

## Chapter 2

# Radiation Oncology and the MGH 1896–1945

### 2.1 The Almost Instantaneous Acceptance of X-Rays into Medicine

Radiology literally erupted onto the medical and scientific community following publication of the paper by Wilhelm Conrad Röntgen on December 28, 1895, describing the discovery of new rays. The immediacy of the impact on the world was strikingly evident by the speed with which physics laboratories, hospitals, and clinics began assembling equipment. Within a year there was a substantial and positive experience using radiographs for diagnosis and a beginning of testing of their very low kVp beams as treatment for superficial lesions. Reflecting the literally fantastic excitement in medicine and physics generated by Röntgen's paper were the >1000 scientific papers and ~50 books during 1896 on the new rays [6].

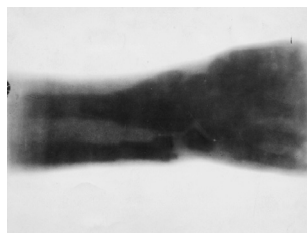
The first documented medical use of x-rays in the USA was that by Edwin Frost, an Assistant Professor of Physics at Dartmouth College on February 3, 1896, and reported in *Science* on February 14, 1896 [10]. This article did not include a medical radiograph. The patient was provided by Frost's brother, a Professor of Medicine at the medical school. The patient, a young man, was proven by this x-ray to have a Colles' fracture of the left ulna as presented in Fig. 2.1 [19]. That February 14 issue of *Science* had several articles on these rays, including a 5-page article by W. Röntgen.

Francis Williams, a physician of Boston City Hospital, began to investigate the potential of the new x-ray images concurrently. For his initial studies, he took patients for

imaging studies to the physics laboratory of R. Lawrence and C. Norton at MIT. A radiograph of the hand demonstrating "anomalies of the phalanges" was published on February 20, 1896, in the *Boston Medical and Surgical Journal*<sup>1</sup> [44]. MGH began use of x-rays in March 1896 along with large numbers of American and European hospitals [11].

That the new rays could injure normal tissues became quite clear within a month of the Röntgen discovery. Perhaps the earliest instance of radiation injury to human tissues was that of Emil Grubbe, an electrical engineer [7, 11]. He was examined at the Hahnemann Medical College of Chicago by three physicians for a "suppurating erythema" of the left hand on January 27, 1896, viz., 1 month after Röntgen's paper was published. He reportedly had tested his x-ray beam by examining the image of his hand multiple times per day. At that visit, the physicians suggested that the radiations might be effective therapeutically. One day later, Grubbe was referred a patient with post-surgical recurrent breast cancer whom he claimed to have treated. He was evidently among the first to employ radiation therapeutically for malignant disease. There has been no published description of the result. Grubbe sustained grievous radiation injuries, some requiring surgery. Elihu Thomson published in *Electrical Engineer*, New York on March 4, 1896 [38], a warning of the potential of injurious effects of these new rays and described protection by enclosing the machine head in a box with only a small aperture for the beam.

The number of severe skin reactions being reported was accepted as proof of a biological effect of these new rays and indicated a potential for these new rays in the treatment of one or more human diseases. Actually, the new rays



**Fig. 2.1** Perhaps the first medical x-ray taken in the USA (February 3, 1896). This demonstrated a Colles' fracture [19]. With permission

<sup>1</sup> This article did not give the author but did state that the picture "is taken from a patient at Boston City Hospital, by the kind co-operation of the Department of Physics at the Massachusetts Institute of Technology with gentlemen connected with the hospital." Williams was a physician at Boston City Hospital, a graduate of MIT, had connections with the physicists, and almost immediately became a specialist in this emerging specialty.

were rapidly being assessed for therapeutic efficacy against virtually the entire spectrum of diseases. Note that the basic nature of most diseases was unknown, the efficacy of available remedies low, and the biological action of the rays on tissues quite unstudied. Hence, a major medical “fishing expedition” ensued.

Although the name of the person(s) who first used radiation with therapeutic intent is not certain, there is clarity of the essentially immediate acceptance of a therapeutic potential of the new x-rays.

The leading academic radiologist in Boston in 1900 was Francis Williams [7], a graduate of MIT (chemistry) and then Harvard Medical School (HMS), in 1877. This was followed by 2 years in Vienna and Paris. Upon return, he practiced medicine at Boston City Hospital. In 1884, Williams was appointed to the faculty of HMS. Williams maintained his connections at MIT. As noted above he was among the first to employ x-rays for medical imaging. Williams was a friend of Elihu Thomson and was rare among radiologists at that time in his acceptance of Thomson’s warning, viz., he enclosed his x-ray tubes in lead-lined boxes with only a small aperture. We have no information as to why this simple method was not implemented at MGH. Of interest is that Williams employed fluoroscopy extensively and lived to the age of 84 years. No injurious effect of his radiation exposure is mentioned in the accounts of Williams reviewed.

In 1901, Williams published a landmark book in radiology: *The Röntgen Rays in Medicine and Surgery* [45]. This most impressive book has 658 pages and 390 figures, principally of radiographic images. William’s book has been reprinted in a special edition in 1988 by the Classics of Medicine Library and a photograph of the book is in Fig. 2.2.

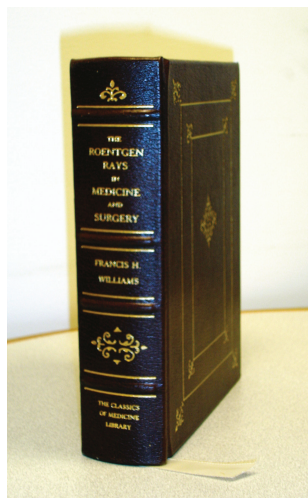
The book opens with 58 pages on technical aspects of radiology. There are 63 pages on radiation therapy, with 22

patient photographs. Williams employed tin foil or white lead painted masks to achieve shaped treatment fields and thereby reduce dose to normal tissues.

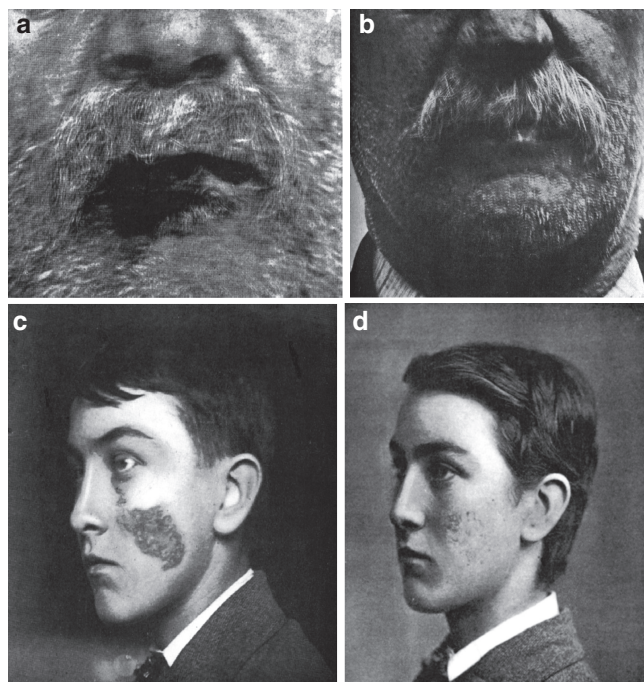
The industry, organizational skills, and efficiency to collect and organize this vast quantity of material, write the text, *sans* computer, submit for publication, and have the book on sale within 6 years of the discovery of Röntgen must be rated as most exceptional. This book is recommended for those interested in the start of radiology by a fine clinician and serious scholar.

