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Presidential Address

RADIATION – FRIEND OR FOE?
Presidential Address to Ulster Medical Society
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The Ulster Medical Society was formed in 1862 with the amalgamation of the Belfast Medical Society (which had been founded originally in 1806) and the Belfast Clinical and Pathological Society (founded in 1853).

The Belfast of those early days of the 19th century was a parish of 20,000 inhabitants and in the second half of the 18th century the Charitable Society Poor House gave shelter to the old, infirm and orphaned children. Linked to the poor house was a small hospital[1]. In 1792 the Belfast dispensary opened a small fever hospital in Factory Row (Berry Street). A 'lying in' hospital was founded in1793 in Donegall Street and in 1815 the General Hospital was built in Frederick Street.

Against this background 19 physicians and surgeons came together in 1806 to form the Belfast Medical Society, with the first President being Dr SS Thompson. However, after discord the Society was dissolved in 1814 and reconstituted in 1822[2].

The Belfast Clinical and Pathological Society was founded in 1853 with its first President being Dr TH Purdon. This new Society, proposed by Dr Malcolm, included town and country doctors and by the end of its first year had 96 members. Remarkably its first President, Dr Purdon (born in Chichester Street, Belfast in 1806) entered Trinity College Dublin, at the young age of 13 years and in due course qualified in Medicine.

However, by 1861 discussions took place about having one single society and on April 30th 1862 the two old societies joined to become the Ulster Medical Society. The first President of the Ulster Medical Society was Professor JC Ferguson – born in Tandragee in 1802. He studied medicine in Trinity College and was appointed the King's Professor of Practice of Medicine in Dublin University in 1845. In 1850 he was appointed to the Chair of Medicine at Queen's College, Belfast[3].

The Society flourished and there were many well-known Presidential names over the years, including William Whitla, Robert Esler, Alexander Dempsey, John Byers, Thomas Sinclair (Professor of Surgery) (to whom I shall return), Johnston Symington (Professor of Anatomy and Fellow of the Royal Society) and so many others – truly giants of Ulster Medicine.

These giants of Ulster Medicine, who became Presidents of the Ulster Medical Society continued throughout the 20th and 21st century to my predecessor Professor Patrick Johnston (President of the Society 2011-12), recent Dean of Medicine in Queen's University and latterly appointed Vice-Chancellor of Queen's University.

One of the remarkable changes in my 40 years of working in medicine has been imaging in diagnosis in all specialties and, of course, the therapeutic value of radiation in the treatment of our cancer patients. However, radiation – either in its diagnostic or therapeutic use, is not without its sequelae and my journey for my Presidential Address and this paper is "Radiation – Friend or Foe?"

IN THE BEGINNING:-

As I have already alluded, Professor Thomas Sinclair was Professor of Surgery in Queen's College and President of this Society in 1895-1896. Thomas Sinclair succeeded Prof Alexander Gordon to the Chair of Surgery at 27 years of age. He was appointed to the Chair in 1886 and held the Chair for 37 years – a great technical surgeon and superb teacher. He was a surgeon to the British Expeditionary Force in the Great War and was appointed CB. He is remembered for performing the autopsy on Baron Richthofen (The Red Baron)[4,5]. It was said of Sinclair – 'No man has ever stood in higher regard with his professional brethren that Professor Sinclair'[5].

During Sinclair's Presidential year of the Ulster Medical Society a world shattering discovery was made on the evening of Friday 8th November 1895 by Roentgen in Wurzburg.

Wilhelm Conrad Roentgen was born on 27th March 1845 in Lennep in the German Rhineland. As a child he moved to Holland and later was expelled from Utrecht school! He later

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studied mechanical engineering in Zurich and was inspired to follow a career in physics in the University of Wurzburg (Germany) – where (in 1883) he became Professor of Physics. (*fig 1*)

Fig 1. Wilhelm Conrad Roentgen, 1845 – 1923

He noticed late on 8th November 1895 that his 'Crookes tube' caused some adjacent barium platinocyanide crystals to 'light up'. The crystals were lying accidently on the adjacent table. He reasoned the tube was emitting some 'new' ray which produced fluorescence – if a metallic object was placed between the screen of barium platinocyanide and the tube, it cast a shadow. Roentgen is supposed to have said to his friend Boveri – 'I have discovered something interesting …..' He coined the phrase X-ray ('X-strahlem' in German) because the nature of the rays was uncertain.

His first paper on the new X-rays was given to the President of the Physical Medical Society on 28th December 1895. In his paper he showed an X-ray picture (the first) of the bones of the hand. (*fig 2*) The paper was printed immediately and an English translation was published in Nature on 23rd January 1896 and within weeks (long before modern communication) the news spread worldwide. Within a year there were 1000 publications on X-rays[6]. Lord Kelvin wrote a congratulatory letter on 17th January 1896 – in which he wrote 'I was very much astonished'[7]. (*fig 3*)

Roentgen worked on after his discovery – as industrious as ever. Honours were heaped upon him – including the Nobel Prize for Physics in 1901. Following the death of his beloved wife in 1919 he was lonely and unhappy and he died in Munich in 1923 of bowel cancer. His ashes were laid to rest in Giessen.

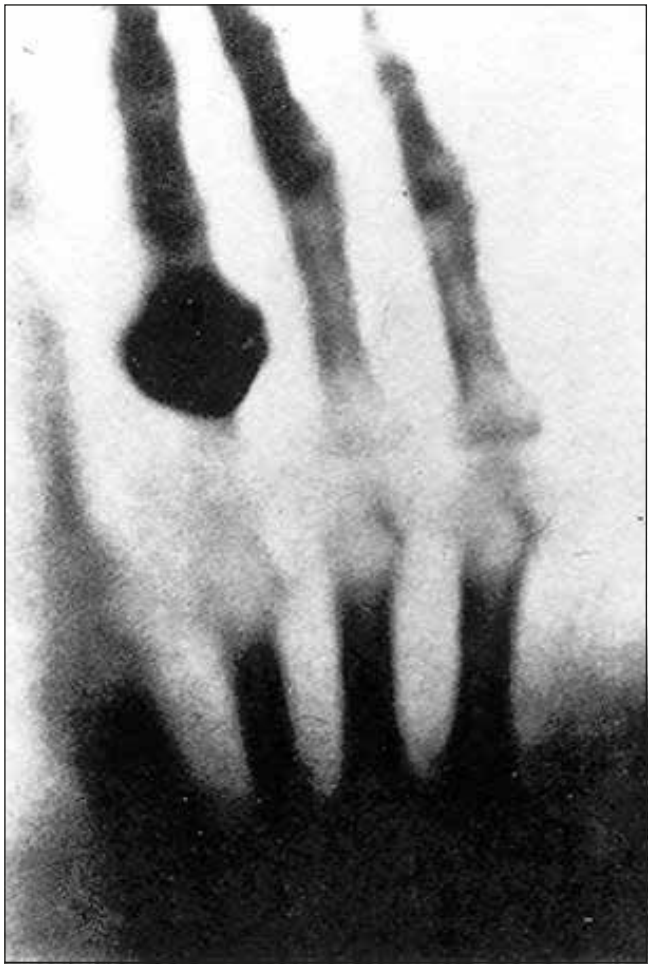


Fig 2. The first X-ray – bones of the hand (possibly Fräulein Roentgen)

His life and work are well reviewed by Mould in 1995[8]. Roentgen was a modest man who shunned publicity – writing only three papers on his remarkable discovery. As with others who have made such discoveries he had his critics – others had made accidental X-ray photographs in the course of research – such as Goodspeed in Philadelphia and Crookes in England (the latter had altered the shape of the cathode ray tube in 1879)[9]. However, neither of these scientists had appreciated the importance of their discoveries[10].

