1.- Cancer as disease, history

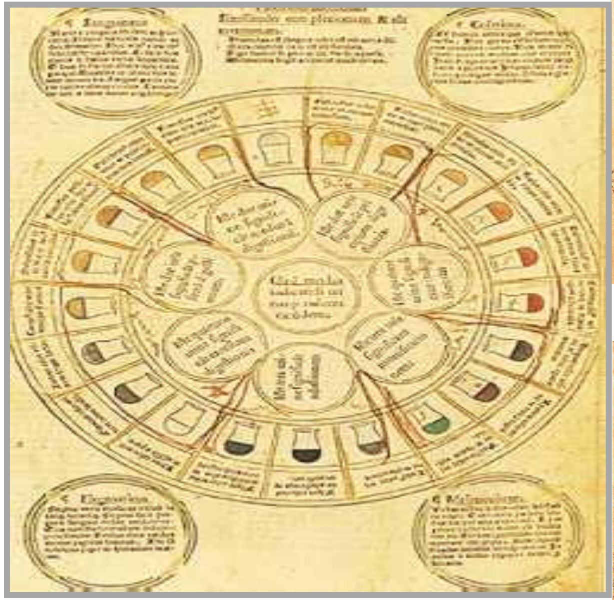
Cancer Described by the Ancient Egyptians

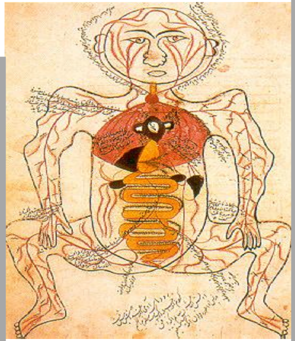
The "Smith" and "Ebers" papyri, dating back to 1600 BC and 2500 BC, respectively, contain descriptions of cancer and prescribe surgical and pharmacological treatments.

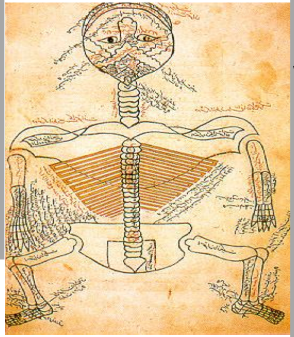
The naming of Cancer

Hippocrates, in 400 BC, gave the name “karkinos”, and “karkinoma” – the Greek words for Crab, to groups of diseases he studied, that included cancers of breast, uterus, stomach, and skin. The hard center and claw-like projections of tumors he observed reminded him of the crustacean. “Cancer” is the word’s Latin form.

Early Theories of Cancer



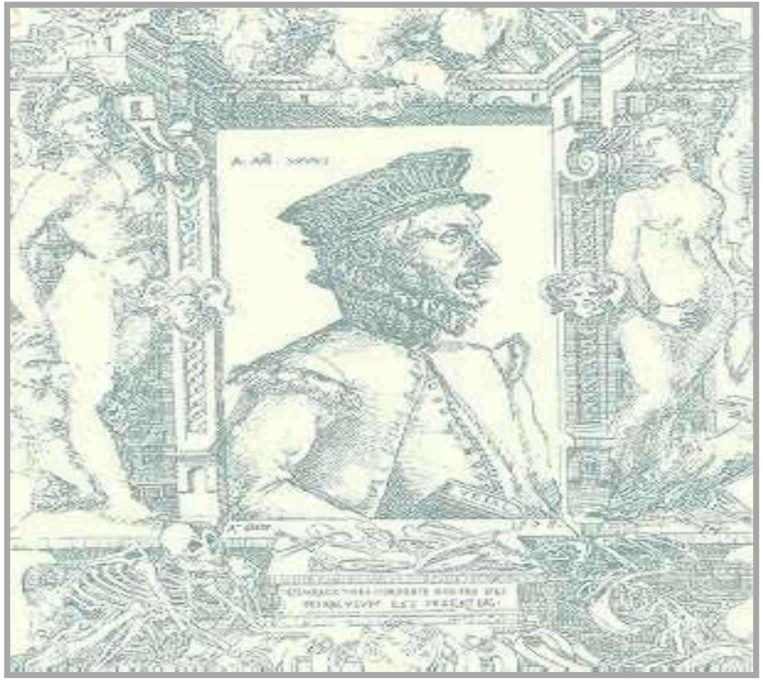




Sin, Satan, Astrology, and the ancient theory of four humors – blood, phlegm, yellow bile and black bile were invoked to explain human illness. Uroscopy charts depicted shades and conditions of urine samples and indicated what diseases might be the cause.

Cancer was explained as a result of an excess of black bile, curable only in early stages.

The Not So Early Theories of Cancer

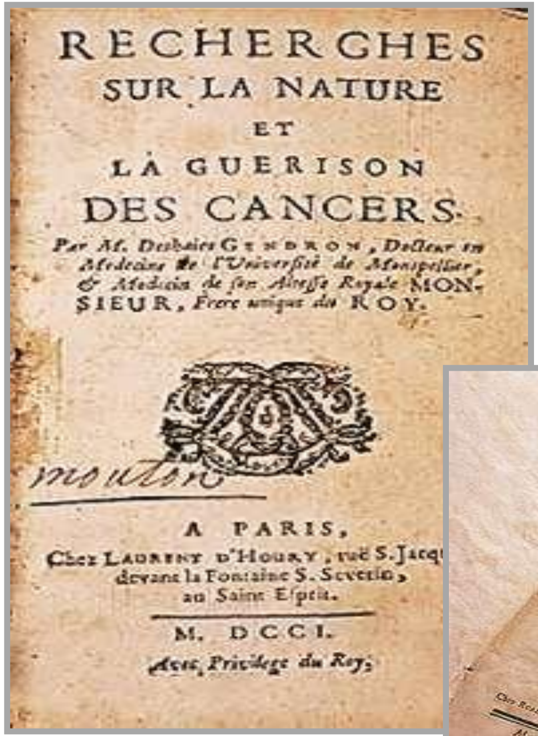


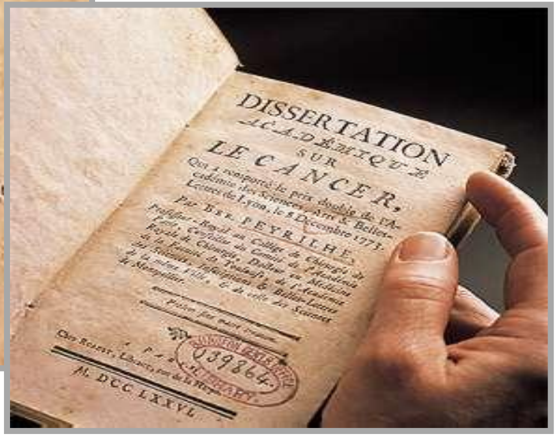
The old theory of disease based on bodily humors was discarded in the 17th century.