Photographs of complete response of a patient with a squamous cell carcinoma of the lip is presented in Fig. 2.3a, b. Quite unrelated to present-day medicine, patients were treated by radiation for lupus vulgaris (TB of the skin). Evidently, complete responses were not uncommon. Figure 2.3c, d illustrates such a patient, from William’s book [45]. The response was almost certainly not the consequence of bactericidal action of the low dose of radiation. Similar results on lupus patients at many clinics served as a stimulus for radiation treatment of patients with pulmonary TB, but evidently not at Boston City Hospital. The treatment was not effective against the pulmonary disease.

As evidence of the tendency to try radiation as treatment for nearly all diseases, examine Fig. 2.4, a photograph of patients treated for epilepsy in 1904 at the Philadelphia Hospital [11] by irradiation of the head. The one clear effect was epilation.



**Fig. 2.2** *Röntgen Rays in Medicine and Surgery* by F. Williams published in 1901 [45]



**Fig. 2.3** (a, b) Squamous cell carcinoma of lip before and following x-ray therapy. (c, d) Lupus vulgaris of the cheek in a young man before and following x-ray treatment [45]. With permission



**Fig. 2.4** Epilation after irradiation of the scalp for epilepsy at the Philadelphia Hospital, 1904 [11]. With permission

## 2.2 The First Experiment in Radiation Biology. *Lancet*. 22, 1896

Grover Lyon suggested that Röntgen rays might have therapeutic use against bacteria in a brief note in *Lancet* of February 1, 1896 [22]. In the February 22 issue of *Lancet* [23], he reported negative results for irradiation of an “impure culture of diphtheritic bacilli” in a test tube at  $35^\circ$  for 12 h. He observed that “considerable growth took place during these 12 hours.” “A pure cultivation of tubercle bacilli exposed at the same time showed a vigorous power of growth afterwards.” He concluded “experiments like these are not, of course final. Increased knowledge and improved apparatus may place the cure of disease by radiant energy within the possibility of the future.” He was referring to bacterial infections. The x-rays were almost certainly of low energy and delivered at a low dose rate to bacteria in a test tube. Estimation of the dose delivered is not feasible due to absence of technical details of the radiation generator, the test tube wall thickness, target test tube distance, etc. Surely the doses were far less than that required to sterilize a test tube loaded with bacteria. At present, ionizing radiations are used extensively in industry to sterilize food and many items. In this department, all of the feed for our mouse colony comes as radiation sterilized by a single dose of 35,000 Gy.

Lyon was a Senior Assistant Physician at the Victoria Park Chest Hospital, London. The alacrity with which he acted after reading of a quite different radiation, planned and performed an experiment, analyzed results, wrote and submitted a paper, and had it published in *Lancet* in less than 8 weeks is clearly impressive.

## 2.3 Advances in Physics, 1895–1900

A fascinating aspect of the manifestly impressive record of multiple and significant advances in physics during the 19th

century is the conclusion by a few very highly regarded physicists that there was little to no prospect for further advances. As an example of such a negative opinion for the future of physics, in 1900 Lord Kelvin, perhaps the most highly regarded physicist at the close of the 19th century, is quoted by multiple sources as stating to a meeting of the British Association for the Advancement of Science: “There is nothing new to be discovered in physics now. All that remains is more and more precise measurement”<sup>2</sup> [39]. This was not a unique view of the future of physics at that time, see the footnote.<sup>3</sup> Even at present, not dissimilar views are articulated by prominent science writers, e.g., Horgan in his book *The End of Science* of 1996. [16]

With significant discoveries popping up at an incredible frequency, pessimism of any physicist is not easily comprehended.

1895: Röntgen discovered x-rays.

1895: Perrin found that cathode rays are negative particles.

1896: Becquerel discovered natural radioactivity in uranium ore.

1897: J.J. Thomson discovered electrons, the first subatomic particle demonstrated.

<sup>2</sup> We found no published statement by Kelvin to this effect.

<sup>3</sup> Albert A. Michelson, in his speech at the dedication of Ryerson Physics Lab, U. of Chicago, 1894, is quoted as saying “The more important fundamental laws and facts of physical science have all been discovered, and these are now so firmly established that the possibility of their ever being supplanted in consequence of new discoveries is exceedingly remote.... Our future discoveries must be looked for in the sixth place of decimals” [27]. Max Planck commented in a 1924 speech: “When I began my physical studies [in Munich in 1874] and sought advice from my venerable teacher Philipp von Jolly... he portrayed to me physics as a highly developed, almost fully matured science... Possibly in one or another nook there would perhaps be a dust particle or a small bubble to be examined and classified, but the system as a whole stood there fairly secured, and theoretical physics approached visibly that degree of perfection which, for example, geometry has had already for centuries” [30].



- 1898: Marconi achieved transmission of signals across the English Channel.
- 1898: The Curies discovered radium and polonium.
- 1898 Rutherford discovered  $\alpha$ - and  $\beta$ -radiation.
- 1900: Planck formulated Planck's constant.
- 1900: Villard discovered  $\gamma$ -rays.

Thus, from December 1895 through 1900, x-rays, the electron, alpha, beta, and gamma rays were discovered [33]. This had to be, without equivocation, quite a remarkable 5 years for physics. The ease of separating these radiations by a magnetic field was an important tool in the discovery of these particles and is illustrated in Fig. 2.5 [12].

This fantastic pace of discoveries in physics continued without abatement. Below is a quite abbreviated listing of advances in physics, 1901–1920 [33].

- 1902: Rutherford and Soddy formulated a theory of transmutation by radiation and were the first to use the term “atomic energy.”
- 1904: Nagaoka proposed the planetary model of the atom.
- 1905: Einstein announced his concept of special relativity plus his proposal of the equivalence of mass and energy.
- 1908: Geiger, Royds, and Rutherford identified  $\alpha$ -particles as helium nuclei.
- 1912: Wegener proposed and presented substantial evidence for tectonic plates.
- 1913: Bohr utilized quantum theory to explain electron orbits in atoms.
- 1915: Einstein announced his theory of general relativity; he predicted the gravitational power of a star to bend light.
- 1919: Rutherford demonstrated the proton in the atomic nucleus.
- 1920: Rutherford proposed existence of the neutron and proposed its name.

The term photon was not proposed until 1926 in the article in *Nature* by G. Lewis [20]. The neutron was discovered in 1932 by J. Chadwick [4] while working in Rutherford's

laboratory.<sup>4</sup> Thus, the three prominent atomic constituents, electron, proton, and neutron, had been discovered by 1932. These are critical players in accelerating advance in nuclear physics. These shortly led to nuclear fission and then the atomic bomb. For medicine, an important result was the availability of a large and expanding number of radioactive isotopes (e.g.,  $^{60}\text{Co}$ ,  $^{137}\text{Cs}$ ,  $^{125}\text{I}$ ,  $^{131}\text{I}$ ) for radiology, diagnostic and therapeutic.