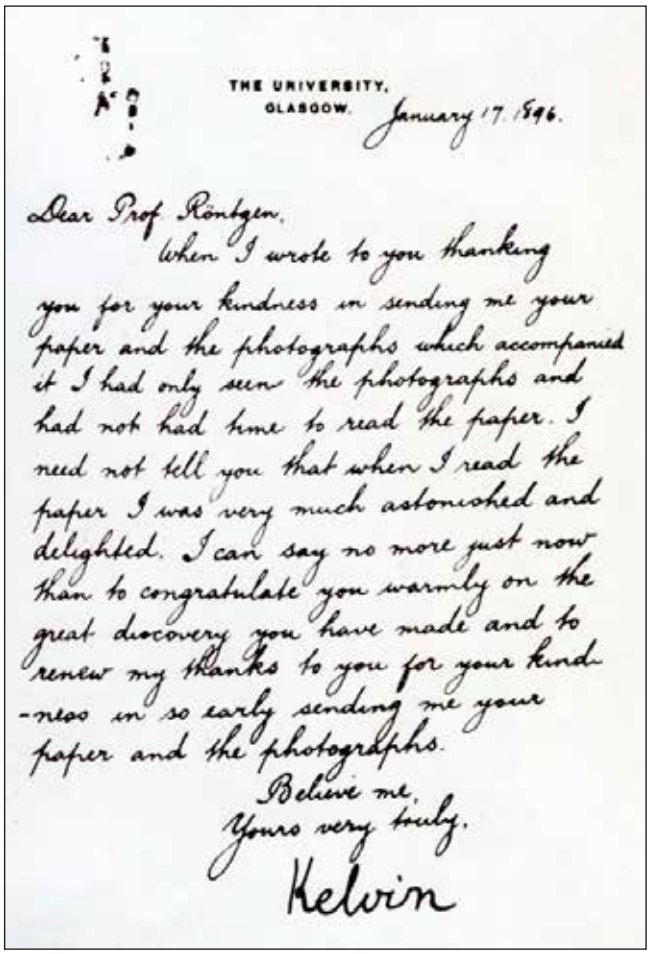
It is remarkable how word spread in the 19th century after Roentgen's discovery – only a day after his announcement Dr JR Ratcliffe in Birmingham, England, X-rayed his hand with a sterilised needle beneath the skin of his palm[9]. A day later a lady with a needle embedded in her hand had an X-ray taken in Queen's Hospital, Birmingham and a surgeon removed the said needle, guided by the radiograph[11].

Remarkably by January 9th 1896 American newspapers published the news of Roentgen's discovery[12]. In February 3rd 1896 a radiograph was taken of the left wrist of a 14

year old boy who had sustained an ulnar fracture[10]. Initially radiographs were used for skeletal abnormalities and location of foreign bodies. The British were the first to use radiographs for war casualties[11].

By 1898 bismuth subnitrate was used to study the gastrointestinal tract of humans[13]. Fluoroscopy, developed in 1896, was used widely in quality control of metal products, detection of fraudulent documents and paintings[11].

The spread of the news of these new 'X-rays' was remarkable. It was first reported in Britain on 6th January 1896 in the Daily Chronicle and the first note in a scientific journal in Britain was in The Electrician of 10th January 1846[14]. The Lancet on 11th January 1896, followed by the British Medical Journal reported the new phenomenon. Robert Jones also reported the use of the new X-ray to locate a bullet in the wrist of a 'lad aged 12 years' – with a 2 hour exposure[14]! There was an explosion of papers in 1896 – 18 published by John McIntyre of Glasgow, including the demonstration of a kidney stone. Over 1000 articles on Roentgen's X-rays were published in 1896. As Posner (1970)[14] has indicated it is difficult to think of any 'event', certainly in medicine which spread throughout the world with such speed until the first heart transplant in 1967 - all the more remarkable for the lack of electronic media which was not widespread until nearly a century later.



THE UNIVERSITY,
GLASGOW. January 17. 1896.

Dear Prof Röntgen,
When I wrote to you thanking you for your kindness in sending me your paper and the photographs which accompanied it I had only seen the photographs and had not had time to read the paper. I need not tell you that when I read the paper I was very much astonished and delighted. I can say no more just now than to congratulate you warmly on the great discovery you have made and to renew my thanks to you for your kindness in so early sending me your paper and the photographs.
Believe me,
Yours very truly,
Kelvin

Fig 3. Congratulatory letter from Lord Kelvin to Roentgen

However, also in 1896, the then President of the British Association for the Advancement of Science, Sir Joseph Lister spoke in Liverpool - his address was "The Interdependence of Science and the Healing Art". Before his address he had his hand X-rayed (photographed). He spoke on Roentgen's Rays and pronounced the following prophetic words "if the skin is long exposed to their action it becomes very much irritated, affected with a sort of aggravated sun burning" – much more was to be revealed as the years followed![14]

In the meantime the use of the new X-rays (Roentgen Rays) became widespread, not only for medical purposes, but also for amusement with mobile apparatus developed for fairgrounds. The apparatus became increasing sophisticated and early protection was developed to protect the users' hands from 'dermatitis' as knowledge of physics grew[7,8]. By May 1896, in New England, Professor Frank Austin used a portable X-ray machine to photograph children's hands for amusement at his daughter's birthday party![15] (*fig 4*)

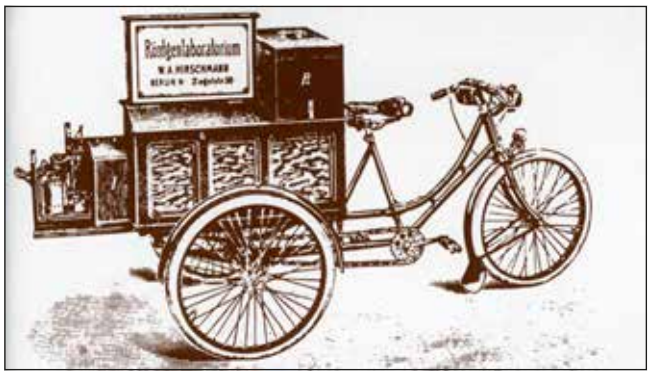


Fig 4. Portable X-ray machine – 19th Century

The spread of the news of Roentgen's Rays reached the USA within days with newspaper accounts[16] and Nature on 23rd January 1896 published a translated copy of his paper[17,18]. On 25th January 1896 Scientific American published a news section 'Professor Roentgen's Wonderful Discovery' with the account having come from Europe by cable. The article contained the sentence 'when the details reach us, the process will probably prove to be of scientific rather than practical interest'[19].

