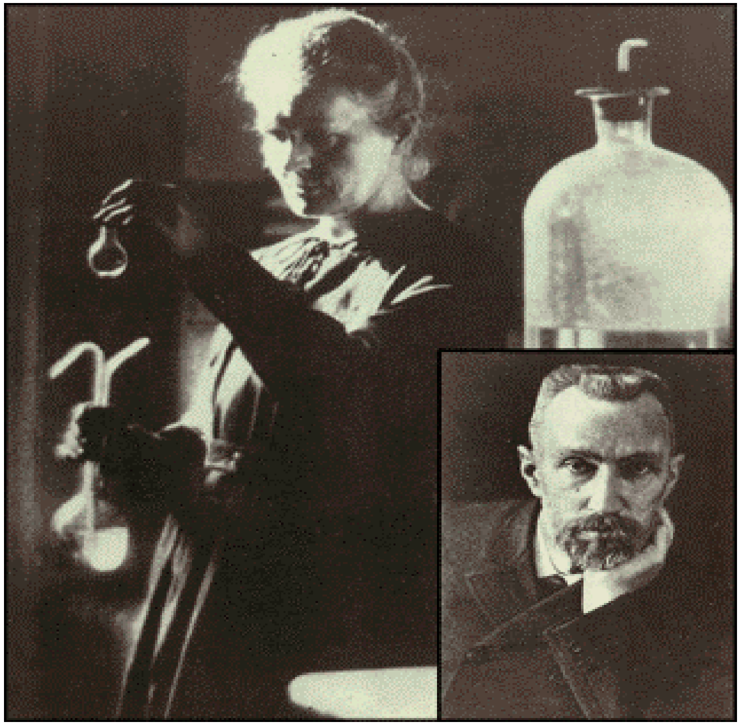
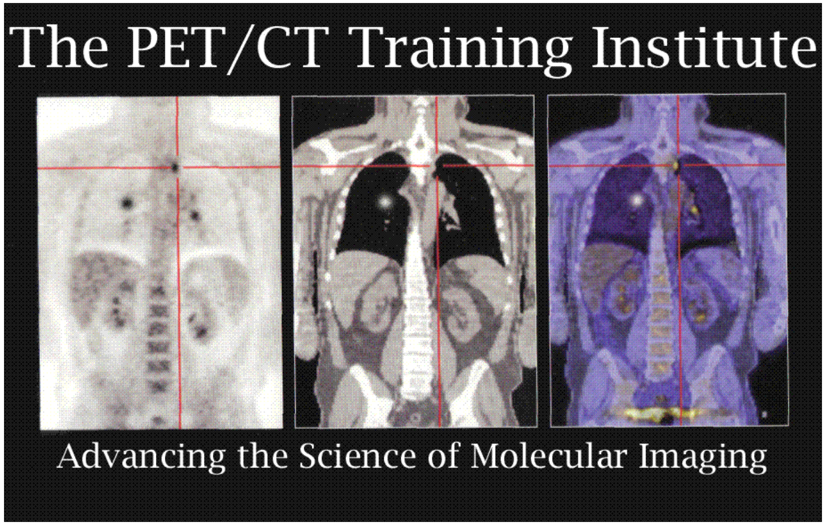


The History of Radiobiology



Tim Marshel R.T.
(R)(N)(CT)(MR)(NCT)(PET)(CNMT)

SNMTS Approved

<u>MIIWIQI: The History of Radiobiology</u>

45 Hr PET Registry Review Course

Reference Number: 028609

1.5 CEH's

Program Objectives

- Discuss the history of radiobiology
- State the Laws of Bergonie and Tribondeau
- Discuss the fractionation theory
- Define mutagenesis
- Describe the effects of oxygen
- Discuss reproductive failure
- Review the first 100 years of radiation therapy
- List the pioneers of radiation therapy
- Discuss the early years of radiation therapy
- Review early uses of radioactivity and radium
- View the newest radiotherapy system on the market today

History of Radiobiology

- **Radiobiology**- the branch of science concerned with the methods of interaction and the effects of ionizing radiation on living systems
- Combination of biology, physics, and epidemiology
- 3 incidents triggered beginning of radiobiology
- Wilhelm Conrad Roentgen's discovery of x-rays in 1895
- Henri Becquerel's observance of rays given off by a uranium substance
- In 1898 Marie Curie discovered radium (radioactivity)
- Early radiobiology observations included:

Skin Erythema – radiation induced skin reddening

Epilation- radiation induced hair loss

Anemia- less than normal number of red blood cells

Law of Bergonie and Tribondeau

- 1906 J.Bergonie and L.Tribondeau exposed rodent testicles to x-rays and observed effects of radiation
- Selected testes since this organ contains both mature cells and immature cells
- **Spermatozoa**- mature cells;
- **Spermatogonia** / **Spermatocytes**- immature cells
- Mature cells (*spermatozoa*) cells do not divide
- Immature cells (*spermatogonia*) cells divide frequently
- **The Law of Bergonie and Tribondeau** states:

1. Stem cells are more radiosensitive than mature cells. The more mature a cell is, the more radio resistant
2. Younger tissues and organs are more radiosensitive than older tissues and organs
3. The higher the metabolic activity of a cell, the more radiosensitive it is
4. The greater the proliferation and growth rate for tissues, the greater the radio sensitivity

Fractionation Theory

- Brought the fractionation theory from France in 1920’s& 1930’s
- Ram testicles were exposed to large doses of ionizing radiation
- Rams could be sterilized with one large dose
- Quantity of radiation caused skin adjacent to ram’s scrotum to have a reaction
- If large dose was fractionated animals would become sterile
- Less damage to their skin

Mutagenesis

- H.Muller discovered that ionizing radiation produced mutations
- Discovered his experiments with fruit flies
- His finding is termed mutagenesis
- Radiation-induced mutations were the same as those produced in nature
- Irradiating the fruit flies did not create any unusual effects
- Frequency of mutations was intensified
- Effects of ionization were not unique to radiation
- Effects could have been caused by other things than radiation

Effects of Oxygen

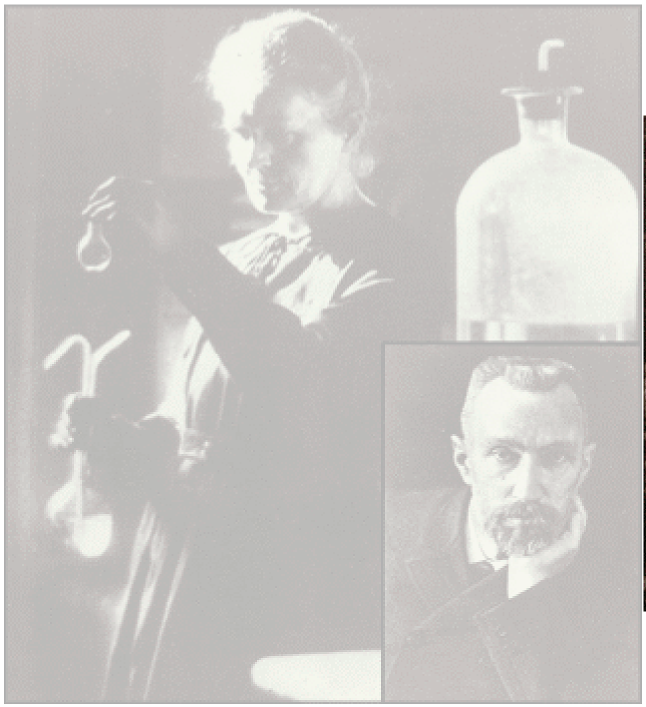
- 1940's & 1950's
- Oxygen is termed a radio sensitizer
- It increases the cell killing effect of a given dose of radiation
- Occurs as a result of the increased production of free radicals when ionizing radiation is delivered in the presence of oxygen

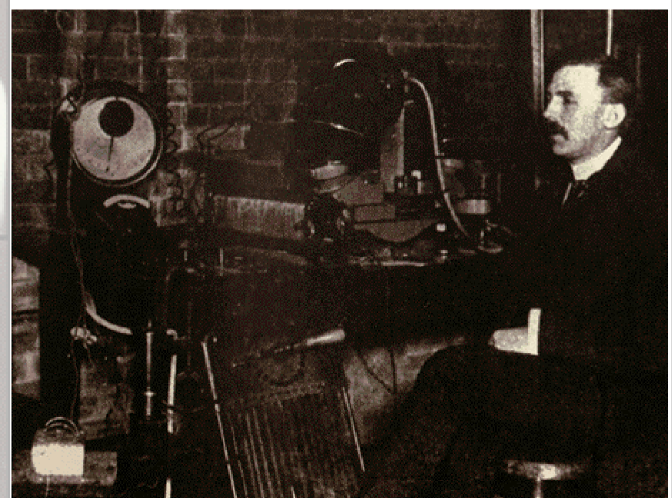
Reproductive Failure

- Puck and Marcus exposed human uterine cervix cells to varying doses of radiation
- Experimentally determined reproductive failure by counting the number of colonies formed by irradiated cells
- Units of measurement were developed to quantify radiation levels
- Also to track effects of exposure by varying the levels of exposure