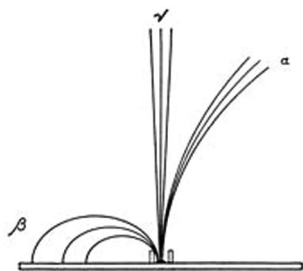
Due to space constraints, the advances in biology chemistry and medicine are not considered here. Mention has to be made of two of the most significant developments in biology in the 19th century. First is the theory and extensive supporting data for evolution of life forms by Charles Darwin, 1859. Second is the work of G. Mendel who published in 1866 [8] results of cross-breeding of hybrids of peas and the basic laws of heredity. His important report was not appreciated until his work was “re-discovered” in 1900, after 34 years. He shortly became famous and is ranked as the Father of Genetics.

## 2.4 The Start-Up of Radiology and Radiation Therapy at the MGH: The Walter Dodd Era

### 2.4.1 Walter James Dodd, 1869–1916. The Developer of Radiology at MGH

This section is taken largely from Macy's *Biography of Dodd*, 1918 [24], and from [21, 25, 26, 43]. The initiator and developer of diagnostic radiology and of radiation oncology at the Massachusetts General Hospital was Walter J. Dodd (WJD). Despite being disadvantaged as a youth, he did achieve an impressive education, largely on his own. He was widely described as possessing exceptional personal charm, initiative, enthusiasm, and well-directed energy. That is a formidable combination and clearly served him well in his efforts to propel the MGH to a rapid entry into radiology at the start of 20th century medicine.

Walter Dodd (see Fig. 2.6a, b) was born in London in 1869. His father was a metal roofer and also quite active in the labor movement. However, he died when Walter was only 8 years old. Due to an insufficient family support system, the boy was sent to Boston to live with a married sister.



**Fig. 2.5** The effect of a magnetic field on the path of  $\alpha$ -,  $\beta$ -, and  $\gamma$ -rays

<sup>4</sup> For a thoroughly fascinating biography of Chadwick, read the book *The Neutron and the Bomb: A Biography of Sir James Chadwick* by Andrew Brown [2]. This book received a full page very positive review in *Nature*. Brown is a radiation oncologist. He had 2 years as a fellow in this department and is now working at the Kennedy School of Government and at a clinic in New Hampshire.



**Fig. 2.6** (a) Walter J. Dodd as a young man. (b) Walter Dodd in his military uniform, 1915 [24]

She did manage for him to attend a public school to age 13, but then he had to “Drop Out.” Dodd worked for almost 5 years at the Oriental Tea Co. as an office boy. He attended a Unitarian Sunday school at the Bulfinch Chapel. There he made a quite positive image for himself due in part to his success as an actor, especially as a comic in the Church theatrical program. His Sunday school teacher was a Ms. Bullard. At age 18, Walter professed interest in life as a seaman and world traveler. However, his sister was opposed to such a life for her brother. Ms. Bullard concurred and arranged for her cousin, Charles Eliot, the President of Harvard College, to meet Walter. Eliot rated the young man favorably and invited him to accept a job as an assistant janitor at a chemistry laboratory. Young Dodd judged this to be more attractive than the sea and accepted Eliot’s offer. He worked there for 5 years, until 1892. WJD was intensely curious about the science discussed in the lectures and laboratory procedures. Reflecting his enthusiasm and obvious intelligence, he was granted permission to sit-in on lectures and to perform the experiments in the general chemistry course. Professor Hill of Harvard wrote of Dodd “While he was in our laboratory, Mr. Walter J. Dodd attended the lectures given in general chemistry and performed all of the experiments required of our students under the direction of one of our assistants. In the following year he was in my own course in Quantitative Analysis. His experimental work was unusually good and he also passed with credit the two written examinations of the course. I think that he profited more from the instruction in the two courses than most of our matriculated students.”

In 1892, he was successful in applying for a position as Assistant Apothecary at the MGH. Almost immediately, Dodd took further chemical courses and became a registered pharmacist. The apothecary was responsible for the hospital’s photography program that had been started by a gift of \$100 in 1887 to provide pictorial records of patients

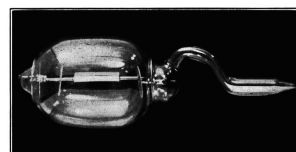
and their course in hospital. Dodd learned photography readily. These combined experiences were important to his MGH career as pharmacist, photographer, and then radiologist.

Dodd’s work was progressing happily when the attention of much of the medical and scientific worlds became highly focused on the December 28, 1895, paper by Wilhelm Röntgen. Dodd was instantly excited by these incredible “pictures” of human bones in patients. He and his assistant, Mr. Joseph Godsoe, immediately commenced development of the technical devices for taking such pictures. Their enthusiasm was shared by many staff at the hospital. Due to his reputation as a photographer, Dodd was given responsibility for implementation of the new technology at the MGH, i.e., a quick shift from photographer to radiographer. Their first radiograph was made in approximately March 1896. This was, of course, simultaneously occurring at hospitals throughout the world. WJD took the first radiograph at MGH according to a later account by George Holmes and by J. Godsoe. However, H. Cushing did claim that he and Codman, very famous physicians at the MGH, made the first MGH radiograph.

From 1896 onwards, WJD and Godsoe made or assembled a series of x-ray generators from bits and pieces of equipment, secured from throughout the hospital. A photograph of an x-ray tube used by Dodd near the start of radiology at the MGH is shown in Fig. 2.7 [15].

In 1897 a Dr. Weld gave an x-ray apparatus to the hospital, a substantial assist in this new program. The roentgenology unit was moved through a series of locations, due to the steeply expanding range of activities. In reality, Dodd was functioning as a “radiologist” prior to becoming a physician. We have no record of WJD knowing of or attempting to interact with Williams at BU or the physicists at MIT or at Harvard.

There is little written record of this early period at MGH in contrast to the book by Williams at Boston City Hospital. Do note that Williams was an established physician from a medical family (his father was the first professor of ophthalmology) and he had the finest education available in this country plus post-graduate education in Europe. In contrast, Dodd was largely self-taught, not a member of an important family, and a recent graduate from pharmacy



**Fig. 2.7** One of the very early x-ray tubes employed by Dodd and Godsoe [15]

school. Perhaps, this partially explains the lack of knowledge by Dodd of Williams' work.

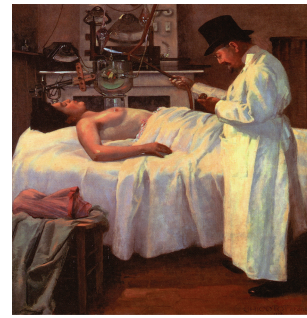
The MGH archives do not reveal records of the MGH early radiation treatments. Almost certainly, Dodd and colleagues were using the new rays against a variety of diseases, especially benign and malignant lesions of skin. Certainly, Dodd was highly active in the use of the new machines. By summer of 1898, he required skin grafting for radiation injury. In 1902, the department had three x-ray machines, viz., clearly a growing program. The work was intense, i.e., many patients but quite limited staff and space.

The following are from unpublished notes by Milford Schulz [36]: "the earliest hospital record of probable use of x-rays for therapy is a note in the Treasurers report of 1900 'expenditures of \$125.24 for x-ray apparatus, \$203.90 for x-ray tubes and \$1062.54 for beer and ale.' In the records of surgical procedures done that year, there appears an item *repair of ulceration and X-ray burns*. 1901 surgical records include one case of x-ray burns. In 1902, two patients were treated for X-ray burns (one of the abdominal wall and one of the groin." In 1909 Dr. C.A. Porter published a paper "Surgical Treatment of X-ray Carcinoma" [31].