By the end of 1896 Dr James Third in Canada had acquired his own X-ray apparatus for Kingston General Hospital and published in 1902 a comprehensive review of diagnostic uses of X-rays[20]. In May 1896 Dr Williams of Boston had an 'X-ray run' in the basement of the library of Boston City Hospital and during the next 19 years he examined 150,000 patients. By the summer of 1896 X-ray apparatus was installed in several London Hospitals. However, by 1903 use of X-rays had increased and the King had opened a new outpatient department with an 'electrical division' containing X-ray apparatus[21].

The X-ray department was often hidden away in the country hospitals of the time – 'if you look for the darkest, steepest and most awkward stair below ground, you will generally find that it takes you to the X-ray department'[21].

The early years of the 20th century led to increasing understanding of the new X-rays with development of apparatus[22] and the awareness of side effects as we will discuss later. To X-ray a hand for bone – exposure would take initially up to 30 minutes, to X-ray a skull or pelvis may take 2-3 hours of exposure[21].

Barium overtook bismuth in 1910 to demonstrate the gastrointestinal tract (because barium was cheaper); the first radiology journal – Archives of Clinical Skiagraphy – was produced in England, and by 1897 X-rays were admissible as medico-legal evidence.

RADIOGRAPHY IN ULSTER

So how did radiology develop in Ulster? From Roentgen in 1895 discovering the X-ray, winning the Nobel Prize of Physics (1901), to Hounsfield's work on CT computed tomography in the EMI labs at Hounslow[23] (also awarded the Nobel Prize) it has been a remarkable 100 years of X-ray use[24].

So to Ireland and in particular Ulster -

The early national journals of the 20th century were full of discussion of the use of X-rays[25] and likewise the Dublin Journal of Medicine[26]. In the meetings of the Ulster Medical Society in 1912, there were frequent discussions of the use of radiology to solve various clinical difficult cases.

So what of X-rays in Ulster – two excellent reviews by DC Porter in 1962[27] and FS Grebell in 1987[28] tell the story – both published in the Ulster Medical Journal a quarter of a century apart.

Porter (1962) describes the giants who before Roentgen also set the building blocks for this discovery – William Gilbert – physician to Queen Elizabeth in the 16th century – was the father of electric and magnetic science. Galileo in the University of Pisa evolved the principle of the air pump. Sir Humphrey Davy (who devised the miners' safety lamp) used electric current to decompose gases. Humphrey Davy's successor as Professor of Chemistry at the Royal Institution, was Michael Faraday who later discovered electro-magnetic induction[27].

Sir William Crookes in 1870 developed cathode ray tubes and indeed, as alluded earlier, may well have stumbled on X-rays but did not recognise, or publish their nature.

Porter describes the rapid advances in X-rays in medicine in the first 15 years of the new century – highlighting the exposure times – in 1896 a chest X-ray of a girl of 10 years had an exposure time of 30 minutes, a wrist - 20 minutes, hip X-ray exposure of one hour, skull X-ray - 45 minutes – leading to loss of hair in 10 days.

In Ulster – the importance of X-rays was quickly realised on 9th July 1896 (only 6 months after Roentgen's announcement) at a medical staff meeting in the Old Belfast Royal Hospital in Frederick Street. Doctors Mitchell and Caldwell were directed to investigate the apparatus for the new X-rays. The first X-rays (photographs) were taken by John Clarke & Co, then in Corporation Street, who dealt with all cases for £1 per month.

During the first year – 50 radiographs had been produced. The work then passed to Lizars of Wellington Place under the auspices of Mr JC Carson, who also provided in his jaunting car, a domiciliary X-ray service at 10 shillings a time! In 1899 Mr John Campbell Rankin was appointed pupil to the hospital and later physician with an interest in 'electrical medicine' – in diagnosis and treatment, and also in sexual transmitted diseases. He learned 'electrical therapy' in Copenhagen and in 1903 he was appointed 'electrician'. He did many X-rays in his home in Mount Charles and in 1911 had a formal darkroom and new X-ray equipment in the hospital. The work expanded during the war and in 1919 Dr Maitland Beath was assistant to Dr Rankin and became an outstanding radiologist and one of the first Presidents of the Faculty of Radiologists[27].

Dr Grebell (1987) in his address at the Annual Oration to the students at the Royal Victoria Hospital continued the story of development in radiology. Mass tuberculosis screening in the UK using chest radiography was introduced by Bentley and Leitner in 1940[29].

Following the discovery of isotopes (Bequerel, the father of nuclear chemistry – Nobel Prize for Physics in 1903), came Lord Rutherford who discovered γ, and β – particles (Nobel Prize for Chemistry in 1908).

CT was invented by Godfrey Hounsfield in 1972 – and many suggest this is the greatest discovery in radiology since Roentgen's X-rays[28]; Hounsfield received a Knighthood and Nobel Prize for his work. The Royal Victoria Hospital got its first CT scanner in 1977.

The principles of MRI (magnetic resonance imaging) go back to Bloch of Standford and Purcell of Harvard, for which they received the Nobel Prize in 1952. Following the introduction of MRI to the RVH in 1993 – today all major hospitals have multi-slice CT scanners and MRI scanners – all with great ability for diagnostics in a wide variety of patients, in particular in cases of trauma (CT) and cancer (CT and MRI).

ADVERSE EFFECTS OF THE ROENTGEN RAYS

The adverse effects of the Roentgen rays became known quickly – even if the long term consequence was not initially clear. Professor John Daniel of Vanderbilt University wrote in March 1896 of a laboratory incident. In his attempt to X-ray his colleague's skull – he placed the X-ray tube 0.5 inch away from his skull and activated the beam for 1 hour – 3 weeks later the hair came out over a space of 2 inches and 'we were both at a loss to account for it, as we had no previous intimation of any effect whatever', Daniel said[30].

Later in the summer of 1896 Mr Herbert Hawks (Assistant to Dr Michael Pupion of Columbia) was demonstrating X-rays in Bloomingdales store and describes, probably for the first time, the severe 'burn' – 'like bad sunburn' on his hands

which caused him to cease work for 3 weeks[30].

The first fatality due to X-ray exposure may have been Clarence Daly – Chief Assistant to Edison – who had many 'radiation burns' on face, hands and fingers. By 1902 he had developed cancer of the skin – he had amputations of both arms but died in 1904.