Aselli's discovery of the lymphatic system suggested abnormalities of lymph as the primary cause of cancer.

Lymphatic drainage became the key factor in developing more extensive surgical removal of cancer.

Oncology’s Arrival in the Age of Reason…



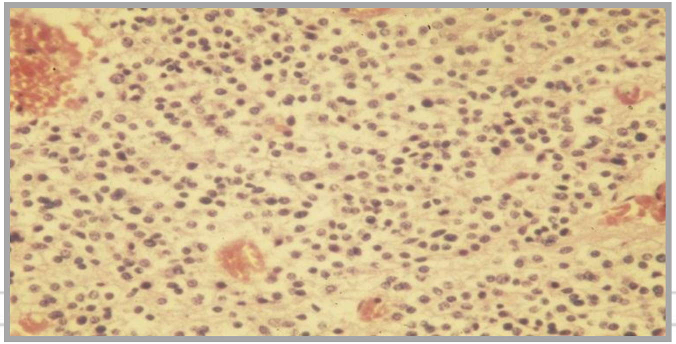


2.- Cancer as disease, definitions

What is cancer?

"Cancer is a single disease and it is a hundred diseases with similar symptoms."

- The uncontrolled growth of abnormal cells derived from normal tissues
- Can spread from the site of origin to other sites



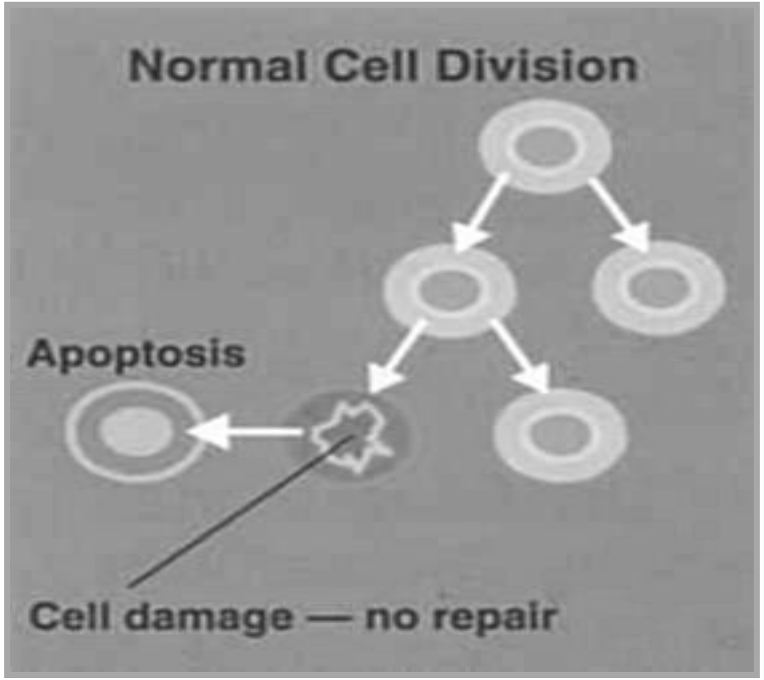
- "A group of diseases in which cells
- grow and spread unrestrained
- throughout the body."

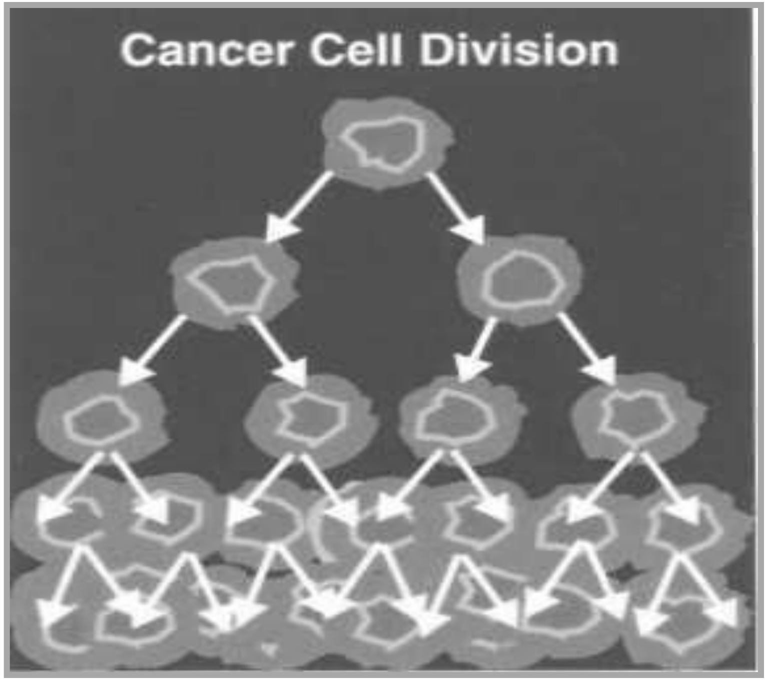
1st characteristic

2nd characteristic

What is cancer?

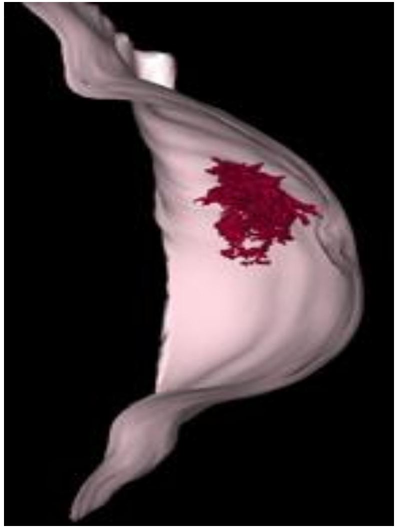
What is cancer?