The MGH was very much alive and increasing its range of activities. This was reflected in statistics of growth in the number of patients and the population base. In 1900, the MGH had 260 beds and the medical program was almost exclusively for the care of the economically disadvantaged. These factors changed rapidly, viz., by 1935, there were 765 beds and medical care was provided to persons of all income levels.

Dodd was sensitive to the rate and scale of change in the practice and that he must increase his medical knowledge base to interact with physicians more effectively. In 1900, he entered HMS for 1 year, but then decided that he had to transfer to Vermont Medical School in order to concentrate on his studies, i.e., to be out of reach of the pressures of the work load at the hospital. On graduation in 1908, he was made röntgenologist (skiagrapher) at MGH. The Röntgenology Department was established, with WJD as Chief, a position he held until his death in 1916. Thus, he had no residency, as they did not exist. His appointment as Chief came almost as a graduation present. Dodd was given the academic rank of Instructor in Röntgenology in 1909, the first appointment in radiology at HMS. The clinical demand was rapidly expanding and there was a series of moves to progressively larger quarters. WJD was active in virtually all areas of radiology. WJD collaborated with the famous Walter B. Cannon in contrast examinations of the GI tract, using bismuth.

There was public appreciation of this new endeavor by physicians and physicists in radiology. Perhaps of interest is Fig. 2.8 [5], the self-portrait by G.A. Chicot in 1907. He was a French painter of substantial repute and a pioneer in



**Fig. 2.8** G. Chicot's self-portrait of the artist treating the breast of a woman, 1907 [5]. With permission

radiology, i.e., a two-career man. In this painting, he portrays himself administering radiation to the breast of a female patient. This 1908 self-portrait is the only painting of a physician administering radiation to a cancer patient known by Dr. Luther Brady, an established art critic (Personal communication, 2007).

1911. WJD received a Dalton Scholarship to investigate radiological images of the GI tract.

1912. Dodd's stated in his annual report "There is great need for some simple but accurate standard of dosage in radiotherapeutic work – we believe that this can be accomplished by the new apparatus recently installed. The great importance of this can only be appreciated by those engaged in this work." Holmes, *vide infra*, was commended for his efforts to measure radiation dose. The Trustee's Report gave encouragement to increase the utilization of radiation post-operatively. Special emphasis was placed on breast cancer. The report also urged that more patients be treated by radiation. By 1912, the department had imaged and/or treated 6574 patients. Of special interest is that despite an extremely small staff, radiology service was available 24 h/day, 7 days per week. The first machine obtained specifically for radiation therapy was a 140 kVp unit.

Although the USA did not enter WWI until 1916, Walter Dodd volunteered in 1915 for service with the Harvard Medical Unit (in the British Expeditionary Force) in France. This reflected his character as a man who had to be involved as a participant, not as an observer. Another contributing factor could well have been his birth in England. He departed for France with recent and incompletely healed extensive surgery on an arm and chest wall. Figure 2.6b is of Dodd in uniform while on duty. He worked with a military unit from June to ~ October 1915.

Walter J. Dodd died on December 18, 1916, of metastatic cancer secondary to multiple radiation cancers. He had had his first in-hospital treatment in 1898, skin grafts for radiation dermatitis of the hands. This was followed by more than 50 surgical procedures with no major infections mentioned in the records (antibiotics were, of course, not available).



Dodd was an early martyr, but not the first in diagnostic and therapeutic radiology [3], but one very close to us. He was exceptionally respected and held in much affection in the hospital.

## 2.5 Advances in Radiation Therapy, 1917–1942, the George Holmes Era

Dodd made a brilliant recruit to his staff in George Holmes from Tufts in 1910. Holmes was a graduate of Tufts medical school (1906) and had worked with F. Williams at Boston City Hospital, Fig. 2.9.

1914. The first radiation physics paper from the MGH was “Some Experiments in the Standardization of X-ray Dosage” by G.W. Holmes [13]. Although most of Holmes’ work was in diagnosis, his interest in therapy was at a high level. His last paper was “Therapeutic Radiology” and that appeared in *Radiology* in 1946 [14]. The number of radiation treatments administered were 923 in 1914 and 1220 in 1915. Due to this expanding clinical load, there were yearly requests for new and better equipment and additional space.

1915. The First Resident in Radiology in the USA was in 1915 and at MGH. This is discussed in Chapter 10 on Education. From 1917 onwards, the MGH department was very active in the organization and teaching of radiology to medical students under G. Holmes. Although one could sub-specialize in diagnostic or therapeutic radiology and be credentialed by the American Board of Radiology as of 1939, the first to do so at the MGH was not until the late 1960s.

1916. Holmes emphasized the need for a lead-lined room and his desire to combine x-ray therapy with radium, which was not then available. Probably the first MGH paper on clinical outcome of radiation therapy was that by Malcolm Seymour in the *Boston Medical and Surgery Journal* “Treatment of Grave’s Disease by the Röntgen

Ray” [37]. This was followed by a paper by Holmes and Merrill in 1919 on 262 patients treated for thyrotoxicosis using 140 kVp units.

1917. George W. Holmes was appointed as successor to Walter J. Dodd as röntgenologist [21]. He continued in that role until his retirement in 1942. Portable x-rays in the operating rooms were introduced that year. There was much interest in use of radiation post-operatively. The Phillips House (private patients) was opened and fitted with a diagnostic unit. A radiation therapy unit was not installed until 1924.

1919. Holmes organized special clinics for thyroid and skin diseases, antecedents of the Tumor Clinic.

1922. MGH was given \$31,000 by Ms. W. Grove to provide for radium therapy. These funds were given to D. Barney, Chief of Urology and not Radiology, but were to be available to the MGH staff beyond Urology. In 1924 a Radium Committee was formed with the Chief of Röntgenology (George Holmes) as the Chair. The radium was stored in a lead safe in the radiology department. At the MGH, there were 40 mg in needles and a small amount in plaques. However, some 500 mg of radium was stored in solution at the Huntington Hospital. The emanation (radon) was available on 48 h notice from the “radon pump” under the control of the physicist, Duane [6]. This program continued until the closure of the Huntington in 1942, when the radium inventory came to the MGH with Milford Schultz. Duane was the first Professor of Biophysics at Harvard and in the USA [6]. At the MGH, surgeons had the responsibility for brachytherapy and intracavitary application while dermatologists used radium in surface applicators. Radiologists functioned merely as advisors until ~1950. Duane was among the first to measure ionization of air by x-rays and to develop instruments for dose measurements, a precursor of first international unit of radiation dose, the R (Röntgen), Fig. 2.10 [6].

1924. The first of several high-energy machines (220 kVp) based on the air cooled, hot cathode, and high vacuum Coolidge tube was obtained. Shielding was by a  $\frac{1}{4}$  inch layer of lead. Treatments were given at 50 cm SSD. This was judged a marked improvement. Note that the dose at 10 cm depth was higher at 35%. These tubes were the sole basis for “deep therapy” at the MGH until 1940 when the new 1.2 Van de Graaff became operational. .

1925. *The First Tumor Clinic in the USA*. The special tumor clinics initiated by Holmes in the Radiology Department in 1919 developed into the Tumor Clinic in 1925. Many patients were referred directly to Holmes. He soon developed the practice of asking a surgeon or dermatologist with interest in the problem presented by the individual patient to come to the department and examine the patient with him. The start of the program was primarily a consultation service for skin disorders and thyroid diseases.