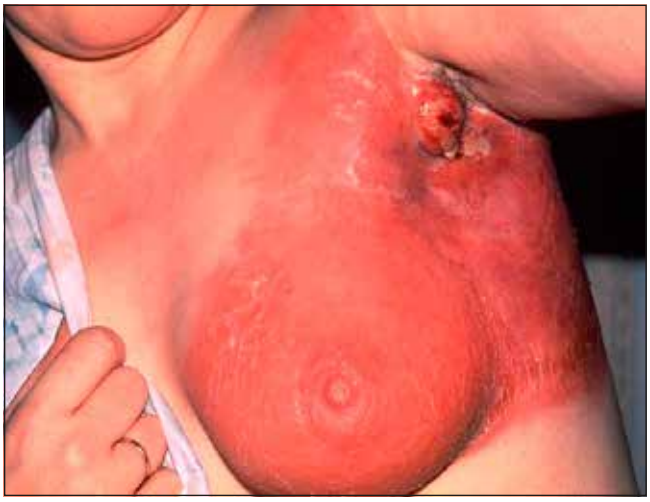


Fig 5. Acute radiation burn – during radiotherapy for breast cancer

Ironically Roentgen constructed a box lined with lead in which he stood when doing his experiments and X-rays only entered through a small aperture. This 'box' was for the purpose of light control and Roentgen's protection from the X-rays was serendipitous – as we have no information that in the early years Roentgen was aware of their carcinogenic potential. In England Dr Hall-Edwards – the physician responsible for the first 'X-ray' photograph in Britain in 1896 later developed cancer of his hands[9].

Later in 1896 the great Sir Joseph Lister postulated 'the transmission of the rays through humans today may not be altogether a matter of indifference to internal organs'[31]. Cancer of the hands was a common adverse effect to the early pioneers[11]. The therapeutic use of X-rays followed quickly from the discovery and a lady with cancer of the breast was treated in 1896[32]. (*fig 5*) Advances followed rapidly – Marie and Pierre Curie identified radium – discovered in 1896 and published in 1898. Eventually Marie was to die from a radiation - induced cancer and yet radiation for cancer was to become a cornerstone of cancer therapies over the ensuing decades. (*fig 6*)

Lentle, the previous Head of Radiology in the University of British Columbia, Vancouver has distinguished the reception of some Victorians to the new X-ray compared to radium discovered only a few years later. The Victorians were apprehensive of the ability of the X-ray to 'see through' the voluminous clothing of the era - an invasion of privacy, discovered by a rather stern man of 'Germanic extraction'. Whereas radium was well accepted as a 'cure all' having been discovered only a few years later by the petite 'feminine' Marie Curie![33] Gradually the early pioneers using radiation in patients realised the harm done could be long lasting.

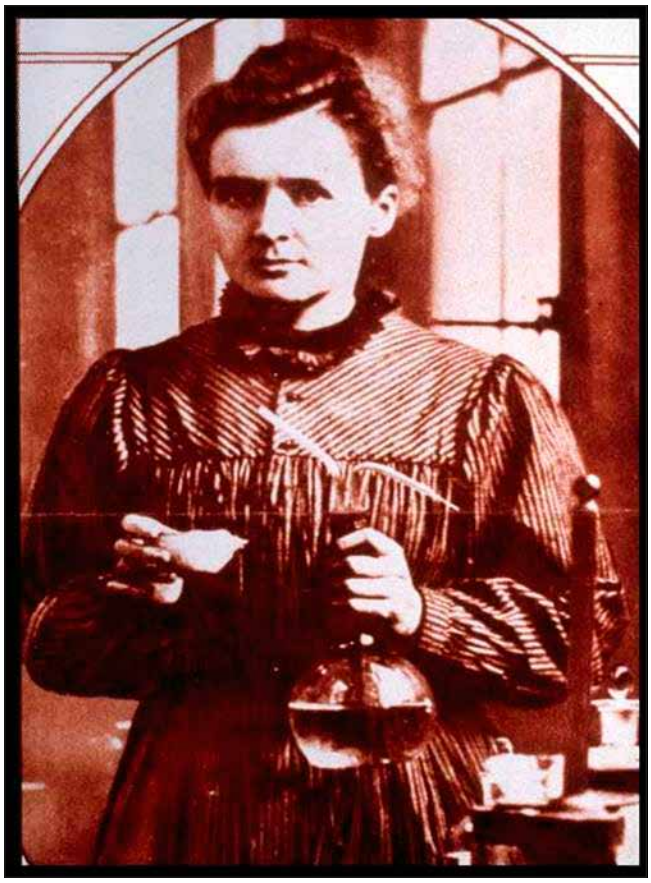


Fig 6. Marie Curie, 1867 – 1934

Dr Walter Cannon, who performed remarkable work on gastrointestinal physiology using radiology, beginning as a medical student in Hanover in 1896, noticed a red rash on his chest and limbs, when he was 59 years of age in 1931 (23 years after he stopped exposure to X-rays). A biopsy in 1932 diagnosed mycosis fungoides[34].

In a well written article DiSantis, in1991, describes the so-called 'wrong turns' in radiology's progress. Despite the early recognition in 1896 of adverse effects of radiology – the lay public would form long lines waiting at public exhibitions for fluoroscopy for amusement[35]. Even Thomas Edison, in 1896, introduced a recreational home fluoroscopy unit – it was Clarence Daly (Edison's Assistant) who became the first American radiological casualty. Training for X-ray physicians was cursory and a study in 1948 showed radiation damage in the hands in 48%[36]. In the USA, in 1920, X-ray units were used in beauty parlours to remove unwanted facial and body hair. (500 rad) (5Gy) for epilation. Perhaps 1000s of women developed skin cancer as a consequence. In the 1950s, in the USA, shops used fluoroscopy as part of shoe fitting- often in children with inadequate shielding with scattered rays affecting children (as high as the pelvis), the assistants and other customers.

Marie Curie's discovery of radium in 1898 sparked 'ray mania' - this new mysterious element discovered by a woman! The new element was incorporated into everything from chocolate to contraceptive jelly – it was perceived as a

panacea! The journal 'Radium' declared in 1916 – 'radium has no toxic effects! It was perceived as a cure of every disease, by 1904, including 'health giving' water impregnated by radium, radium toothpaste, radium roulette, radioactive china and radium beverages were fashionable in the 1920s. Radium paint, which fluoresced, was everywhere! However, the same workers who painted radium paint developed a mysterious and profound anaemia and osteonecrosis. To 'point' their brushes they used their tongues and they could light a fluorescent screen with their breath! Their deaths mounted and the first 'shadow' appeared on the new radium 'cure all'![35] Marie Curie, herself died from radiation induced aplastic anaemia.