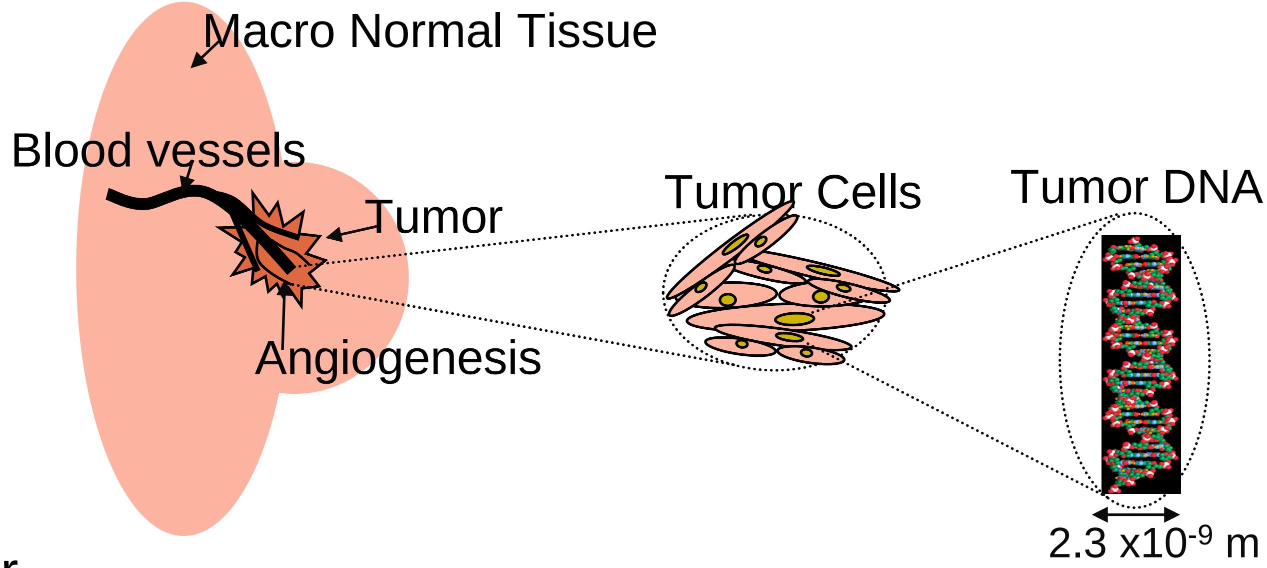


Tumors

Tumors are disorganized tissues that **expand without limit**, compromising the function of organs and threatening the life of the organisms.



A real breast tumor

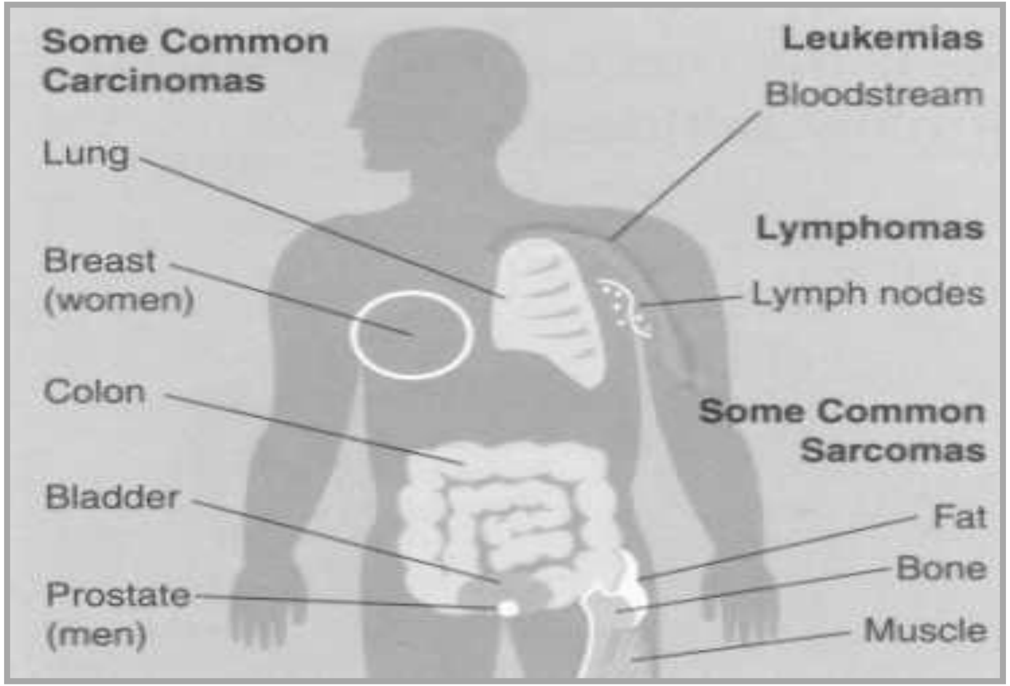


Invasion is the signature and the unifying aspect of malignant tumors.

Classification

There are an estimated 200 different kinds of cancers.

- Carcinomas
- Sarcomas
- Lymphomas
- Leukemias



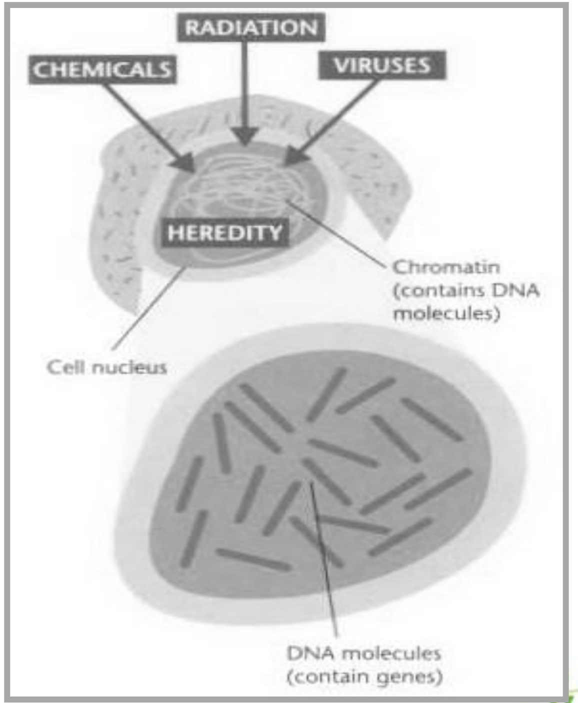
Cancer biology

"Cancer is a disease of the genes"

Chemicals and radiation → **Damages**

Viruses → **Introduce their own DNA**

Heredity → **Passes alterations**



Cancer staging

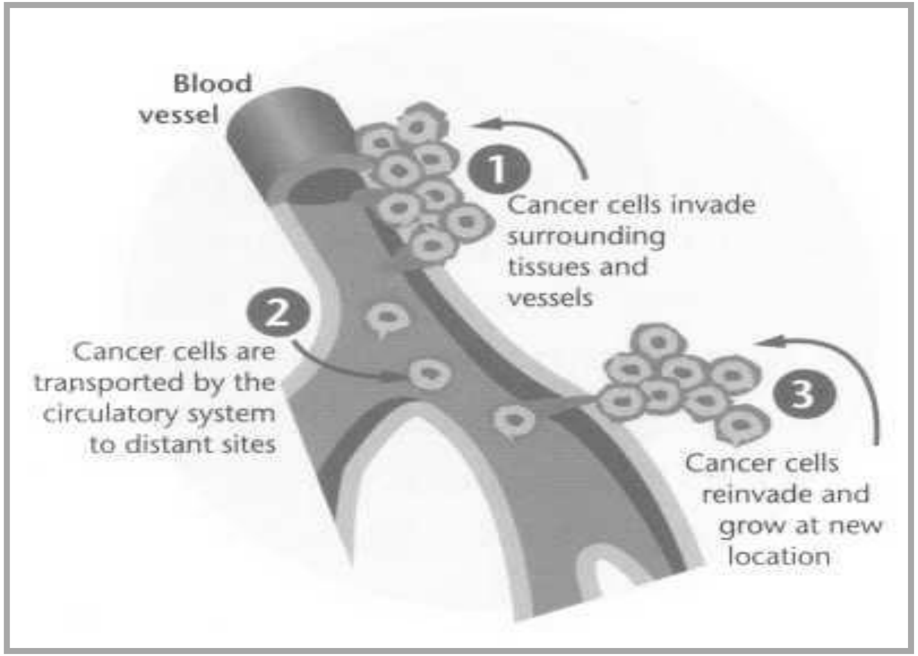
Objectives:

- Estimate prognosis
- Determine the best course of therapy
- Facilitate investigation

- The stage of a tumor describes:
  - Size
  - Extent of regional lymph node spread
  - Presence or absence of metastasis

Cancer staging – tumor invasion

- Direct invasion of local tissue
- Metastasis to regional/distant lymph nodes
- Metastasis to distant organs



Staging systems

- T N M Classification System:

  T= size and extent of primary tumor

  N= degree of nodal involvement

  M= presence and extent of metastasis

Treatment principles

- Curative or Palliative

- Curative: The intention is to eradicate the tumor and keep the patient free of disease.

- Palliative: The intention is to prolong life and offer the patient an acceptable “quality of life” when cure is not a possibility any more.

Treatment: Multi-modality approach

- Surgery
  - Works best for tumors that are well contained and accessible; some are neither
- Radiation Oncology
  - Teletherapy
    - Conventional/Conformal
    - Intensity Modulation (IMRT), Volumetric Modulated Arc Therapy
    - Stereotactic RT
    - IORT (Intra-op)
    - IGRT (Image Guided Therapy)
  - Brachytherapy (LDR-MDR-HDR)
  - Nuclear Medicine - Non sealed sources
- Chemotherapy
  - Antimitotic Drugs/Growth Factors (GF)
  - Biologic Response Modifiers
  - Angiogenesis Inhibitors

Multi-disciplinary approach: Integrated patient care

- Combination of different treatment modalities available, with the intent of improving treatment outcome in terms of survival and quality of survival which result in better local control of the disease.

  - Surgery
  - Radiation Therapy
  - Clinical Oncology (Chemotherapy)

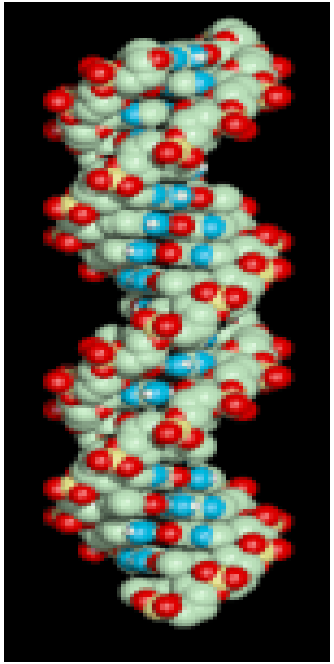
Principles of radiotherapy

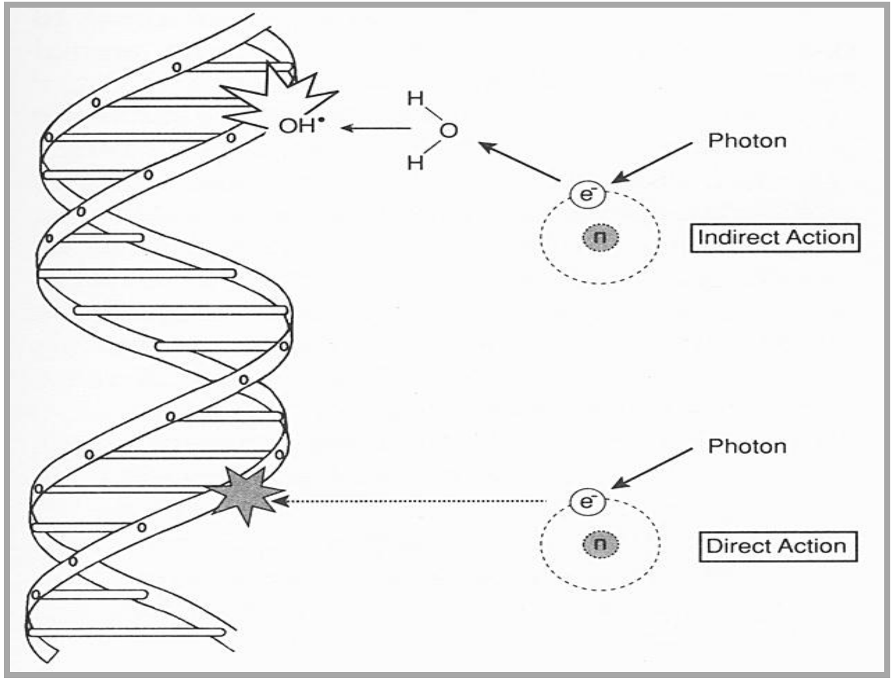
- Radiation Therapy is used in cancer treatment to destroy tumor cells, while minimizing damage to normal cells.

- Radiation is not selective, it damages both normal cells and tumor cells. Fortunately, healthy cells can repair themselves more readily than tumor cells, under some conditions.

- Treatment should be planned in such a way that allows to deliver the largest possible dose to the "target volume," minimizing the effect of ionizing radiation on healthy surrounding tissue and critical structures.

Radiobiology





~**60%** of all damage

Why fractionate treatment?

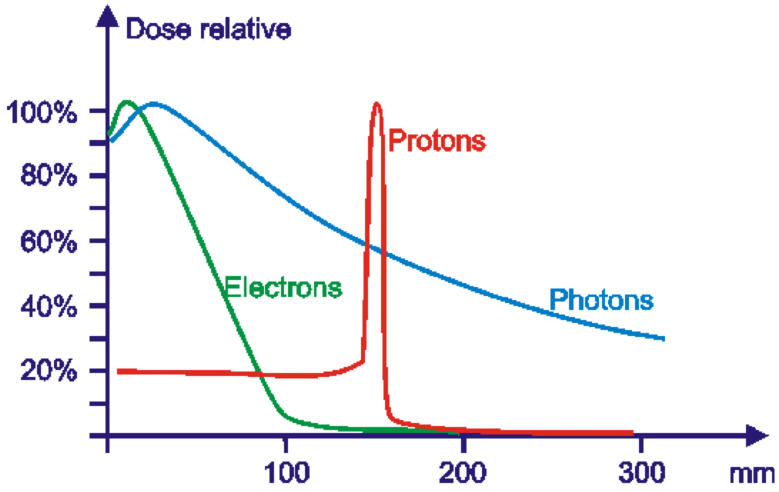
- *The biological response of tissue to radiation depends on the combined action of 4 different factors (the 4 R's):*