**Fig. 2.9** Dr. George W. Holmes. MGH Chief of Radiology, 1917–1942 [21]



**Fig. 2.10** William Duane, Professor of Biophysics, Harvard University [6]

This rapidly expanded to include cancer patients. As his clinics were working well, he concluded that there would be a gain for patients to be seen jointly by the radiologist and the appropriate surgeon or dermatologist.

Holmes and his partner in this development was surgeon Robert B. Greenough who had been an assistant to John C. Warren. He and Holmes were convinced of a clinical benefit by concentration of medical talent and facilities at one locus in the hospital. Holmes insisted and prevailed for the Tumor Clinic to be sited within the Radiology Department. Clinic hours were 9:00 to noon Monday through Saturday, with different patient categories seen on each of the 6 days. That is, the patient would experience *one* appointment in *one* setting. This was judged to be beneficial for patient care and resulted in the formation of the Tumor Clinic in April 1925, the first such clinic in the USA. There was the important gain of a central record for each patient. Referring or bringing patients to this clinic was entirely voluntary.

Specialties participating included internal medicine, pathology, GU, neurosurgery, and nose/throat surgery. From the various accounts, the clinic operation was pleasant and effective. A large fraction of the patients were from the House Service and the Out-Patient Department. At the opening of the White Building in 1939, the Tumor Clinic was transferred to space adjacent to the radiation therapy area.

1928. Holmes described the department in the summer issue of *Methods and Problems of Medical Education*, a publication of the Rockefeller Foundation. Parts of his report are reproduced here [21]:

The department is on the ground floor of one of the older buildings of the hospital, occupying 7000 square feet of space. Located in a part of this space is a clinic for diagnosis and follow-up work in connection with the treatment of tumors. The protection of the operator is obtained by enclosing the tube, and

by the use of a small screen in front of the control board. No special operating booths are considered necessary. On the opposite side of the waiting room are examining booths for the observation of patients receiving treatment and for the follow-up of such cases as require it. Near these booths, separated by a corridor, are two rooms for preparation and application of radium, one of which is equipped for minor surgery.

About 20 percent of the patients who are seen come for treatment or observation. In the therapeutic division there are three machines capable of delivering a maximum current of 10 milliamperes at a voltage of 220 kVp. These much higher energy machines were based on inventions of the hot cathode and high vacuum tube by W D Coolidge. His machine achieved a major increment in operating voltage and the tubes had a long life and were relatively stable.

They also developed or obtained special apparatus for the measurements of Röntgen-ray and radium dosage. The measuring instruments employed are the ionization chamber of Duane, the electroscope developed by Dessauer-Bach, and the ionization chamber recommended by Weatherwax. There are also special standard milliamperes and voltmeters which were used as controls.

During the year the entire department has been rewired and the current for energizing the x-ray machines had been changed from direct to alternating; this allowed us to do away with rotary converters. There was then a constant source of trouble and risk, and has given us a more stable power supply.

An important advance for all uses of x-rays and  $\gamma$ -rays was the adoption of the R or Röntgen as the internationally accepted unit of radiation dose by the International Congress of Radiology in 1928. The Röntgen, the R, was defined as “the quantity of X or gamma radiation such that the corpuscular emission per 0.001293 gram of air produces, in air, ions carrying 1 esu of quantity of electricity of either sign.” The mass of 1 cm<sup>3</sup> of dry atmospheric air at 0°C and 760 mmHg pressure is 0.001293 g [12].

This was an era of quite dramatic discoveries in all of science and medicine. Among these in physics were the uncertainty principle (Werner Heisenberg), 1926; the cyclotron (E. Lawrence), 1929; the expanding universe (E. Hubble), 1929; the Van de Graaff accelerator (Van de Graaff), 1931; the neutron (Chadwick), 1932; fission of lithium by accelerated protons (Cockcroft and Walton), 1932; and an extensive array of other important discoveries. There were also many discoveries beyond radiation oncology, e.g., insulin (Banting and Best), 1922; penicillin (Fleming), 1929; and the first vaccines for tuberculosis and for yellow fever (1927 and 1932). The science of genetics became a very serious research area. The arts were advancing into quite new concepts and styles in painting, sculpture, and architecture. As one example of this remarkably free spirit, examine Fig. 2.11. This is a 1926 painting by Juan Miro, “Harlequin’s Carnival.” This is a dramatically new and different form of artistic expression. This is included as an example of the exploration and acceptance of new thinking.

Returning to the progress in radiation oncology at MGH by years:





**Fig. 2.11** Harlequin's Carnival by Juan Miro, 1926 [28]. With permission

1929. Reports on the radiation treatment of patients with angina pectoris, carcinoma of the prostate, and carcinoma of the breast were published. That radiation would have been given to patients for angina pectoris certainly gets our attention and gives pause to consider the extent of counterproductive procedures in medicine in general. At HMS, radiology was transferred to the Department of Medicine from the Department of Surgery.

1930. At the Clinical Congress of the American College of Surgeons in Philadelphia, Dr. Greenough presented a paper describing the origin of the Tumor Clinic and how it had operated in the previous 5 years. The Baker Memorial Building was opened and the radiology section was equipped with a therapy unit.

1931. In a GEC report, the comment was made that cancer clinics similar in concept and function to the MGH Tumor Clinic have been established in many hospitals around the country.

The department staff consisted of three full-time radiologists (George Holmes, Aubrey Hampton, William C. Martin) and three part-time radiologists (Richard Dresser, John Meachen, and Robert Vance) and one consulting physicist, Howard Stearns.

1937. Gay ward was demolished to provide space for the new White building scheduled to open in 1939. Radiology was allotted a substantial new space for expansion of its programs. A new 1 MV or higher energy x-ray machine was planned to be installed in the new building.

In the late 1930s, Carl T. Compton, President of MIT, was enthusiastic to assess the clinical value of the uses of some of the radioactive isotopes in medicine, with special interest in isotopes of iodine. He arranged for discussions with Howard Means of the MGH Department of Medicine. The result was that the MGH was one of the first in the medical use of artificial radioisotopes. This close work between MGH clinicians and MIT scientists led to the establishment of Scientific Advisory Board in 1947, with Dr. Compton as the first chairman. Additionally, MIT Professor Francis O. Schmitt was appointed to the MGH Board of Trustees.

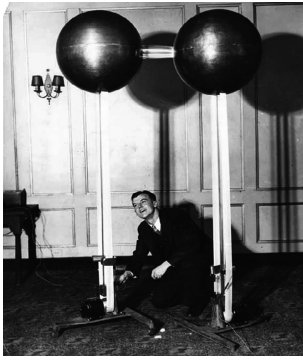
## 2.6 Robert J. Van de Graaff and His Accelerator

Van de Graaff (VdG) was born in 1901 in Tuscaloosa, AL [18, 34], from which he graduated with BS and MS degrees in mechanical engineering. After 1 year with the Alabama Power Company, he received a grant from the state that he combined with personal savings to study at the Sorbonne from 1924 to 1925. There he attended lectures and demonstrations by M. Curie and other notables in physics. While there he won a Rhodes Scholarship to Oxford University where he did well and was awarded the D.Phil. (the Oxford designation of the Ph.D.) in physics in 1928. During this period, he became familiar with the work of Rutherford and team at the Cavendish Laboratory, Cambridge University. His interest was greatly stimulated by their concepts of the potential of causing disintegration of atomic nuclei by the impact of energetic particles on atomic nuclei. Were there to be success, this would lead to increased understanding of atomic nuclei. This was a provocative concept and Van de Graaff commenced planning for a particle accelerator.