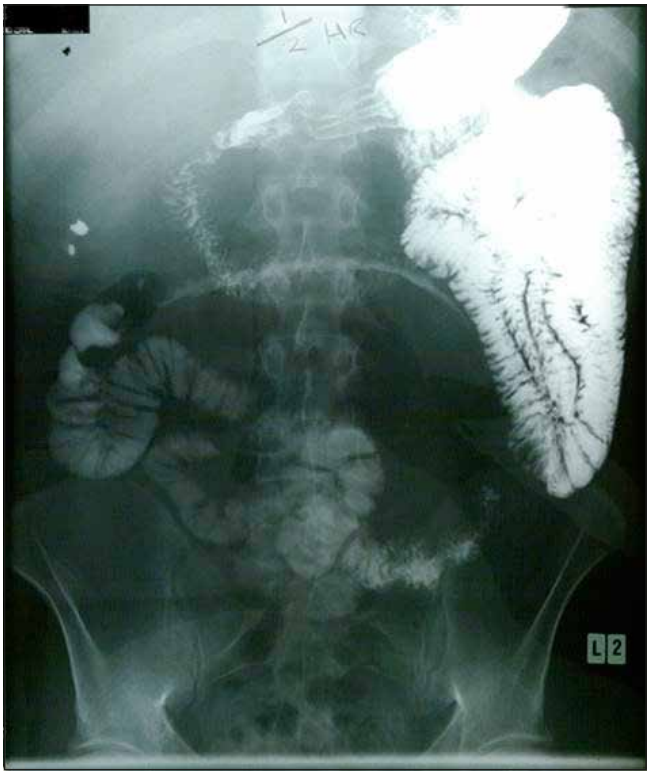


Fig 7. Radiation stricture to small bowel

The American physicist, Thorson, first found the direct relationship between exposure to X-rays and side effects – he deliberately exposed his left index finger to an X-ray tube for 30 minutes per day, for 3 days, developing swelling, erythema and pain[37]. Rollins in 1901 reported radiation could kill animals on prolonged exposure and advised X-ray users to wear radio-opaque glasses[38]. Rollins was the true pioneer in radiation protection[39] but it was not until 1921 that the British X-ray and Radium Protection Committee (1921) issued their report on radiation protection measures[40]. In the USA the United States Advisory Committee on X-ray and Radium Protection came into being in 1929[41] and, henceforth, protection measures became rigorous in, at least, the developed world.

THERAPEUTIC USE OF RADIATION

Marie Curie discovered and reported radioactivity of polonium in July 1898 and radium in December 1898[42,43] and the use of radium seeds and rod implants were greatly advanced by Patterson and Parker at the Christie hospital in Manchester[44]. Over the subsequent decades a large number of radionuclides were used for brachytherapy[45], the delivery of which optimised since the development of sophisticated computers in the 1970s.

External radiation was developed in the two decades before World War II and the earliest super-voltage unit (IMV) was placed in St Bart's Hospital London in 1937. The first medical accelerator (8MV) was installed in Hammersmith Hospital, in London in 1953. A quarter of a century later multi-dimensional computerised 3D planning was described in 1979[46].

With these, and other advances in radiation therapy it is now estimated that two-thirds of the 1.5 million new cancer cases diagnosed annually in USA – will undergo some form of radiation therapy[47]. Despite careful planning, including the use of radio-sensitisers, radio-protectants, non-cancerous cells are affected resulting in many clinical side effects – from fatigue, and depression[48], to secondary malignancy such as breast cancer in women who have had mantle radiotherapy for lymphoma when young[49].

The side effects are both early and late and can affect all major systems *(fig 7)* – from skin - dermatitis, radiation recall[50], cardiovascular disease after radiation for lymphoma[49,51], pneumonitis[52] mucositis, oesophagitis[53] enteritis[54], proctitis[55], cystitis[56], erectile dysfunction[57], and infertility[58].

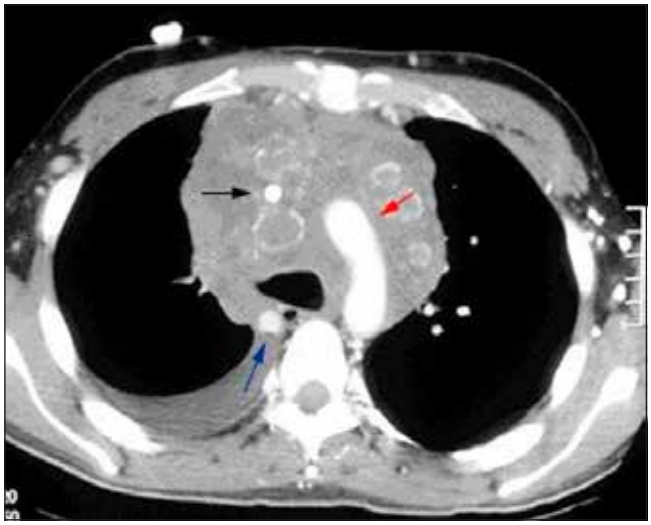


Fig 8. Hodgkin's disease requiring mantle radiotherapy

Most of these side effects are well recognised by physician and patient and for some complications, such as breast cancer after radiotherapy for Hodgkin's disease have guidelines for surveillance. (*fig 8*)

These adverse effects of radiation may lead to problems distinguishing side effects from recurrence or de novo cancer[59] but undoubtedly radiation therapy has produced improvement in survival in many cancers over recent years[60]. The mechanism of damage to cancer cells (and normal cells) is increasingly well defined with breaks in the DNA double

helix being the main method of cell damage[61]. While the management of the adverse effects of radiation therapy is not ideal, many treatment strategies are in practice[62].

Therefore, with the huge amount of literature both published and on the internet including the standard oncology text books such as DeVita[63] , there is great awareness in the public, the press and medical profession of the benefits and side effects of radiation therapy in the 21st century.

DIAGNOSTIC RADIOLOGY IN THE 21ST CENTURY – CT SCANNING - ? A PANACEA

Let us now turn to the remarkable changes in diagnostic imaging especially that of CT – with the huge benefits in non-operative management of trauma eg the conservative management of gunshot wounds, liver and splenic injuries including the use of CT in endovascular aneurysm repair and follow-up –as we now approach 120 years since Roentgen's remarkable discovery.

CT scanning is a remarkable advance for diagnosis - it has huge value in the assessment of medical and surgical patients; diagnosis of a myriad of conditions especially trauma and cancer and follow up after treatment of such patients. (*Fig 9*)

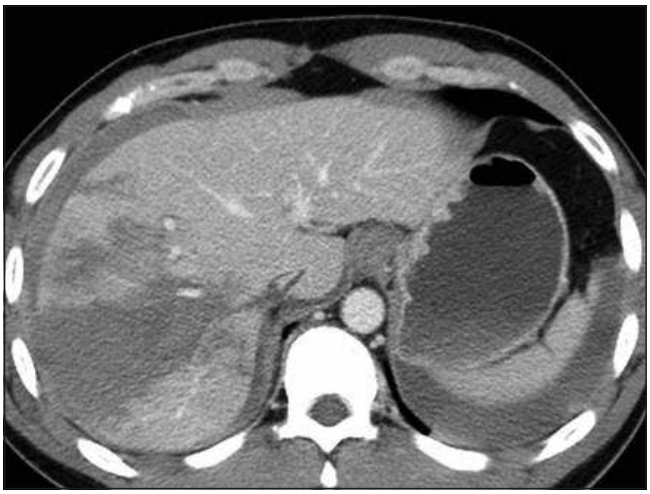


Fig 9. CT scan of liver trauma (reproduced with kind permission of Dr Barry Kelly)

In many surgical and medical emergencies CT scanning is invaluable as evidenced by any recent text book on surgical emergencies[64]. It is central to the conservative management of splenic trauma[65] and the recent suggestion of the non-operative management of gunshot wounds[66]. *But has the pendulum of imaging, particularly CT scanning swung too far to the detriment of clinical acumen? Has a fear of litigation pushed the clinician to over-investigate with imaging, especially CT?*

A Dutch paper in 2014 looked at the role of CT and MRI in the differentiation of simple appendicitis and perforated appendicitis![67] (*fig 10*) Furthermore, the quality of modern CT scanning picks up incidental lesions such as adrenal nodules and small pulmonary nodules – previously undetected in patients free from symptoms. Since the development and widespread use of helical CT in the 1990s; the detection of lung nodules as small as 1-2mm in diameter is common. It is now recognised that the majority of smokers undergoing thin section CT have small (usually <7mm) lung nodules – the majority of which are benign[68,69]. (*fig 11*) They have been increasingly found in studies of CT screening for lung cancer[70].