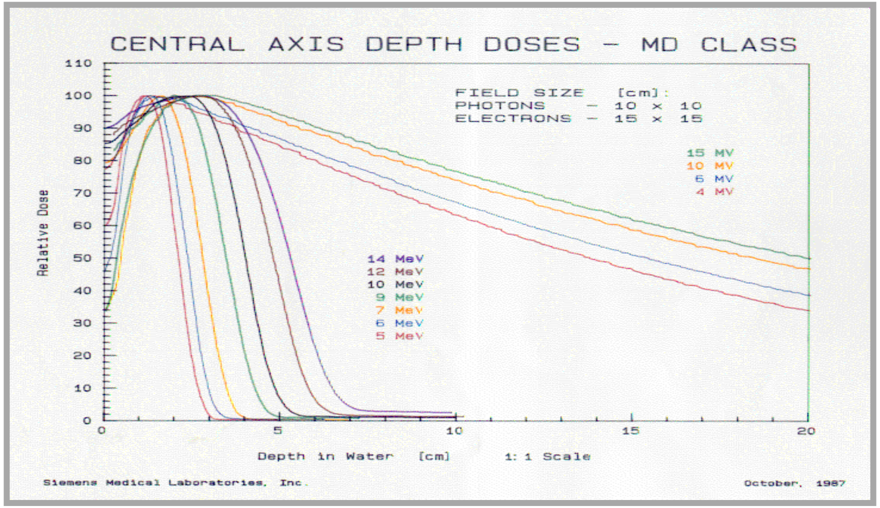
- **Repair** of sub-lethal DNA damage
- **Repopulation** or the division of surviving cells
- **Reoxygenation** of "hybernating" cells located far from a blood supply
- **Reassortment** of cells in all phases of the cycle

Remember: Normal tissues repair well if the damage is not too intense.

And: We *can't* kill all the tumor cells at once due to the latter 3 "R"'s.