Young VdG was again fortunate in 1929 in winning a National Research Fellowship to join the Palmer Physics Laboratory at Princeton University and work in the laboratory of Karl Compton. He promptly commenced his project and within the year had assembled a special electrostatic accelerator; this Mark I device developed 80,000 V. This was a powerful encouragement for him and his supporters to initiate building a series of accelerators of increasing energy.

Compton was recruited to the Massachusetts Institute of Technology as President in 1930. The next year he brought Van de Graaff to MIT as a research associate. At the time of the inaugural meeting of the American Institute of Physics in November 1931, VdG exhibited his most recent model. That machine achieved energy levels above 1,000,000 V. This was a signal success for his career and for the smartly advancing field of nuclear physics. Figure 2.12 is a photograph of VdG with one of his early machine.

At MIT, Van de Graaff proceeded to construct an exceptionally powerful and quite large unit. This was built in an aircraft hangar. It featured two polished aluminum spheres, each 15 ft in diameter. These were mounted on insulating columns that were an impressive 6 ft in diameter and 25 ft in height. At its debut on November 28, 1933, the performance was a huge success and received national attention. Namely, the *New York Times* for November 29, 1933, report on the machine was titled "Man Hurls Bolt of 7,000,000 Volts" [41]. That Van de Graaff was thinking deeply



**Fig. 2.12** Robert Van de Graaff, the inventor of the Van de Graaff accelerator [42]

regarding the potential of nuclear reactions and forces can be seen from the footnote.<sup>5</sup>

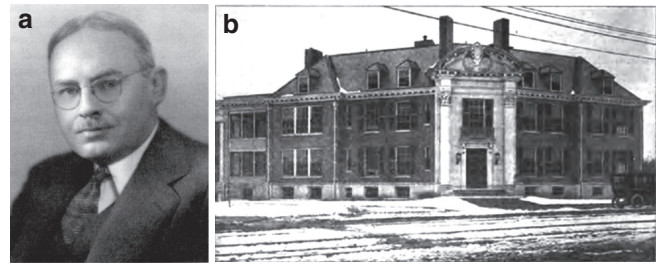
By the time of Robert Van de Graaff's death in January 1967 more than 500 Van de Graaff particle accelerators were in use in more than 30 countries. Of these, ~53 were used for radiation therapy.

## 2.7 The 1 MV Van de Graaff Accelerator at Huntington Hospital in 1937

A lecture on the clinical needs of improved radiation sources was given by G. Holmes at MIT in 1932. Van de Graaff and his assistant John Trump did not attend the lecture but learned that there would be serious clinical interest in their high-energy machines for treatment of cancer patients. Thus stimulated, they arranged to meet with George Holmes to discuss such an option. Holmes was interested in such a

<sup>5</sup> VdG wrote this letter to Karl Compton on March 20, 1931, "homogeneous beams of protons at voltages that may be expected from the present work could be used for many simple experiments of fundamental nature. Among them would be the investigation of the effect of their impacts on uranium and thorium. These nuclei are already unstable, and it would be interesting to see if an impacting proton of great speed would precipitate immediate disintegration. On the other hand, it might be that the proton would be captured by the nucleus, thus opening up the possibility of creating new elements of atomic number greater than 92." "Near the other end of the series of atomic numbers is lithium. Now suppose that a proton is shot into the  ${}^7\text{Li}$  nucleus, supplying the second component for the second alpha particle group. A consideration of Aston's curve and Einstein's law shows that a nuclear reaction might take place as follows:  $\text{VLi} + \text{aH} \sim 2\text{ }^4\text{He} + 16\text{ MV energy.}$ "

In his obituary of VdG, Peter Rose wrote, "This was one year before Cockcroft and Walton split the atom by bombarding  ${}^7\text{Li}$  with protons and eight years before element 93 was artificially produced in an accelerator! He once told me that he wanted to include in his 1931 letter his belief that useful amounts of nuclear energy might be liberated by the disintegration of uranium or thorium, but he felt Compton would think this too bold!" [35]. See also the obituary by L. Huxley [18].



**Fig. 2.13** (a) Richard Dresser was the Chief of Radiology (major interest in therapy) at the Huntington Memorial Hospital and part-time staff at the MGH [21]. (b) Huntington Memorial Hospital of the Harvard Cancer Commission [17]

machine for the MGH but had no space. He was anticipating adequate space in the new White Building in 1939.

Richard Dresser was a radiologist who had a major interest in radiation therapy (Fig. 2.13a). He had a part-time staff position at the MGH and his main appointment was at the Huntington Memorial Hospital. He learned of the meeting and the machines that had been built by Van de Graaff. He arranged to meet John Trump and discussed a generator of  $\geq 400\text{ KeV}$  to be used in the Huntington Memorial Hospital. Trump replied "make it 1 MV and we might be interested" [35]. Dresser obtained a Hyams Trust grant of \$25 K to build a 1 MV generator. Dresser and Trump began work in 1935 on a new class of clinical x-ray therapy machine at the Huntington Memorial Hospital, the cancer research hospital of the Harvard University. Trump and Van de Graaff described their design for the 1 MV machine in 1937 [40]. It had 25 beds, major laboratories, and was sited on the corner of Huntington Avenue and Shattuck Street<sup>6</sup> (Fig. 2.13b).

Patient treatments began in April 1937 [36]. The scale of this Van de Graaff machine is evident by its six charging belts of 1 m width that carried negative charges to the dome at 4000 ft/min or 45 mph. Surely, this was not a quiet machine. The machine was definitely impressive in size. There was ample space to walk inside and examine or repair as needed. The interior was air insulated and maintained at a constant temperature. The operation was based on clever manipulation of electric charge: charge is applied to the belts at the lower level and transported rapidly to the top of the

<sup>6</sup> The Huntington Hospital developed from the impact of the gift of \$100,000 by a Ms. Croft that resulted in the establishment of the Harvard Cancer Commission. This was followed by an additional gift, viz., Ms. Collis Huntington gave \$292,000. These were sufficient to commence the planning and construction of the small hospital for cancer research and patient care in 1912 by the commission. This hospital had the first 1 MV machine for clinical use [40]. Additionally, Duane was the world's first to devise the method for "pumping radon or as he called it emanation from a solution of radium salts" into glass capillary tubes which were then inserted into tumors. This pump was brought to the MGH by Schulz in 1942.

run. Negative charges from corona points are accelerated in the run-down to the target [12]. The dose rate was considerable for machines of that era, viz., of 40 R/min at 80 cm [36]. The first clinical treatment in April 1937 was a historic point in the development of radiation oncology, viz., the first clinical use of an x-ray beam of 1 MV. One of the first patients treated by the 1 MV beam at the Huntington in 1937 was a dentist with bladder cancer. According to Milford Schulz, the patient was alive and well 4 years later. This was the site of the first “supervoltage” clinical machine in the world, a 1 MV Van de Graaff.

In 1938, a 1 MV resonant transformer machine was installed at Memorial Hospital, New York. St. Bartholomew Hospital in London began treatment with an x-ray machine designed to operate at 1 MV but was operated at 0.7 MV from 1937 to 1939, then the unit was upgraded and commenced treatments at 1 MV.