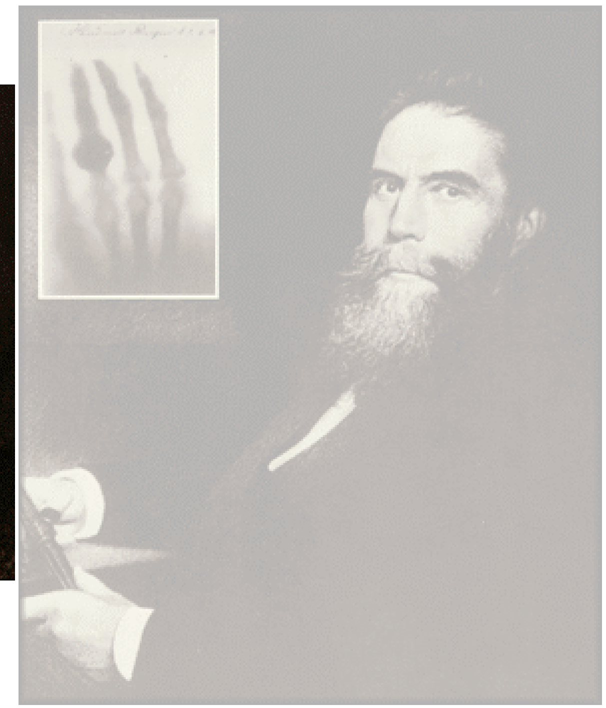
Lets take a glance at…
Radiation Oncology:
100 Years of Therapy

The Early Pioneers





Ernest Rutherford
(1871-1937)



Pierre Curie (1859-1906)
Marie Curie (1867-1934)

Wilhelm Conrad Roentge
(1845-1923)

The first century of radiation oncology has seen numerous pioneering advances in healing, patient care, and scientific knowledge.

The history of the field is an integration of the various components--clinical medicine, medical physics, dosimetry, pathology, and radiation biology.

•Roentgen's magical rays discovered 1895.

•Applied to both benign and malignant conditions within weeks of the first news of the strange "new light" in 1896.

•X-rays were seen as one of the miracle cures of the new age. Soon the natural radiations of radium would be added to treat an increasing range of surface and deep-seated ailments.

•Even the news that the rays could cause burns or more serious sequellae did not dampen enthusiasm or diffuse the general astonishment that the rays which could see through living human flesh could also cure disease.

Roentgen's work was in the mainstream of nineteenth century physical investigations into light and energy. Seeking to better understand the nature of light, Roentgen built on the work of many other investigators but, in the process, came upon something entirely unexpected.

Site of discovery. Roentgen's lab where, on 8 November 1895, he noticed an extraordinary glow while investigating the behavior of light outside a shrouded cathode tube. To his astonishment, he saw the shadows of the bones of his hand when held between the tube and a fluorescent screen. Within two months he had published a carefully reasoned description of his work and the famous radiograph of his wife's hand. Aware of the immediate implications for medical diagnosis, Roentgen did not envision more direct applications.

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- Emil Grubbe, a Chicago electrician and metallurgist, first treated the recurrent breast cancer of a 55-year-old woman in the last days of January 1896--only weeks after the announcement of Roentgen's discovery.
- John Daniel described scalp epilation during a diagnostic exposure in 1896.
- William Pusey (1898) reported beneficial effects on hypertrichosis and acne
- Heber Robarts editor (1902) could list over 100 different surface and deep-seated conditions treated by 1902.
- Leopold Freund pioneered the use of the rays in benign conditions in 1898 (pediatric nevus and lupus vulgaris)
- Frands Williams published on the X-ray cure of a cancer of the lower lip (1901).

Many early researchers suffered painful injuries or death from their work with the rays. Efforts to devise practical dose measurement and protective shielding soon followed (clockwise from upper left): Emil Grubbe, like many of his colleagues, experienced severe radioepidermatitis of the hands; in Philadelphia, C.L. Leonard advocated lead and leather shielding, while George Pfahler worked with filtration and selective absorption; Thomas Edison, here seen in 1896 fluoroscoping the hand of his ill-fated assistant, Clarence Dally; Mihran Kassabian photographically documented his own serial amputations; and Francis Williams who, in his 1901 text, advocated protective shielding for tube and patient.

Early cures. In 1899, in Stockholm, Thor Stenbeck initiated the treatment of a 49-year-old woman's basal-cell carcinoma of the skin of the nose (above), delivering over 100 treatments in the course of 9 months. The patient was living and well 30 years later. At the same time, Tage Sjörgen cured a squamous cell epithelioma with fifty treatments over 30 months (below). Many patients marveled at the experience of receiving radiations.