Particles, energies, etc



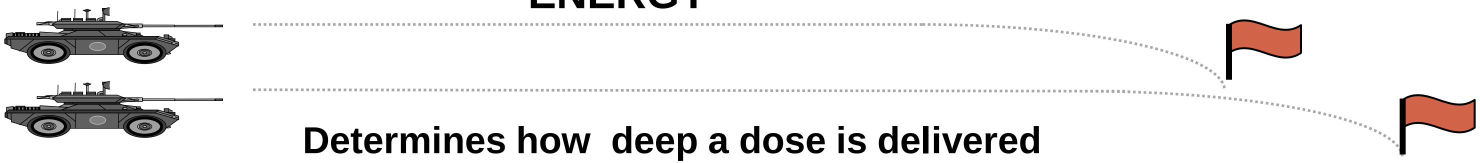


Definitions: Dose, Energy, Dose Rate

ENERGY

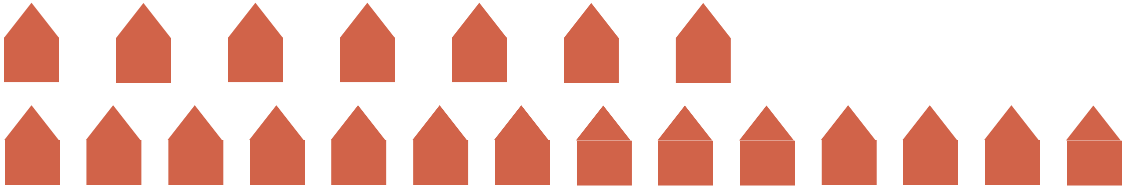
6 MV

10 MV



Determines how deep a dose is delivered

DOSE

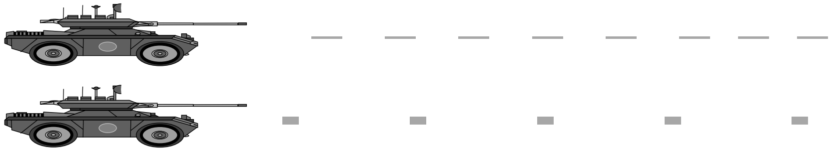


200cGy

300cGy

Determines how much ionizing radiation is delivered

DOSE RATE

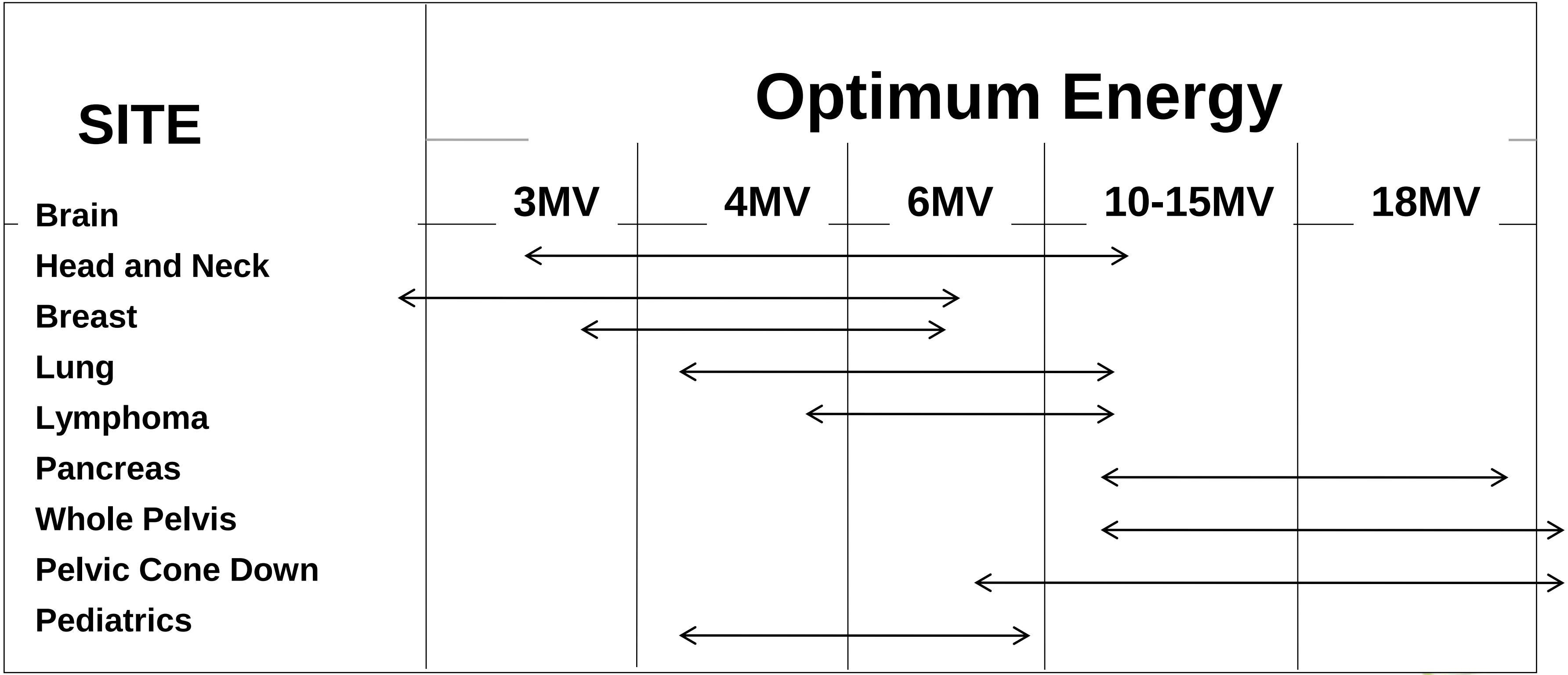


200MU/min

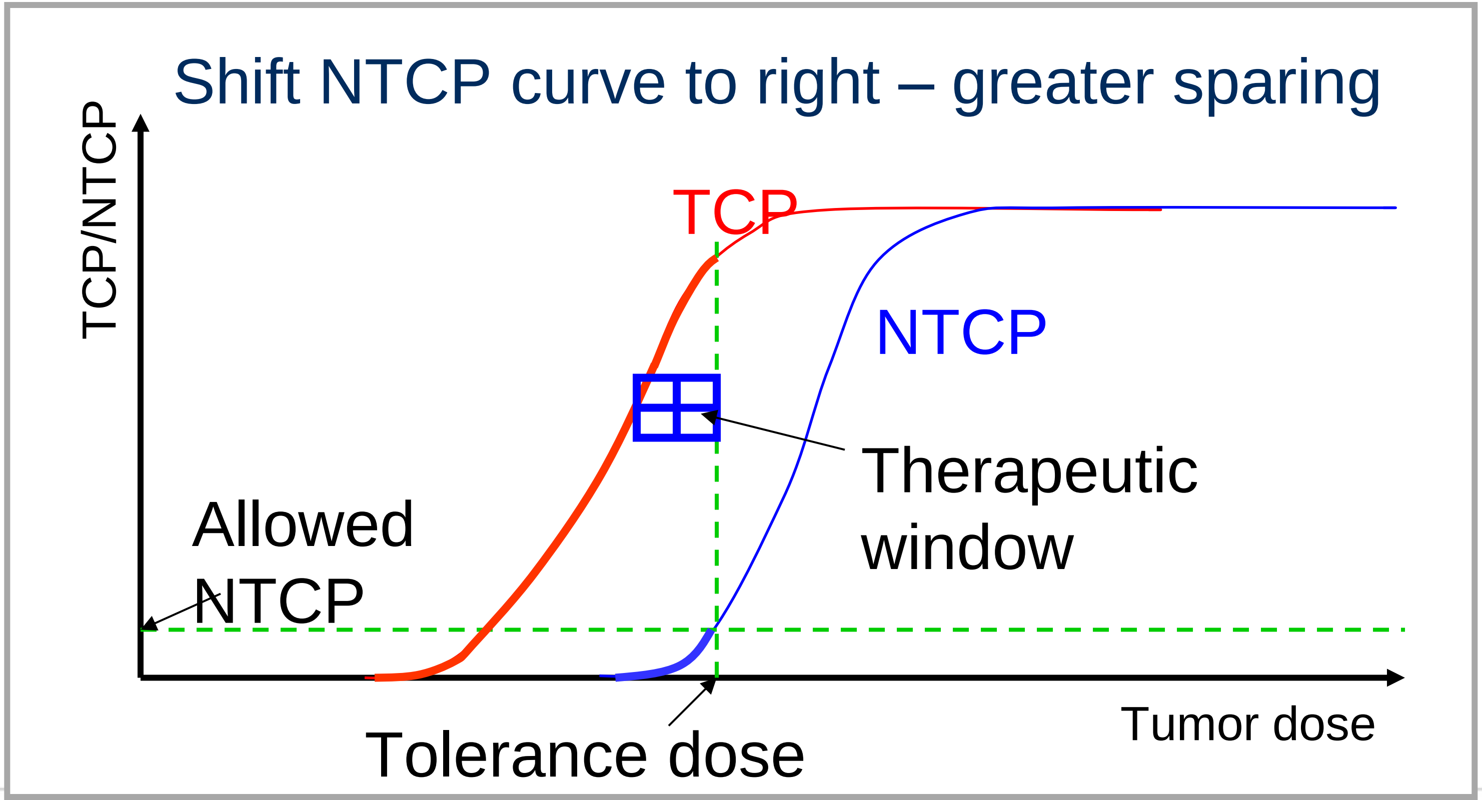
100MU/min

Determines how fast the dose is delivered

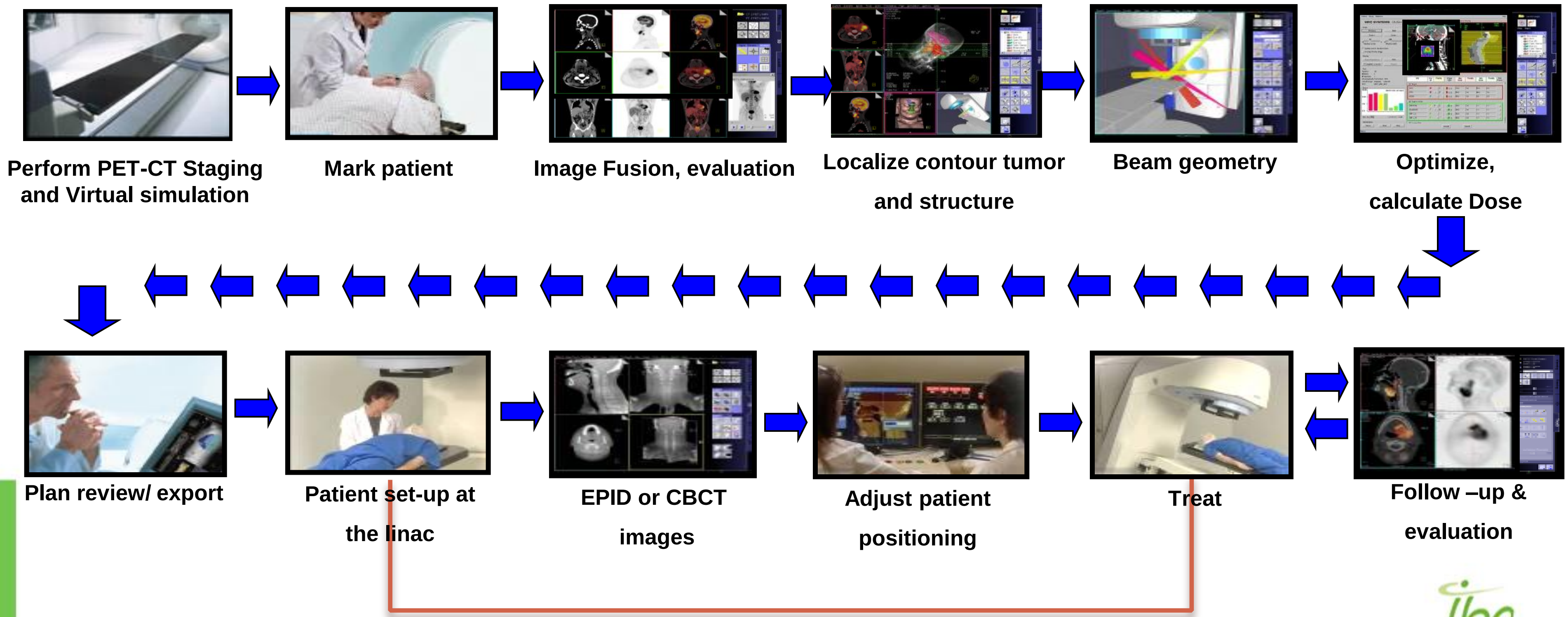
Useful clinical references

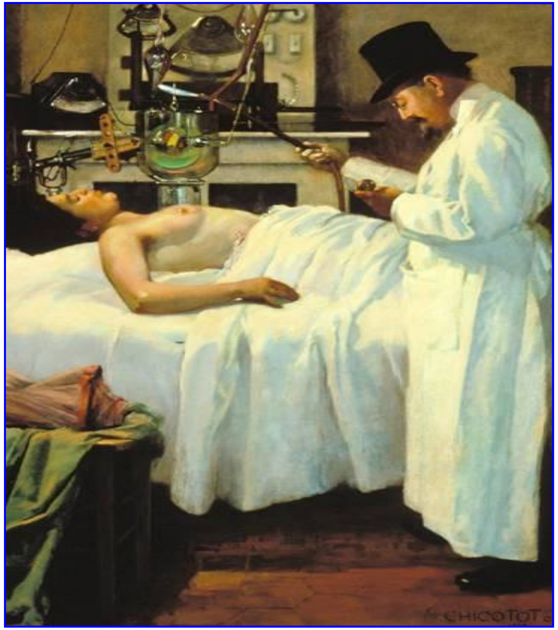


Therapeutic Window



Multi-modality Oncology Workflow





4.- Radiation Therapy: History

Historical review of Radiation Therapy Physics.

Rarely does a single discovery change the course of human existence, yet such was the case with Roentgen's magical rays. Along with other innovations resulting from these rays, the therapeutic value of ionizing radiation is being celebrated in this centennial of Roentgen's discovery. 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.

