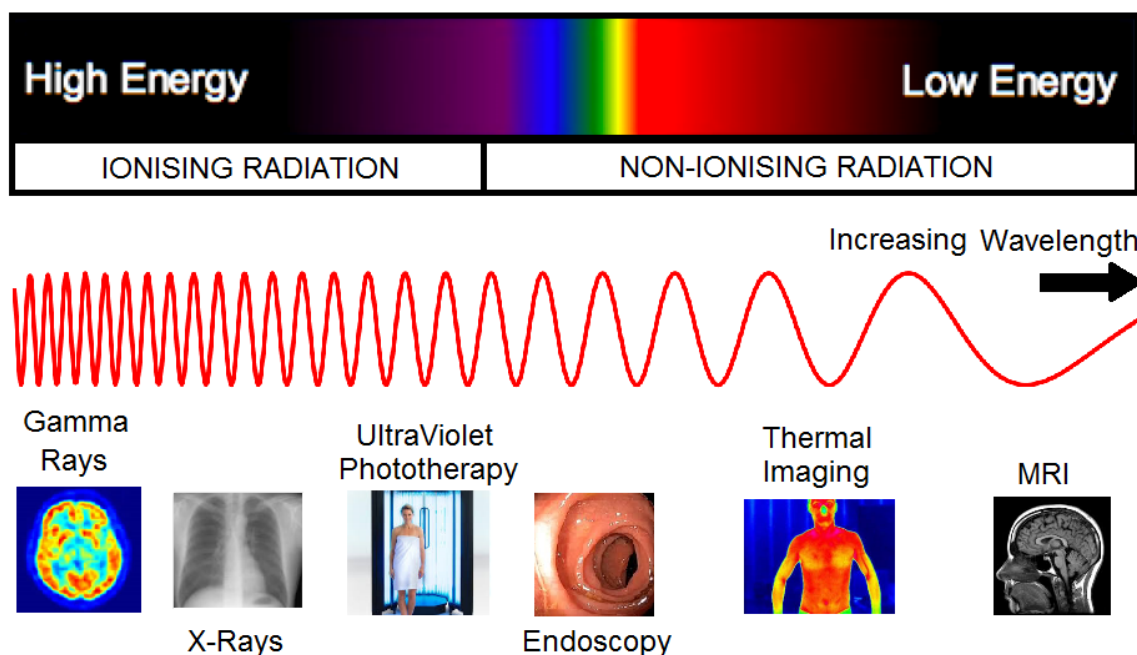


Figure 1: The electromagnetic (EM) spectrum, and applications in modern medicine. Ionising radiation is a term used to describe radiation with enough energy to cause damage to the cells of the human body while non-ionising radiation does not have enough energy to damage cells.

MEASUREMENT OF RADIATION EXPOSURE

It is useful to know when considering radiation exposure how it is physically measured and how it is quantified. “Radiation exposure” is a term that accounts for the potential damage by certain types of radiation, as well as the radiation sensitivity of the biological tissue subjected to the exposure. In its most fundamental form, a basic parameter called “absorbed dose” is the amount of radiation energy absorbed per unit mass (Joules per kilogram (J kg^{-1}), otherwise known as the Gray (Gy)). A further parameter is the “effective

dose”, which is the absorbed dose multiplied by a radiation weighting constant (i.e. the constant for X-rays = 1, the constant for neutrons = 20) and a tissue-weighting constant (i.e. skin = 0.01, bone marrow = 0.12). The effective dose parameter has the unit of Sieverts (Sv), and is a crude (although internationally accepted) attempt to quantify the biological effects of exposure to radiation.



BIOLOGICAL EFFECTS OF RADIATION EXPOSURE

Exposure to ionising radiation can lead to two different effects known as ‘deterministic’ effects and ‘stochastic’ effects. Both effects apply to the exposure pattern of the Hulk and Radioactive Man. Firstly, deterministic effects occur upon receiving a large dose of radiation over a short amount of time (i.e. in the case of Bruce Banner being exposed to gamma rays from a nuclear blast), and damaging biological effects are certain to occur above a well-defined threshold. Examples of deterministic effects include reddening of the skin (between an absorbed dose of 2-10 Gy), sterility (above a dose of 2.5-6 Gy to the ovaries/testes), and cataracts (above 1.5 Gy to the eyes) [8]. A summary of deterministic effects measured in mSv representing the effective dose to the whole body is shown in Figure 2, accompanied by a severity scale. For Bruce Banner, it is difficult to calculate the effective dose or the absorbed dose that he received. In the original 1962 comic [3], it is mentioned that he was “many miles from the blast”, and given that he did not die within weeks, we can estimate that he might have received an effective dose of less than 6000 mSv. Although radiation dose decreases with distance from the blast, so far,

superhuman strength has not been observed to be a side effect.