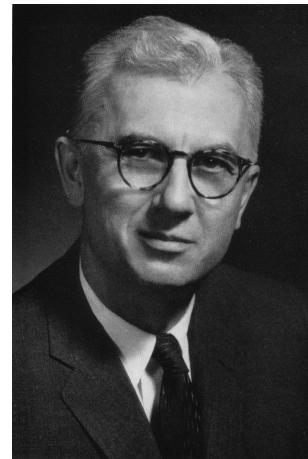
## 2.8 The 1.2 MV Van de Graaff Machine at the MGH

The Hyams Trust supported development of a 1.2 MV Van de Graaff accelerator for MGH in the new space for radiology on the second floor of the White Building. Van de Graaff and Trump worked on this installation. This new machine was the first clinical unit to operate at more than 1 MV. Also of practical importance, it was vastly reduced in all dimensions relative to the Huntington unit and delivered 80 R per minute at 1 m. Installation was in 1940 with no full-time physicist on the MGH staff.

In that year, the department had the 1.2 MV Van de Graaff, four orthovoltage units (two in the White building, one each in the Baker and Founders buildings) and radium. Some 5000 treatments were administered in 1940. Dispersal of important equipment around the hospital appears to have been an inefficient operation and was prejudicial to sub-specialization.

We move to another big event in our history, viz., the appointment of Milford Schulz to the MGH staff in 1942 (Fig. 2.14). Milford started life in Sister Bay, WI, in 1909 and moved to Chicago for his medical education and residency in radiology at Northwestern. James T. Chase was the chief, a very highly regarded radiologist. Milford’s interest in the most modern radiation therapy was evident in his move in 1939 to the Huntington Hospital to work with the 1 MV x-ray beam. At that time there were only three 1 MV machines: Boston, New York, and London.

The Huntington Hospital closed late in 1941 and virtually the entire research and clinical staff moved to the MGH at the beginning of 1942, at the time of US entry into WWII. These included Milford Schulz, Joseph Aub, Ira Nathanson, Rita Kelly, and Paul Zamecnik. Each was to be central player



**Fig. 2.14** Milford D. Schulz. Radiologist at MGH, 1942–1970. Radiation Oncologist, 1970–1976

in the development of oncology at MGH. Milford’s arrival was indeed a fortunate event for the MGH, viz., obtaining one of the extremely few radiologists with substantial experience with 1 MV x-ray beams and whose principal medical interest was therapy. This obvious good luck was not fully appreciated as evidenced by a letter from A. Hampton, Chief of Radiology, to Faxon, the General Director of the MGH. Hampton made the appointment temporary, with the proviso that Milford might be dismissed at the end of the war with the return of staff from military duty. This was despite the near certainty that the patient load would continue to increase and that none of the returning staff were even remotely comparable to Milford in experience with high-energy x-ray therapy. The reality was that many of the returning radiologists moved to other hospitals. Milford was definitely needed and he remained.

Milford was one of the few to work at the hospital throughout WWII, as he did not pass the army physical examination. During WWII, most of the department staff had joined the military leaving the MGH quite depleted of radiologists. The military recruitment policy during WWII was that the most experienced physicians were recruited and the least experienced left to care for the civilians. As Robbins was the “boy” or the youngest among the staff, he was left at the MGH. At the end of the war in 1945, many of the returning staff retired or moved to other hospitals. Larry was rewarded for his good service under war time conditions by being made Chief of Radiology in February 1946.<sup>7</sup>

<sup>7</sup> The contributions to diagnostic radiology by Larry Robbins were very well regarded as evidenced by these honors: Gold Medals of ACR and RSNA; President of ABR; Chancellor of ACR; director and president of James Picker Foundation. Additionally, he wrote the eighth edition of *Röntgen Interpretation* in 1955. He retired in 1971 with the appointment of Juan Taveras as his successor.





**Fig. 2.15.** (a) Acute and (b) late skin reaction after high-dose irradiation by orthovoltage x-ray beams. (c) The extremely severe late skin changes after low dose per fraction treatment of eczema that resulted in slight to no acute reaction [15]

The rationale for the enthusiasm for radiation beams of  $\geq 1$  MV photons was remarkably straightforward. There are four critical advantages for the 1 MeV relative to orthovoltage beams: (1) surface dose (skin dose)  $\sim 40$  vs 100%; (2) marked increase in depth dose; (3) sharply decreased differential absorption of radiation between muscle, lung, and cortical bone; and (4) much reduced penumbra width.

The severe moist skin reaction that developed in virtually all patients treated to radical dose levels by orthovoltage machines is illustrated by Fig. 2.15a [15]. The patient was at  $\sim 2$  weeks after treatment. These reactions required non-trivial nursing care and constituted a serious discomfort for the patient. The late reaction in a different patient treated by orthovoltage radiation is that of prominent telangiectasia and contraction/fibrosis, Fig. 2.15b. For supervoltage x-irradiation, the acute skin reaction is usually that of a dry dermatitis and occasionally a patchy short-lived moist change followed by minimal to modest fibrosis. That severe late reactions can develop following minimal acute reactions is powerfully illustrated by Fig. 2.15c.

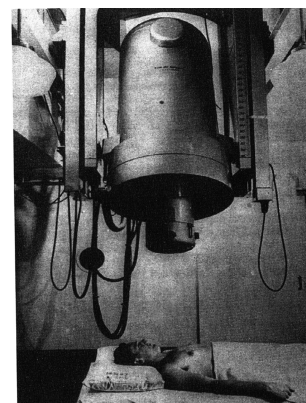
In other centers there had been use of  $\gamma$ -beams of  $\sim 1$  MV from radium teletherapy units, “Radium Bombs.” These had important disadvantages, viz., very low dose rate, short source surface distances, small field sizes, large source size, and wider penumbra than high-energy x-ray machines.

Milford could not limit his practice to radiation therapy as sub-specialization was not permitted. Although there was no designated radiation therapy section within the department, Schulz functioned as the de facto head of the therapy activities. G. Holmes, the Chief, was quite active in radiation therapy and supported Milford.

In 1944, there was a serious radiation accident. During work on the installation of the 1.2 MV Van de Graaff, several workers got into the path of the cathode beam. There were no fatalities but a few persons developed significant injuries. Use of the newly available antibiotics was credited for some of the success in caring for the injured.

The four war-time years provided few to no opportunities for innovation due to shortage of staff and essentially all manufactured goods. Despite these constraints, there were serious considerations for post-war improvements. One impressive result was the effort by Milford and Larry Robbins that led to the purchase, installation, and then the start of treatment in 1948 on a 2 MV Van de Graaff machine. Figure 2.16 is a photograph of such a machine. The MGH machine was in clinical service from 1948 to 1975. This was one of the first clinical units that operated at 2 MV. However, in that same year, a patient was treated at University of Illinois on the first clinical Betatron, a 22 MV machine.

The MGH 2 MV VdG was installed with no full-time physicist on the staff. There was an extraordinary problem in its installation. Lead was a protected item during the war and even by the time of the installation of this machine, lead was difficult to obtain and was pricey. The MGH arranged for a large quantity of lead from the storage unit at MIT to be used as shielding. From that newly acquired lead, 20 tons were stolen. After some protracted discussion, the lead was returned. In 1950 Holmes and Schulz published an



**Fig. 2.16** A photograph of a 2 MV Van de Graaff [11]

extremely fine and lucid textbook on therapeutic radiology. They opened with 73 informative pages on physics and radiation biology. The Holmes and Schulz book had 347 pages with 111 figures. Their book was the first MGH book on radiation oncology and was one of three widely used radiation therapy textbooks in English of that era (1950). The other two were *The Treatment of Malignant Disease by Radium and X rays* in 1948 by R. Paterson of the Christie Hospital and Holt Radium Institute, Manchester, UK, and *Clinical Therapeutic Radiology*, edited by U. Portmann, of the Cleveland Clinic, in 1950 [29, 32].