- From: Radiation Oncology: 110 Years of Therapy and Research - 1896 - 2007

Historical review of Radiation Therapy Physics.

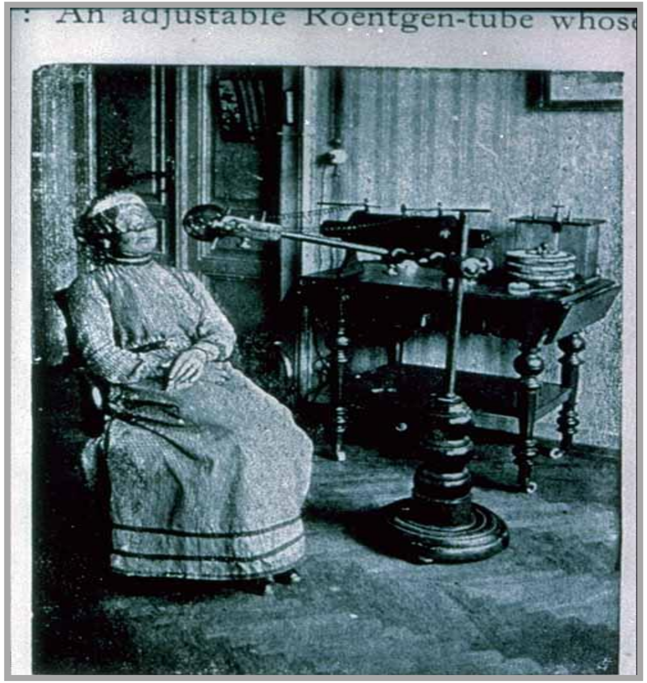
The first century of radiation oncology has seen numerous pioneering advances in healing, patient care, and scientific knowledge. The practitioners have evolved during three eras, from empirical experimentalists, through years as therapists advancing clinical observations and techniques, to today's multidisciplinary approach to individual cancer care. The history of the field has been graced by the many dedicated professionals whose integration of the various components--clinical medicine, medical physics, dosimetry, pathology, and radiation biology--have redefined the public and scientific perception of radiation oncology.

- From: Radiation Oncology: 110 Years of Therapy and Research - 1896 - 2007

Roentgen's magical rays

The famous picture…..

Fast medical use

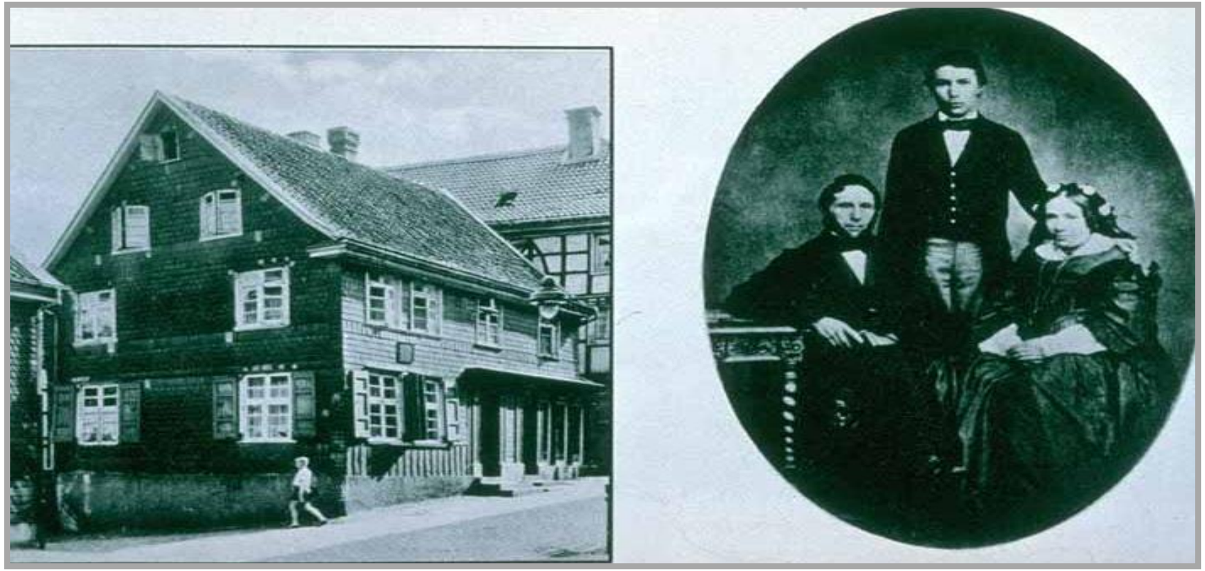


Amazing X-Rays

And their unknown consequences.