In reality, any person exposed to a large dose of radiation at a single time is highly likely to develop acute radiation sickness. There are well known cases of death due to radiation from accidents in nuclear reactors in power plants [9], submarines [10] and also from lost radioactive sources intended for use in medicine [11]. More recently radiation has been used for criminal purposes such as murder, as was the case with Alexander Litvinenko, whose tea was spiked with highly radioactive Polonium in a London restaurant [12]. His death from multiple organ failure 3 weeks later clearly demonstrates the negative biological effects of acute radiation sickness. Litvinenko’s kidneys and bone marrow received an absorbed dose 7-10 times greater than the absorbed doses known to cause detrimental organ complications [12]. Due to radiation poisoning, conditions such as leukopenia (a reduction in white blood cells that affects the body’s ability to fight infection), thrombocytopenia (a reduction in platelets that affects the ability of blood to clot) and aplastic anaemia (a reduction in the production of red blood cells that affects their ability to carry oxygen around the body) are known to develop [13].



RADIATION DOSES Millisieverts (mSv)

10,000	Acute radiation poisoning - death within weeks
6,000	Typical dose received by Chernobyl nuclear plant workers who died within one month of accident
3,000	Survival rate approximately 50 percent
2,200	Reading found near tanks used to store radioactive water at Fukushima plant, Sep 3, 2013
1,000	Causes radiation sickness and nausea, but not death. Likely to cause fatal cancer many years later in about 5 of every 100 persons exposed
700	Vomiting, hair loss within 2-3 weeks
500	Allowable short-term dose for emergency workers taking life-saving actions
400 per hour	Peak radiation level recorded inside Fukushima plant four days after accident
350 per lifetime	Exposure level used as criterion for relocating residents after Chernobyl accident
250	Allowable short-term dose for workers controlling 2011 Fukushima accident
100	Lowest level linked to increased cancer risk
20 per year	Average limit for nuclear industry workers
10	Full-body CT scan
2.4 per year	Person's typical exposure to background radiation
0.01	Dental x-ray

Figure 2: Summary of deterministic biological damage after radiation exposure to the entire body. A very rough estimate would put Bruce Banner's exposure level at less than 6000 mSv (given that he didn't die) (1 milliSv = 0.001 Sv). Figure reproduced with permission [13].

In comparison to deterministic effects, the second category of biological effects is more difficult to quantify. These are called stochastic effects, and are biological effects that have a probability of occurring, but there are no absorbed dose thresholds below which the probability is zero. With radiation the assumption is that the probability is linearly proportional to radiation dose received, a theory known as the 'linear no threshold hypothesis' (LNT) [14]. A stochastic risk that is familiar to many is smoking. If a person smokes 20 cigarettes a day for 40 years, it is not a certainty that the person will develop lung cancer. However, stochastically, it is more likely to happen if you smoke than if you do not smoke.

The same thought process could be applied to developing diabetes from consuming sugar, and similarly to the increased risk of development of cancer after exposure to ionising radiation.

In the case of Radioactive Man or Dr. Chen Lu, he exposes himself to ionizing radiation over an unknown time period. It is likely that he took "breaks" during the "treatment" such that he would have exposed himself to radiation for perhaps a few minutes per day, which would have allowed his body time to recover from the radiation damage in the intervening time. In effect, he would have been training his immune system to withstand various doses of radiation in the same manner



that some organisms can survive in the exclusion zone around nuclear accidents [15, 16]. On the other hand, if he received an effective radiation dose of 100 mSv or more (see Figure 2), he would more likely have developed chronic radiation sickness from repeated exposure to high levels of radiation. In addition, there would have been a much greater risk of developing some form of cancer. Such exposure processes led to the demise of many famous pioneers of Nuclear Physics, who were unaware of the dangers of ionising radiation and handling very highly radioactive sources. Marie Curie, Pierre Curie and Henri Becquerel (who apparently kept radioactive sources in his pockets) all died from biological conditions such as aplastic anaemia, which was directly attributable to their exposure to ionising radiation (known today as radiation poisoning) over many years. Even now Marie Curie's original notebooks from 1890 are considered a radioactive hazard to handle, anyone wishing to read them must wear special protective clothing [17].