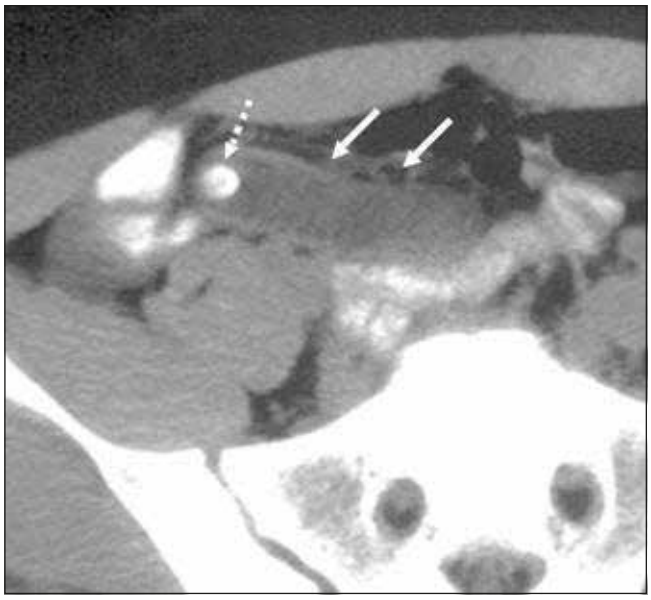


Fig 10. CT scan of acute appendicitis (reproduced with kind permission of Mr Stephen Badger)

The current guidelines in the literature are from the Fleischner Society and follow up depends on the size of the nodule and whether the patient is high or low risk. Unless the nodule is less than 4mm in size, in a low risk patient then all require CT follow-up – for example a nodule over 8mm would need repeat CT at 3, 6, 9 and 24 months[68].

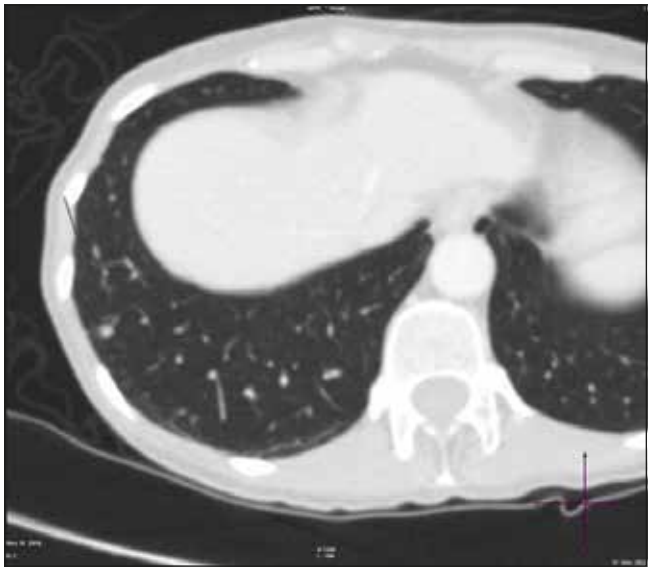


Fig 11. CT scan of an incidental benign lung nodule (reproduced with kind permission of Dr Barry Kelly)

While the benefit of such follow-up is that a small number will be early cancers, the majority are benign – and the

'downside' of this approach includes the possibility of morbidity/mortality for surgery for benign nodules, costs, patient anxiety and increased radiation to patients having repeated CT scans[71].

Such nodules are exceptionally common in CT lung cancer screening trials. The Mayo Clinic Lung Cancer Screening Trial was reported by Swensen in 2003[72] - After 3 annual CT scans in 1520 smokers (>50 years old) -at 2 years 2832 non-calcified pulmonary nodules were identified in 1049 subjects (69% of participants), 36 lung cancers were diagnosed by CT (2.6% of participants, 1% of nodules). Only one cancer was diagnosed in a nodule smaller than 5mm. Midthun has calculated that less than 1% of nodules less than 5mm were malignant. Cancer risk in a nodule <3mm was 0.2%; 0.9% for 4-7mm; 18% for 8-20mm, and 50% for nodules larger than 20mm[73].

With the current risk of malpractice in UK and USA it is difficult for the radiologist and clinician not to follow-up, as per these guidelines, these small indeterminate nodules – even though the risk for malignancy for the very small nodule is small[74] ~ nonetheless most of these patients are subjected to a series of at least three CT scans over a period of 24 months with the ensuing radiation dose and possible consequences. However, to improve lung cancer survival early diagnosis is essential[75] and we await the outcome of national lung cancer screening trials.

Lung cancer CT screening has been well reviewed by Bach and colleagues who have reviewed 8 randomised trials and 13 cohort studies[76]. The most impressive results come from the National Lung Screening Trial (53,454 participants), with 3 annual rounds of CT screening – resulted in a 20% relative decrease in deaths from lung cancer[77] but data from other studies were less clear[76].

RADIATION EXPOSURE IN PRACTICE

The overview paper described the radiation dangers of these repeated CT exposures in lung cancer trials[76]. The effective radiation dose in one of the trials was calculated to be 1.5 mSv per examination compared to a diagnostic CT of chest (8mSv)[78] or 14mSv in PET – CT scan[77]. The effective dose of radiation in a chest X-ray is 0.02mSv and a diagnostic CT of chest is equivalent to 400 chest X-rays. There are now clear data on the cancer risks of radiation based on medical imaging and the atomic bomb explosions[79,80,81].

Modelling predicts that in lung cancer screening cancer death is caused by radiation from CT per 2550 persons screened[76]. This risk becomes manifest 10-20 years later. For older patients the benefit of lung cancer screening may lie with those screened and found to have early cancer, but it is questionable for younger persons – ie the potential risks of lung cancer CT screening in non-smokers and those aged under 42 years outweighs any benefit[82]. In recent years the issue of the investigations of the solitary lung nodule, even outwith the context of lung cancer screening trials, has concerned the literature of the impact of radiation from CT in diagnosis and follow-up[83]. At the moment the Fleischner Society guidelines with subsequent (usually up to 3) sequential CTs are used as practical guidance[68,84]. A good editorial by O'Connor and Hatabu has again emphasised the risks of CT radiation – cancer induction in lung cancer screening[85].

CT SCANNING AND CANCER

A major study (from 15 countries) has shown that somewhere between 0.6% to 3.2% of cancers below age 75 years may be attributable to diagnostic imaging, especially CT[86]. There has been a huge increase in the use of CT in UK, Europe and USA. In a study of USA HMO's; the use of CT increased from 52 per 1000 clients in 1996 to 119 per 1000 in 2010 – an annual increase of 8% - leading to a doubling of the mean per capita radiation in each year[87].