Extraordinary follow-up. In November 1896, Leopold Freund in Vienna irradiated a four-year-old girl with an extensive dorsal hairy nevus. Although the immediate result was a painful moist radioepidermatitis, permanent regression followed. The young woman led a normal life, bearing a healthy son. Photographs taken at 74 years of age, however, reveal lumbar skin scarring, kyphoses, keratoses, and sequelar osteoporosis.

Radioactivity and radium. Parisian physicist Antoine Henri Becquerel's 1896 discovery of natural radiations emanating from uranium salts. The Curies isolated the elements emitting Becquerel's natural radioactivity. During 1898 they announced their discovery of two such elements, polonium and radium. In 1903 Becquerel and the Curies shared the Nobel Prize in physics for their work on radioactivity. After Pierre's death in a cycling accident, Marie continued her researches and won a second Nobel Prize in 1911. She died of aplastic anemia in 1934.

Early radium treatment. The Curies loaned small amounts to various Paris physicians, including Louis Wickham and Paul Desgrais who in 1907 treated this child's erectile angioma using a crossfire technique. Below, early applicators were devised in a number of shapes and sizes-flat for surface work and cylindrical for intracavitary use.

Medical Record

Margaret Cleaves, M.D., (1848-1917) on radium. In Light Energy, published in 1904, this New York physician described inserting radium into the uterine cavity of a patient with carcinoma of the cervix.

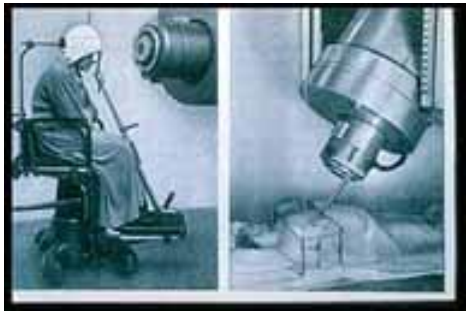
The Coolidge Tube. William Coolidge of GE with his "hot" cathode tube, developed in 1912 and 1913. The tube provided a reliable beam with improved hardness and penetration, and eliminated the guesswork of "gas" tubes. The Coolidge tubes also made possible the development of orthovoltage kV X-ray therapy, which was improved by Lewis Gregory Cole of New York and James Case of Michigan.

International cooperation. Friedrich Dessauer advanced the so-called 'laws of homogeneous irradiation,' promoted filter-hardened radiation beams and central axis treatment planning, and worked on total body irradiation. Here he is seen in Germany in 1920 (left) with visiting colleagues 0. Seeman, William Coolidge, Walter Friedrich, and Otto Glasser.

Divergent theories. Baclesse (center, bottom) summarized two opposing dose methods. Wintz (center, top) and Holzknecht (at fluoroscope) advocated the delivery of the largest possible dose in the shortest possible time. Others, like Leopold Freund (right, bottom) and Claudius Regaud (right, top) favored repeated numbers of smaller doses, or fractionation. Robert Kienbock's (center) emphasis on proper dose measurement and Coutard's 1920s reports of patient cures helped radiation therapy evolve into a legitimate medical science.

Telecurietherapy. Popular into the 1930s, these apparatus included (left) the Sluys-Kessler radium bomb, with an applicator array designed to conform to the required volumes, but requiring long treatment times. Failla's radium bombs, like that at Roosevelt Hospital, N.Y.,(right) refined radium strength and offered higher dose rates, longer SSDs, and improved shielding and collimation.

1 MeV Metropolitan Vickers Unit, St. Bartholomew's, London, 1937. Dr. Ralph Phillips and physicist George Innes devised this 30' long X-ray tube and 600 kVp generator, with variable field sizes, moving couch, vacuum system, parallel plate monitoring, light field localization, and vertical/rotational capabilities. Others were soon in place in Seattle, New York, and California.



First clinical van de Graaff generator, 1933-37. Robert van de Graaff devised a direct current electrostatic generator in 1929. A 2 Mv dedicated radiotherapy unit installed at Huntington Memorial Hospital in Boston used the van de Graaff and boasted pre-treatment planning, wedge filters, and various orientations. The Royal Marsden unit shown had a turntable and set-up lines, but due to field size and insufficient output was not clinically practical.

Mullard (Philips) 4 MV double.gantry linac. First installed at Newcastle Hospital, 1953. This unit featured a nearly isocentric mount, a 1 meter traveling waveguide, 2 MV magnetron, and a false floor.

Siemens (Applied Radiation Co.) Mevatron VIII, a pioneering device for dual photon beams, which underwent further upgrades after its initial appearance in 1966.

Varian Clinac treatment unit, 1990s. Today's integrated medical linac has been enhanced by computerized controls and easier operation in the quest for optimal treatment in cancer.

Today's Radiation Therapy Systems…..

Radiotherapy

Gamma Knife

…and the new kid on the block….**Cyberknife**