RADIATION AND MUTATIONS

Think of mutations, and you are likely to think of superheroes such as the Hulk, Radioactive Man and the X-Men. The DNA in your body or any organism is a genetic code analogous to computer code but much more complex. Ionisation alters this code by damaging atoms

in certain parts of the code. As ionisation events are random, random parts of the code can be damaged during radiation exposure and affect many of the trillion cells in the organism. There are a range of events that may happen after damage from ionisation – the cell may die, the cell may repair itself, or the cell may have a transcription error, meaning that when the cell divides it carries that genetic error forwards into the next generation of cells. This last process is better known as “mutation”, where each change is another error in the organism's genetic code. Unfortunately random mutations such as those occurring from exposure to radiation are not organised enough to make a superpower, and although the effects are generally unpredictable, they are more likely to cause detrimental health effects as the likelihood of random changes being good for the organism is infinitesimally small. A more likely way to develop superpowers along the lines of Radioactive Man might be through the structured transfer of genetic information (ionisation is random, not structured) into cells before a child is born through the use of specifically coded stem cells. However, researchers are more focused on using stem cells to aid in the elimination of inherited genetic and metabolic diseases rather than creating humans with superpowers through ethically questionable experiments.



Figure 3: (Left): The resulting damage suffered by one of the “Radium Girls” from ingestion of radium in the 1920s [18]. (Right): Comparison of a pale bluegrass butterfly from the area directly surrounding Fukushima (bottom) and the same species from an unaffected area of Japan (top) [19]. Figures reproduced with permission.

There are many examples of people living with mutations (visible and invisible) following radiation exposure. Unfortunately none of these people exhibit superpower abilities. Groups of people have been exposed to ionising radiation that emanated from nuclear weapons testing in Kazakhstan, the United States, United Kingdom, and Russia as well as nuclear plant accidents in Chernobyl (Belarus), Fukushima (Japan) and Three-Mile Island (United States). An interesting and strange example of radiation exposure relates to the tragic story of the “Radium Girls”, who were employed at clock factories in the 1920s in the United States to paint “harmless” self-luminous paint onto dials to make them glow in the dark [20]. The women would lick the paintbrushes to make a sharp point for painting, and in some cases, they even wore the paint as nail varnish. It transpired that the paint was actually highly radioactive radium, which emits ionising radiation and, is most dangerous when ingested (at the time small

amounts of radium were actually believed to be beneficial and it was put in toothpaste, milk and blankets [21]). Over the course of months and years, the women developed anaemia (a lack of red blood cells causing a lack of oxygen to the tissues and organs), disintegrating jawbones, facial abscesses, mouth ulcers, tooth loss, bone cancers and severe facial deformities from their prolonged exposure to radium. These genetic mutations (although unknown at the time) were directly attributable to radium. Given that as human beings we inherit the genes of our parents, these mutations were passed on to the women’s children (through mutated DNA in ovary stem cells), some of whom even now 100 years later still suffer effects such as syndactyly (fused fingers), dental and digestive issues initiated by their ancestors exposure to radium generations ago [22].

Other flora and fauna are also not impervious to the detrimental effects of radiation. For example within nuclear accident



sites such as Chernobyl, animals and insects across a range of taxonomic groups have been reported with smaller brains, reduced reproductive capacity, albinism and eye cataracts [23]. Microbes have been reported to display very unusual behaviour, and trees grow much slower than normal and with growth abnormalities and deformed pollen [24]. Mutated butterflies with strangely shaped wings and bodies have been found in the area around Fukushima after the nuclear accidents of 2011 in addition to spiders building ineffective and erratic webs [19]. With the freedom of animals in areas abandoned by humans, these mutations can be spread throughout other population bases in the environment.

FIGHT THE POWER – RADIATION RESISTANCE

Unfortunately for us mortals who wish to emulate superpowers stemming from radiation exposure, it is certainly not good news. Many groups of people exposed to nuclear weapons, nuclear accidents or the resulting radioactive fallout have a greater risk of cancer. For example, general cancer rates in adults near Hiroshima and Nagasaki rose by 10%, and childhood leukaemia by 50% [25]. In fact, the worrying amount of radioactive fallout produced by nuclear weapon testing in Russia and the United States in the 1960's led to an international ban on "above-ground" or surface nuclear weapon testing [26]. American and British military personnel involved in atomic weapons testing in the Pacific islands in the

60's (such as Bruce Banner) were approximately 14% more likely to die from leukaemia, 20% more likely to die from prostate cancer, and more than 20% more likely to die from nasal cancer than soldiers not involved in those tests [27].