Brenner has studied radiation risks associated with full body CT screening[88]. Especially in USA, there is interest in full body CT screening for healthy adults[89], with uncertain benefit[90,91] Brenner has calculated radiation doses in full body CT scanning includes 16mGy to lung, 14mGy to digestive organs and 10mGy to bone marrow. The average organ dose is 12 mSv[88]. To put these figures in perspective we need to look at studies of long term atomic bomb survivors[92,93]. Those survivors who were exposed to a dose from 5 to100mSv (mean 29mSv) had a significant increase of cancer risk. Even a dose of radiation exposure as low as 5-50mSv has a small increased cancer mortality risk. Brenner has calculated that a single full body CT scan in a 45 year old adult would result in a lifetime cancer mortality risk of 0.08% - if the 45 year old continued annual CT full body scans until age 75 years these 30 CTs would produce a 1.9% life-time cancer mortality risk[88]. CT full body screening in the USA has increased in popularity (less so in UK) to detect lung cancer, coronary artery disease and colon cancer[94], - nonetheless our patients should be advised of the radiation exposure and subsequent cancer risk?

The comprehensive Lancet paper of De Gonzalez from a decade ago looking at 15 countries (including UK) estimated cumulative cancer risk due to diagnostic X-rays[88]. Previously, in 1981, Doll and Peto, in1981 estimated that 0.5% of cancer deaths in the USA were due to diagnostic radiology[95]. The Lancet study (2004) estimated in the UK 0.6% of the cumulative cancer risk to age 75 years to be due to diagnostic radiation. In the UK this would be equivalent to 700 cases per year. In another 13 countries the risk was 0.6% to 1.8% - such as Australia (1.3%), Canada (1.1%), USA (0.9%), Norway (1.2%); in Japan the risk was 3.2%[88].

In men bladder cancer, colon cancer and leukaemia were the highest number of radiation induced cancers and in females colon, lung and breast cancers made the major contribution. Most cases arose after age 40 years (56% of cases occurred between 65-74 years of age). Of the diagnostic X-rays the largest number of cases were caused by CT, followed by barium enemas, hip and pelvis X-rays. Current evidence is that there is no lower threshold below which radiation does

not cause cancer[96]. Brenner has estimated that the cumulative risk of cancer mortality for CT in USA is 800 radiation - induced cancers in children under age 15 years[97].

A recent study from Australia looked specifically at CT scans in children and adolescents up to age 19 years. 680,211 patients who had a CT scan were studied and compared in a linkage study to 11 million unexposed individuals. Overall cancer incidence was 24% higher for exposed, compared to unexposed, individuals. There was a dose response association with each additional CT scan[98].

A measured editorial in the British Medical Journal in 2013, which accompanied this article put this in the context of numbers ie one excess cancer per 4000 head CTs at the modern CT dose of 2mSv[99]. Sodickson emphasises a balanced measured approach to the need of CT scans and risk benefit in a context where CT is indispensable in trauma, cancer diagnosis and follow up[99].

ENDOVASCULAR TECHNIQUES – RADIATION RISK

Since the publication of the EVAR I & II trials in the Lancet in 2005[100,101] and The Dream Group publication in The New England Journal of Medicine in 2004[102], and the subsequent longer term data published in 2010 by the EVAR Group[103,104], endovascular stenting for aortic aneurysm has become widely used. (*fig 12*)

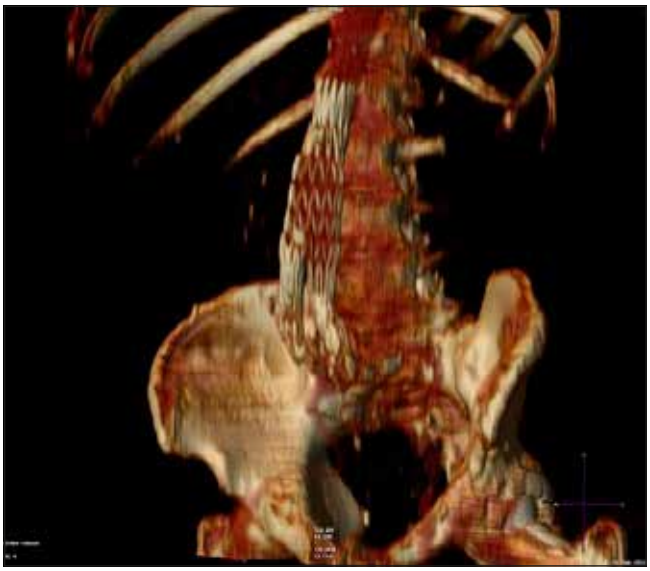


Fig 12. CT scan with endovascular stent in situ (reproduced with kind permission of Mr Stephen Badger)

Preoperative CT is essential for the placement of the stent, to determine the vascular anatomy[105]. After the procedure stenting CT was performed, in earlier series, at 1, 3 and 12 months postoperatively and annually thereafter (EVAR I, II, 2005). The patient is, therefore, exposed to significant CT radiation[106]. One series from Belfast of 320 elective patients undergoing EVAR found a mean screening time of 29.4 mins ± 23.3 minutes and a radiation dose during the procedure of 13.4 ± 8.6 mSv. During the first postoperative year follow-up CT scans exposed the patients to 24.0mSv, and then 8.0mSv in subsequent years. Abdominal X-rays added a further 1.8mSv per year. This adds up to substantial radiation with subsequent long term carcinogenic risks[107]. (*fig 13*) Of course many of these patients are elderly, but younger patients with aortic aneurysm are not uncommon and this radiation dose may be clinically relevant in these patients in years to come. The dose of radiation during EVAR procedures may be close to that during coronary angiography which is highest of all (16.0mSv – equivalent to 800 chest X-rays[108]. (*fig 14*)

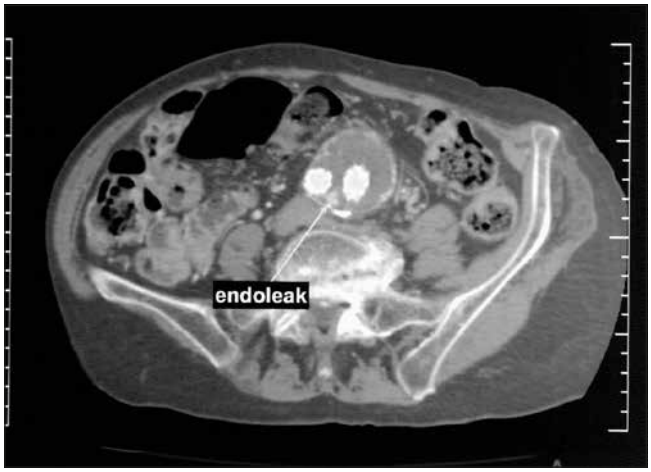


Fig 13. Scan showing endoleak post EVAR detected at follow-up CT (reproduced with kind permission of Mr Stephen Badger)