Despite the large number of patients and minimal support staff, Milford made regular contributions to radiation oncology. Milford was a member of the group that revised the staging system for laryngeal carcinoma, authored papers on staging and end results for carcinoma of the thyroid, radiation in management of myasthenia gravis, spinal cord compression, advanced lung cancer, and radiation secondary sarcoma. He designed applicators for treatment of scleral lesions. Additionally, he commented on ethical issues in advertisements.

Milford was the only MGH radiologist working near full time in therapeutic radiology 1942–1953 when C.C. Wang joined him. Then some 15 years later, Melvin Tefft and George Zininger also joined his team. The patient load progressively enlarged but no increase in space or equipment after 1956, when Milford oversaw the removal of the 1.2 MV Van de Graaff and installation of a 55 cm SAD  $^{60}\text{Co}$  unit.

Milford Schulz enjoyed a very high reputation as a clinician and one very well informed in physics and technology. As evidence of his national status these distinctions and awards are noted:

Member of Board of Chancellors of the American College of Radiology  
 President. American Radium Society, 1958–1959  
 Gold Medalist and Janeway Lecturer of the American Radium Society, 1974  
 Founding Member of American Society of Therapeutic Radiology and Oncology  
 President of American Society of Therapeutic Radiology and Oncology (1971–1972)  
 President. New England Röntgen Ray Society, 1962–1963  
 President. American Cancer Society, Massachusetts Division  
 Member of the International Commission of Radiological Units for many years  
 Shortly after creation of the department, Milford was promoted to Professor of Radiation Oncology at HMS  
 Chair of the Group of 75 C45 (Radiology) Committee for Revision of the American Standard definition of electrical Terms – American Institute of Electrical Engineers

Milford's Janeway lecture "The Supervoltage Story" was a serious and scholarly account of the diverse actors and devices in the development of x-ray machines that produced beams of  $>1$  MV [35]. The transition from 250 kVp to  $\geq 1$  MV is really a fascinating and central technical development in our specialty.

For the MGH program in radiation oncology, Milford was an energetic, articulate, and effective force in moving the hospital to recognize the necessity of a quite major upgrading of the space and facilities for the radiation therapy program. His memoranda to the administration on these needs for radiation oncology were not ambiguous in the least. See his letter to the MGH General Director of 1963 reproduced in Chapter 3. He had strong support from Benjamin Castleman (Chief of Pathology) and Howard Ulfelder (Chief of Gynecology). In the 1960s there was an increasing appreciation of the positions articulated by Milford that contributed to the decision to build a cancer center and establish a separate department of radiation therapy.

## 2.9 Nobel Prize to an MGH Staff

In 1944, Fritz Lipmann discovered co-enzyme A and its role in intermediary metabolism. For this he was awarded the 1953 Nobel Prize. This was shared with Hans Krebs of the UK.

In 2010, Jack Szostak received the Nobel Prize Physiology or Medicine for his role in the discovery of the mechanism by which telomeres and the enzyme telomerase protect chromosomes.

## 2.10 Establishment of the National Cancer Institute (NCI)

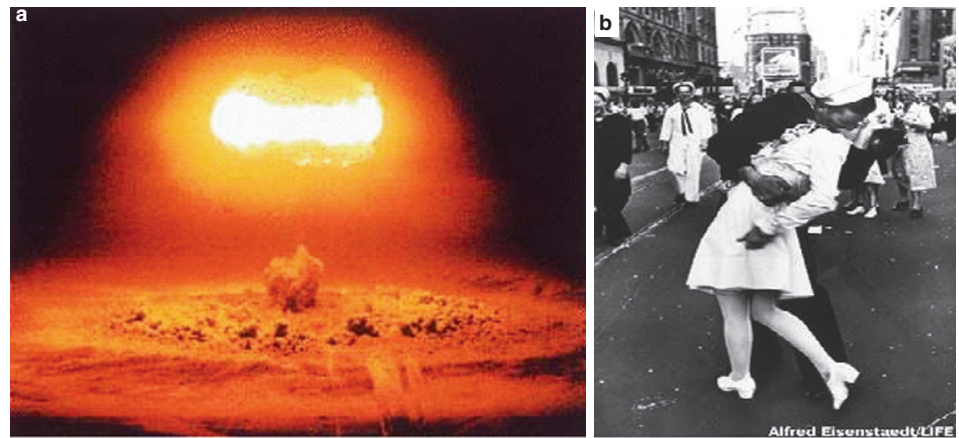
Laboratory and clinical research of our department has been generously funded by the NCI. This is also true for nearly all US cancer research centers. The NCI was the first of the institutes of the NIH. The accomplishments of the NCI in the US program in cancer research and education constitute a national record of achievements of which not only US citizens but all humans can be intensely proud.

Several steps in the US government involvement in health matters and the formation of the NCI are listed [46].

1836: The Library of the Office of the Surgeon General was established (the present National Library of Medicine).

1879: The National Board of Health was created by law, the first, national medical research effort of the US government.

**Fig. 2.17** (a) Explosion of a test atomic bomb on July 16, 1945, near Alamogordo, NM [1]. (b) A spontaneous kiss in Times Square reflecting the intense excitement at the news of the end of WWII [9]



1912: The Public Health and Marine Hospital Service became the Public Health Service (PHS).

1930: The Ransdell Act redesignated the Hygienic Laboratory as the National Institute of Health, authorizing \$750,000 for construction of two buildings for NIH, and creating a system of fellowships.

1937: The National Cancer Institute Act was signed on July 23.

1938: The National Advisory Cancer Council recommended approval of the first awards for fellowships in cancer research.

1938–1942: Ms. Luke Wilson made a series of 5 gifts of land to the NIH, for a total of 92 acres in Bethesda, MD. Her gifts constitute the nucleus of the NIH present site of 306 acres. NIH moved to Bethesda in July.

1946: The Research Grants Office was formed at NIH to operate a program of extramural research grants and fellowships.

Of special interest to us is the fact that the first application to the NCI was in 1937 from a Harvard scientist for “cancer research”; the amount requested was \$4350 and was not funded. The first application funded was to Louis F. Fieser of Harvard on November 27, 1937, for \$27,550. He had proposed to investigate the structure and carcinogenic activity of several chemicals. Grant number was 1C3 (Personal communication, Frank Mahoney, 2007).

## 2.11 The End of WWII

We come to the end of the 50-year period, 1895–1945. WWII ended almost immediately after the explosion of an atomic bomb on Hiroshima, August 6, 1945, and on Nagasaki, August 9, 1945. The destructive power of an atomic bomb is illustrated by the first test explosion that occurred on July 16, 1945, at 05:29 AM, in the Jornada del Muerto (Journey of Death) desert 210 miles south of Los Alamos,

near Alamogordo, NM, Fig. 2.17a [1]. There ensued a most powerful and broad interest in nuclear physics not only for military applications, but also for medicine and biological research.

The uninhibited joy that greeted the news of the end of World War II is powerfully illustrated by the Eisenstadt photograph of a sailor grabbing and kissing a nurse in New York, Fig. 2.17b. This was published on the cover of *Life* magazine issue of August 14, 1945 [9]. A statue of that impulsive kiss was erected in Times Square in August 1995, i.e., the 50th anniversary of the kiss and the end of the war.

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