However, there are less complex organisms shown to be more impervious to radiation than humans for many reasons such as slow cell reproduction rate (in insects such as wasps) [28], single cell organisms that do not divide (and hence have no issues with DNA damage on division), and bacteria with an incredible ability to regenerate their DNA after receiving very high levels of radiation [29]. In a recent study, the bacteria *Escherichia coli* (*E.coli*) was bombarded with high-energy radiation until 99% of the population had died, and a new generation of *E.coli* was grown from the survivors. This new cell population had the ability to repair their DNA strand breaks at a rate that was 4 times better than the rate of their ancestors, proving that in simple cases radiation resistance can be pre-programmed in a form of accelerated bio-adaptive evolution to the habitat [30]. The future implications of this research on other species is interesting if further investigations can decipher the mechanism behind how the bacteria's resistance to radiation is coded into the DNA sequence of genes. Future research could include applying these principles to gene therapy to make humans more resistant to radiation, which is important for astronauts who receive a very high radiation dose of between 50-2000 mSv during a 6 month stay on the International



Space Station [31] (important data for any future mission to Mars), or for example to develop a new strain of bacteria to clean up radioactive waste at sites such as the Fukushima site in Japan [32].

ARE LOW DOSES OF RADIATION BAD FOR US?

The short answer is no. Although the previous discussion focuses on serious health risks when large doses of radiation are received (i.e. nuclear fallout, explosions), low effective doses of radiation received (approximately <100 mSv) present a more complex situation. The current internationally accepted assumption is the LNTH (linear no threshold hypothesis), which assumes a linear relationship between the severity of effect and radiation dose at all levels of radiation dose based on such a relationship at high levels of dose (see Figure 4). The LNTH has been applied to the low dose-rate region (i.e. effective dose <100 mSv) even though epidemiological studies lack significant statistical power to determine the health risks from low dose exposures. The LNTH has been criticized for its lack of a solid scientific basis on many occasions, although it still forms the principles of the legal regulations of radiation safety in countries that legislate on radiation use [33].

Radioactive Man's superpowers developed after exposure to small amounts of radiation over a large period of time, rather than a large amount of radiation over a short period of time. This may not be all that far removed

from reality, and has been the subject of active investigation. Low dose exposures may give the body time to adapt to small doses of radiation, and perhaps build up tolerance in the same way as vaccines made from a weakened form of a microorganism can provide the body with immunity to a particular microbe. This is a process that some researchers refer to as "radiation hormesis", whereby low doses of radiation are actually good for you, and stimulates the active repair mechanisms that protect the body against cellular damage. The theory is that continuous low doses stimulate protective responses, whereas high doses overwhelm the body's protection mechanisms [34]. The 2015 Nobel Prize in Chemistry (awarded to Tomas Lindahl, Paul Modrich and Aziz Sancar) detailed the biological mechanisms on how damage to DNA strands from UV radiation can be repaired by the body's cells during DNA replication, safeguarding the genetic information through constant monitoring and adjustment [35]. So it may be that small amounts of radiation might not be that bad for us after all. However, this conclusion is still far from certain and further research is necessary.

Despite many people thinking they will never be exposed to radiation, we are all exposed to some level of radiation every day. Radiation in the environment is present in many forms, but primarily arises from naturally occurring radioactive elements, such as uranium, thorium, and radon, that can be found in bedrock in the ground underneath us. The



amount of radiation dose you receive from rocks is dependent on what part of the world you live in with some areas having higher amounts of natural radioactive elements than others. A standard effective radiation dose received annually by a person living in the United Kingdom is quoted as 2.2 mSv/year [36], and in the United States is 3.0 mSv/year [37]. Data from China suggests that Radioactive Man would have been exposed to a natural background of 2.3 mSv/year [38]. There are areas in the world where this value is much higher, such as Ramsar, Iran (which has been populated for many centuries) where the background radiation received by the population is 260 mSv/year [39]. Adding weight to the argument that not all radiation exposure is bad, and that radiation hormesis may exist,

genetic studies show no significant differences between people in the high radioactive background areas compared to people in normal radioactive background areas. After exposing a sample of white blood cells from the population of Ramsar and a control group to a high level of ionizing radiation (an absorbed dose of 1.5 Gy to the white blood cells), further investigation revealed that the Ramsar population actually had less chromosome aberrations following the exposure than the white blood cells from the control group [39]. It transpires that the idea from 1963 (long before investigations into radiation hormesis) behind the adaptive response of Radioactive Man's immunity to radiation may not have been so far-fetched after all.