Similar data have been shown in USA[109] and Europe[110]. In an effort to decrease this CT radiation load recent data from the USA and Europe have indicated that the frequency of postoperative CT may be reduced[111] and some imaging may be replaced with ultrasound[112]. Similar data using colour Doppler duplex ultrasound are now emerging from UK[113,114] and Europe[115]. Clearly radiation exposure to the surgeons

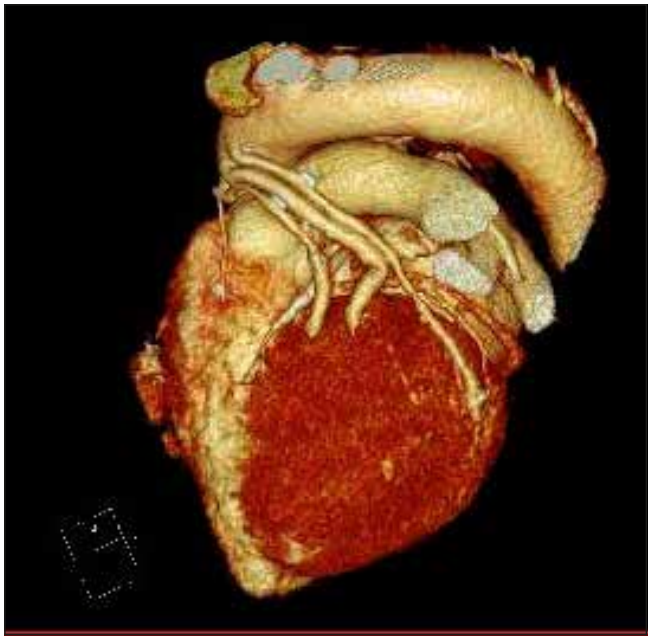


Fig 14. CT coronary angiogram (of the author!) following cardiac bypass

and radiologists performing EVAR procedures need careful monitoring[116].

THE FUTURE

The growth in radiological skill and advances in technology are remarkable from my early days as a student of medicine in 1971. Undoubtedly the advances from the discovery of X-rays by Roentgen in 1895 over the past centuary have had massive benefits for patients both as a diagnostic and therapeutic tool.

The demand for imaging and CT, in particular, has increased exponentially as a diagnostic tool in trauma and cancer, as a follow-up to gauge response in many diseases, but especially in cancer. It has a major role in endovascular procedures and may have a future role in cancer screening such as lung.

However, while the risks of radiation have been known for over a century and, of course, are well known to radiologists it is only recently that clinicians, the press and patients are becoming more aware. Even so the knowledge of clinicians and patients of the risks of imaging are not known in any depth. Only interventional radiological procedures require a consent form to be signed and routine CT does **not** require written consent. Only in the past decade have the cancer risks of CT been discussed widely in the general literature[71,88,98,108]. In 30 years there has been a 20 fold increase in CT scans in USA annually, in the UK similarly CT numbers have doubled in the last decade[108].

Only recently has Queen's University taught radiology as a formal subject in 4th year and few of today's clinicians really understand the various units used in radiation exposure in imaging. The biological effect is best measure in millisiverts (mSv) (the product of the absorbed dose (Grays, Gy) and a quality factor (Q) (which depends on the organ irradiated, the radiation type and regime).

However, in discussion with our patients, students and other clinicians, perhaps the equivalent radiation of an investigation such as CT, is best explained in terms of numbers of chest X-rays. This may be the best communication for comparison (and easiest to understand for patient and clinician) (eg CT chest = 350 chest X-rays, CT abdomen = 400 chest X-rays), CT coronary angiogram = 800 chest X-rays - as well laid out in Davies 2011, British Medical Journal article[108]. The annual background radiation (such as radon) gives each person 2.4mSv exposure per year.

While carcinogenic effects are the major radiation concern[82], other effects include disabilities in children of mothers exposed to radiation in pregnancy, cataracts, skin damage and increased cardiovascular disease. In the USA 6-11% of all CT scans are performed in children and it remains to be seen, with the prolonged lag phase, what future numbers of radiation - induced cancers will emerge[78].

Patients already have IPAD 'apps' to calculate radiation doses of their investigations[108]. In the UK there is reasonable adherence to College of Radiologists Guidance (2007) for investigation, for example head injury scans are guided by NICE guidelines. Recent debate centres around – 'what should patients be told'[108,118]. Informed consent is not required in the UK for routine imaging, outwith interventional radiology, but should patients be told of the potential benefits of a particular scan (versus adverse effects). Patients who request 'full body CT scans' – for a check-up (more common in USA) should be advised of its limited benefit and that the finding of incidental nodules such as in adrenal or lung in the long term – will usually lead to repeat CT scans. Those patients entering lung cancer screening trials will need detailed counselling, about possible adverse effects.

The risk of any one CT scan in an adult is low but those needing repeat CT for cancer (usually benefits exceed the risks) or after endovascular surgery (less frequent CT may now be appropriate) need more detailed advice/counselling. Risks need to be put into lay man's terms for example – the additional risk of death from cancer is 'minimal' at a dose of 1mSv – (X-ray abdomen), 'very low' – 10mSv – CT brain/chest/abdomen; over >100mSv – risk is 'moderate' ie repeat CT scans.

Minimal risk is 10^{-5}, very low risk is 10^{-4} and moderate risk is 10^{-2}. To help explain in lay terms - risk of death during a flight of 4500 miles is 'minimal', risk of death in a car accident in a drive of 2000 miles is in the 'very low' category[118].

For those children/adolescents having repeated CT scans for lymphoma/leukaemia follow-up records (dose/frequency) should be meticulous. The recent literature has revealed an increasing interest and understanding of radiation risk of imaging especially in paediatrics[119].

In the future patients may keep their own radiological imaging history on a smart phone!

CONCLUSION

It is well over a century since Roentgen discovered X-rays and the remarkable advances since 1895 are incredible. Without doubt of all the advances in medicine it must rate at the top, alongside the discovery of antibiotics and anaesthesia.

Notwithstanding the consequence of the atomic bomb, in Japan, and the disaster of Chernobyl (1986)[120] and Fukushima (2011)[121] (*fig 15*) overall radiation has been mostly a 'friend' as opposed to a 'foe'. However, with the advances in imaging and CT in particular, and the exponential increase in use, we must remain conscious of the possible long term adverse effects such as cancer. Maybe we are now at the stage of better information for patients (with modern technology – such as smart phones) and clinicians.

I applaud the early pioneers from Roentgen in 1895 (by all accounts a quiet modest man), I remain amazed at the spread of knowledge of his discovery being known worldwide within days, long before modern media.

Finally, I stand in awe of my colleagues in radiology who have transformed the care of our patients, preventing us

doing unnecessary surgery in our cancer patients, and their remarkable diagnostic accuracy in trauma and cancer. I remain in huge respect of my colleagues in interventional radiology, with their catheters embolising even tiny vessels in the cerebral circulation and dealing so well with the 'bleeding patient' who nowadays, much less frequently requires surgery.

Fig 15. Chernobyl, 1986

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