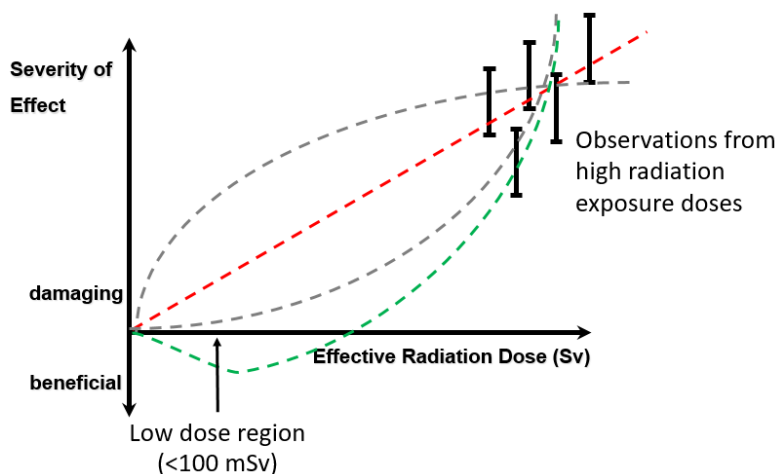


Figure 4: The “linear no threshold hypothesis” of radiation exposure (red line) stating that the severity of radiation exposure at high dose rates can be extrapolated linearly and used to predict radiation effects at lower exposure levels. However many other potential curves may fit the data (grey lines). For example, a case where low levels of radiation are actually good for humans (less severity of effect on the graph) is also included on the graph (green curve). This effect is called “radiation hormesis” [40].



MEDICAL USES OF RADIATION EXPOSURES

Thanks to trailblazers like Wilhelm Rontgen, Henri Becquerel and the Curies, the good and bad effects of radiation have been employed in medicine where the effects of ionization radiation have far more advantages than disadvantages. The uses of X-rays in computed tomography (CT) and plane-film X-ray imaging has allowed physicians to non-invasively see inside the human body. Surgery is now routinely performed with X-ray guidance, which allows surgeons to use minimally invasive techniques, and in turn leads to shorter hospital stays, lower risks of infection, and faster recovery times [41]. Imaging using radioactive isotopes and cancer treatments using high energy X-rays in radiotherapy have also matured to become routine processes in many hospitals around the world. These techniques show that even with the slightly increased risks of cancer development based on the LNTH, the benefits of a clear medical diagnosis or reduction of tumour volume far outweighs the negligible risks associated with a purposeful and controlled exposure to radiation.

An interesting area in medicine and related to Radioactive Man is the field of nuclear medicine, where patients are injected with a radioactive drug known as a radiopharmaceutical, which is a combination of a small amount of a radioactive isotope and a drug. A wide range of pharmaceutical agents can be made to radioactively “tag” to a large variety of biochemical pathways inside the body

(i.e. certain chemical receptors expressed only by tumours), or to certain specific organs. Once the radiopharmaceutical becomes trapped in the tissue of interest, images of the distribution of the radiopharmaceutical can be made using a special scanner that detects the location of the radiation called positron emission tomography (PET) or single photon computed tomography (SPECT) scanners [42]. Clinical investigation of organ function in diseased states can be performed such as organ metabolism of glucose, lung ventilation, neurotransmitter activation in the brain, imaging of different forms of cancer-related proteins, heart metabolism as well as many other investigations. When injected in even higher amounts, the radiation can actually be used to treat different forms of cancer by selectively destroying tumour cells (due to the ‘tagging’ process), thus isolating the damage to non-cancerous tissue to a minimum. This treatment is called molecular radiotherapy and the radiation doses to the areas of cancer can be large, with absorbed doses up to 200 Gy to tumours being quite common [43, 44]. Patients injected with radiopharmaceuticals actually stay radioactive for a time related to the half-life of the radioactive isotope used for injection, and patients being radioactive for a few weeks after treatment is common. Patients of nuclear medicine can be considered as real-life radioactive men and women, as once they are injected they will remain radioactive and go about their daily business with large amounts of radiation inside them and no visible effects that



they are radioactive. Contrary to popular belief radioactive people don't glow green!

A similar principal is applied in radiotherapy whereby special machines called linear accelerators (Linacs) are used to "shoot" very high energy X-rays into patients as part of their cancer treatment. The X-ray beam is shaped so as to efficiently target the beam to the site of the tumour, while minimising the radiation exposure to the non-cancerous tissue. For most cancer treatments, patients will return a number of times for radiation therapy, in some cases up to 30 times over the course of a month as the entire radiation dose in one session would cause excessive damage to the non-cancerous tissues of the body [45]. There is also a form of radiotherapy known as "total body irradiation (TBI)", which as the name suggests, exposes a patients' entire body to large amounts of ionising radiation. The effect of this radiation is to deliberately suppress the

patients' immune system by destroying lymphocytes (a type of white blood cell) in the body that fight foreign invaders, which in turn prevents the rejection of transplanted bone marrow or blood stem cells [46]. Radiation exposure by TBI leads to very high rates of infertility in both men and women, and recovery of proper functionality has only been seen in 10-20% of men and women [47].

The situation of TBI sounds remarkably similar to how Radioactive Man developed his powers (which at the time could have been potentially influenced by the recent invention of the linear accelerator), who made himself impervious to the effects of radiation over the course of time. However with patients it is more ideal if they actually become more sensitive to the radiation over time rather than impervious, as radiation is more likely to lead to a successful outcome for their cancer treatment.



Figure 5: (Left): A PET scan of a patient showing the distribution of a radioactive tracer for glucose metabolism. The PET scan (in orange) is overlaid onto a computed tomography (CT) scan for anatomical localization. The image shows normal use of glucose in the brain but abnormal distribution in the mouth cavity. Middle – a linear particle accelerator (Linac) used in radiotherapy treatments of cancer. The entire unit rotates around the patient, which allows the X-ray beam to conform to the tumour volume as accurately as possible. Image courtesy of Varian Medical Systems. (Right): A patient about to undergo total body irradiation (TBI) to greatly reduce their immune system for bone marrow transplant.



CONCLUSION

In the cases of both Radioactive Man and the Incredible Hulk, exposure to ionising radiation enabled the damaged DNA of their bodies to react in a harmonized way that generated abilities beyond that of normal human beings. In terms of the biological effects of radiation on humans, this scenario is unfortunately likely to remain a product of science fiction given that DNA in trillions of cells with many different functions does not all react in the same manner to radiation. The real effects of resulting mutation as described above not only includes observable and drastic physical differences such as the blue grass butterfly and effects suffered by the Radium Girls, but also functional abnormalities such as increased occurrences of cancer and hereditary effects passed down to the next generation. As with all mutations, the fields of genetics and epigenetics (the study of changes in organisms caused by modification of gene expression) determines if these mutations can become dominant or recessive (i.e. if the mutation survives in the chromosomes of the descendant population or not) [48].

In theory, we as human beings are already immune to some level of radiation due to exposure to background radiation from underground sources. There is however no clear relationship yet between how much radiation dose humans can receive and the onset of any clinically observable effects. A clinical trial would be the best solution to establish threshold levels of ionising radiation

(in terms of absorbed dose) for the onset of certain detrimental medical complications. Such a trial however would be highly unethical given the known detrimental effects of high doses of radiation, and is extremely unlikely ever to receive the necessary regulatory approvals to be performed. Until such a time comes when mankind further understands the effects of low effective doses of radiation, the LNTH (Figure 4) will continue to form the principles for regulation of radiation throughout the world.

In summary when it comes to radiation, there are some benefits to society as a whole when it is carefully used and controlled, in well-established cores of knowledge such as generation of nuclear power, diagnosis of medical conditions in nuclear medicine, or in life saving medical procedures such as radiotherapy and interventional radiology. Certain aspects regarding the biological effects of radiation such as resistance and hormesis have elements of truth to them at some level, and are areas of active investigation such as how resistance to radiation can be manipulated, deeper understanding of how radiation causes DNA damage and also new applications of radiation in medicine. Currently the ability of the human body to coherently harness the energy of ionising radiation in order to develop superpowers unfortunately will remain firmly in the science fiction world for the foreseeable future.



REFERENCES

1. Fitzgerald, B.W., *Secrets of Superhero Science*. 2016, the Netherlands: BW Science.
2. Lee, S. and R. Bernstein, *The Mysterious Radio-Active Man!*, in *Journey into Mystery*. 1963, Marvel Comics.
3. Lee, S., *The Hulk*, in *The Incredible Hulk*. 1962, Marvel Comics.
4. Leterrier, L., *The Incredible Hulk (motion picture)*. 2008, Marvel Studios.
5. Lee, A., *Hulk (motion picture)*. 2003, Universal Pictures.
6. Ward, J.F., *DNA damage produced by ionizing radiation in mammalian cells: identities, mechanisms of formation, and reparability*. *Prog Nucleic Acid Res Mol Biol*, 1988. **35**: p. 95-125.
7. Watson, M., D.M. Holman, and M. Maguire-Eisen, *Ultraviolet Radiation Exposure and Its Impact on Skin Cancer Risk*. *Semin Oncol Nurs*, 2016. **32**(3): p. 241-54.
8. IARC Working Group on the Evaluation of Carcinogenic Risk to Humans, *Ionizing Radiation, Part 1: X- and Gamma (γ)-Radiation, and Neutrons*. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, No. 75. Vol. 75. 2000, Lyon, France: International Agency for Research on Cancer.
9. Yablokov, A.V., *7. Mortality after the Chernobyl catastrophe*. *Ann N Y Acad Sci*, 2009. **1181**: p. 192-216.
10. Amundsen, I., et al., *The Kursk Accident*, in *Strålevern Rapport 5*. 2001, Norwegian Radiation Protection Authority: Østerås, Norway.
11. International Atomic Energy Agency, *The Radiological Accident in Goiania*. 1988, International Atomic Energy Agency: Vienna, Austria.
12. Harrison, J., et al., *The polonium-210 poisoning of Mr Alexander Litvinenko*. *Journal of Radiological Protection*, 2017. **37**(1): p. 266-278.
13. Crick, M. and F. Shannoun, *Radiation Effects and Sources*, A. Steiner, Editor. 2016, United Nations Environment Program: e.
14. Brenner, D.J., *Extrapolating radiation-induced cancer risks from low doses to very low doses*. *Health Phys*, 2009. **97**(5): p. 505-9.
15. Galvan, I., et al., *Chronic exposure to low - dose radiation at Chernobyl favours adaptation to oxidative stress in birds*. *Functional Ecology*, 2014. **28**(6): p. 1387-1403.
16. Moller, A.P. and T.A. Mousseau, *Are Organisms Adapting to Ionizing Radiation at Chernobyl?* *Trends Ecol Evol*, 2016. **31**(4): p. 281-289.
17. Simcox, L. and J. Taylor, *Curies Contaminated Notebook: An analysis of a notebook and papers, originally belonging to Marie Curie, which are now retained by the Wellcome Collection, London*. 2016, Aurora Health Physics Services Ltd: London, UK.
18. Mullner, R., *Deadly Glow: The Radium Dial Worker Tragedy*. 1999: American Public Health Association.
19. Hiyama, A., et al., *The biological impacts of the Fukushima nuclear accident on the pale grass blue butterfly*. *Sci Rep*, 2012. **2**: p. 570.
20. Clark, C., *Radium Girls, Women and Industrial Health Reform: 1910-1935*. 1997, Chapel Hill, USA: University of North Carolina Press.
21. Gott, M., J. Steinbach, and C. Mamat, *The Radiochemical and Radiopharmaceutical Applications of Radium*. *Open Chemistry*, 2016. **14**: p. 118-129.
22. Moore, K., *The Radium Girls: The Dark Story of America's Shining Women*. 2017: Sourcebooks.
23. Mousseau, T.A. and A.P. Moller, *Genetic and ecological studies of animals in Chernobyl and Fukushima*. *J Hered*, 2014. **105**(5): p. 704-9.
24. Mousseau, T.A., et al., *Highly reduced mass loss rates and increased litter layer in radioactively contaminated areas*. *Oecologia*, 2014. **175**(1): p. 429-37.
25. Goodman, M.T., et al., *Cancer incidence in Hiroshima and Nagasaki, Japan, 1958-1987*. *Eur J Cancer*, 1994. **30A**(6): p. 801-7.
26. Rusk, D., D. Home, and A. Gromyko, *Treaty Banning Nuclear Weapon Tests in the Atmosphere, in Outer Space and Under Water*, t.U.K.o.G.B.a.N.I. Governments of the United States of America, and the Union of Soviet Socialist Republics, Editor. 1963: Moscow, USSR.
27. Darby, S.C., et al., *Further follow up of mortality and incidence of cancer in men from the United Kingdom who participated in the United Kingdom's atmospheric nuclear weapon tests and experimental programmes*. *BMJ*, 1993. **307**(6918): p. 1530-5.
28. Ducoff, H.S., *Causes of death in irradiated adult insects*. *Biol Rev Camb Philos Soc*, 1972. **47**(2): p. 211-40.
29. Gross, L., *Paradox Resolved? The Strange Case of the Radiation-Resistant Bacteria*. *PLoS Biology*, 2007. **5**(4): p. e108.
30. Byrne, R.T., et al., *Evolution of extreme resistance to ionizing radiation via genetic adaptation of DNA repair*. *Elife*, 2014. **3**: p. e01322.
31. Cucinotta, F.A. and M. Durante, *Cancer risk from exposure to galactic cosmic rays: implications for space exploration by human beings*. *Lancet Oncol*, 2006. **7**(5): p. 431-5.
32. Shuryak, I., et al., *Microbial cells can cooperate to resist high-level chronic ionizing radiation*. *PLoS One*, 2017. **12**(12): p. e0189261.
33. Marcus, C.S., *Destroying the Linear No-threshold Basis for Radiation Regulation: A Commentary*. *Dose Response*, 2016. **14**(4): p. 1559325816673491.
34. Baldwin, J. and V. Grantham, *Radiation Hormesis: Historical and Current Perspectives*. *J Nucl Med Technol*, 2015. **43**(4): p. 242-6.
35. Lindahl, T., P. Modrich, and A. Sancar, *The 2015 Nobel Prize in Chemistry The Discovery of Essential Mechanisms that Repair DNA Damage*. *Journal of the Association of Genetic Technologists* 2016. **42**(1): p. 37-41.
36. Oatway, W.B., et al., *Ionising Radiation Exposure of the UK Population: 2010 Review*. 2010, Public Health England: London, UK.
37. Schauer, D.A. and O.W. Linton, *NCRP Report No. 160, Ionizing Radiation Exposure of the Population of the United States, medical exposure--are we doing less with more, and is there a role for health physicists?* *Health Physics*, 2009. **97**(1): p. 1-5.



38. Kudo, H., et al., *Comparative dosimetry for radon and thoron in high background radiation areas in China*. Radiat Prot Dosimetry, 2015. **167**(1-3): p. 155-9.
39. Ghiassinejad, M., et al., *Very high background radiation areas of Ramsar, Iran: Preliminary biological studies*. Health Physics, 2002. **82**(1): p. 87-93.
40. Doss, M., *Linear No-Threshold Model VS. Radiation Hormesis*. Dose Response, 2013. **11**: p. 480-97.
41. Siskin, G., *Outpatient care of the interventional radiology patient*. Semin Intervent Radiol, 2006. **23**(4): p. 337-45.
42. Sharp, P., *Practical Nuclear Medicine*, ed. F. Sharp, H.G. Gemmell, and A.D. Murray. 2008, London, UK: Springer.
43. Strigari, L., et al., *Twenty years of radiobiology in clinical practice: the Italian contribution*. Tumori, 2014. **100**(6): p. 625-35.
44. Strigari, L., et al., *The evidence base for the use of internal dosimetry in the clinical practice of molecular radiotherapy*. Eur J Nucl Med Mol Imaging, 2014. **41**(10): p. 1976-88.
45. Baskar, R., et al., *Cancer and radiation therapy: current advances and future directions*. Int J Med Sci, 2012. **9**(3): p. 193-9.
46. Wills, C., et al., *Total body irradiation: A practical review*. Applied Radiation Oncology, 2016. **5**(2): p. 11-17.
47. Sanders, J.E., et al., *Pregnancies following high-dose cyclophosphamide with or without high-dose busulfan or total-body irradiation and bone marrow transplantation*. Blood, 1996. **87**(7): p. 3045-52.
48. Fraser, P. and W. Bickmore, *Nuclear organization of the genome and the potential for gene regulation*. Nature, 2007. **447**: p. 413-417.