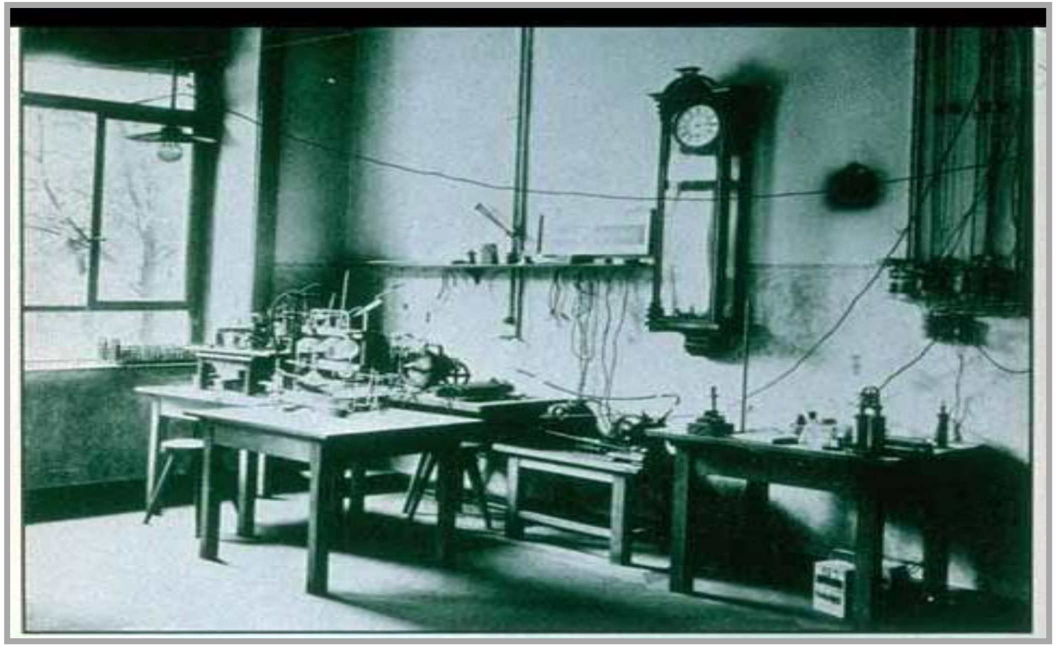
Dangerous X-Rays

Roentgen’s family



Roentgen family roots.
Born in 1845 in the Westphalia town of Lennep, Wilhelm Conrad Roentgen was the son of a German textile merchant and Dutch mother. After a doctorate in "physics-chemistry" he became a university professor, making his great discovery at the age of fifty at the University of Wurzburg.

Roentgen’s laboratory



Medical Records - 1902

From: MEDICAL RECORD (1902)

Emil H. Grubbe

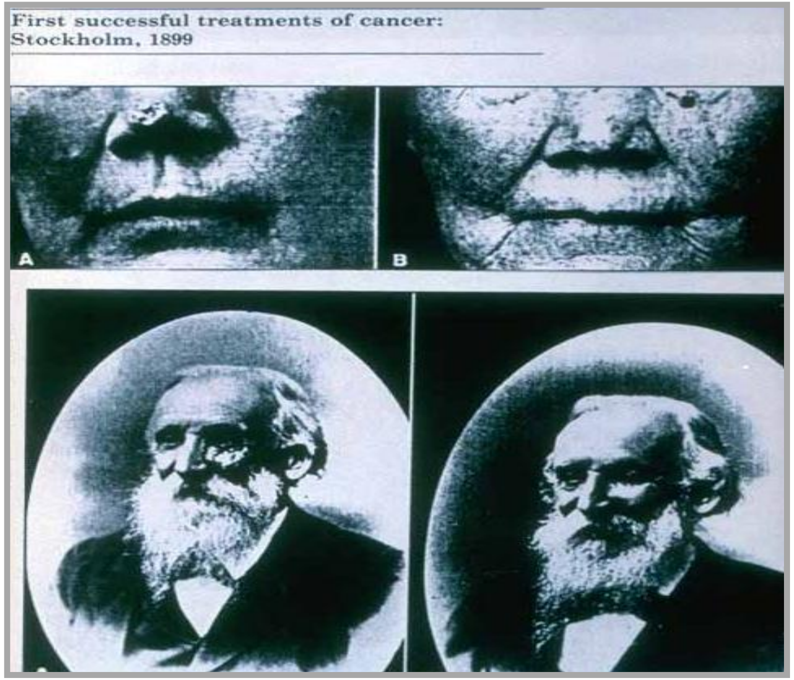
We have a number of other patients who have taken *x*-ray treatment, and who have remained free from recurrence for periods ranging from six months to a year and a half. Many other cases could be cited, but time and space forbid.

In conclusion, we wish to submit the following deductions:

1. The *x*-ray is the most remarkable therapeutic agent of the last decade.
2. In properly selected cases of so-called "incurable conditions" the *x*-ray has brought about remarkable results.
3. Relief from pain is one of the most prominent features of the treatment.
4. Retrogressive changes are noticed in all primary cancer or tuberculous growths.
5. The *x*-ray has a pronounced effect upon internal cancers.
6. The greatest value of the *x*-ray is obtained in treating post-operative cases to prevent recurrences.
7. The proportion of clinical cures by this treatment is greater than that obtainable by any other method of treatment.
8. We are positively justified in assuming an idiosyncrasy to *x*-rays.
9. The peculiarities of each case must be studied in order to get the best results, *i. e.* no strict rules for treatment can be laid down.
10. Dermatitis, if properly produced, is within certain limits a desirable feature of *x*-ray treatment.
11. Since the vacuum of an ordinary *x*-ray tube changes constantly, such tubes are useless for radio-therapeutic work, and only tubes which allow of perfect control of vacuum should be used.
12. The *x*-ray has a selective influence upon cells of the body; abnormal cells being effected more readily than the normal.
13. Hemorrhages and discharges are decidedly lessened and, ultimately, cease in the majority of cases.
14. Even in the hopeless, inoperable cases, the *x*-ray prolongs life, makes the patient comfortable, and the last hours free from pain.

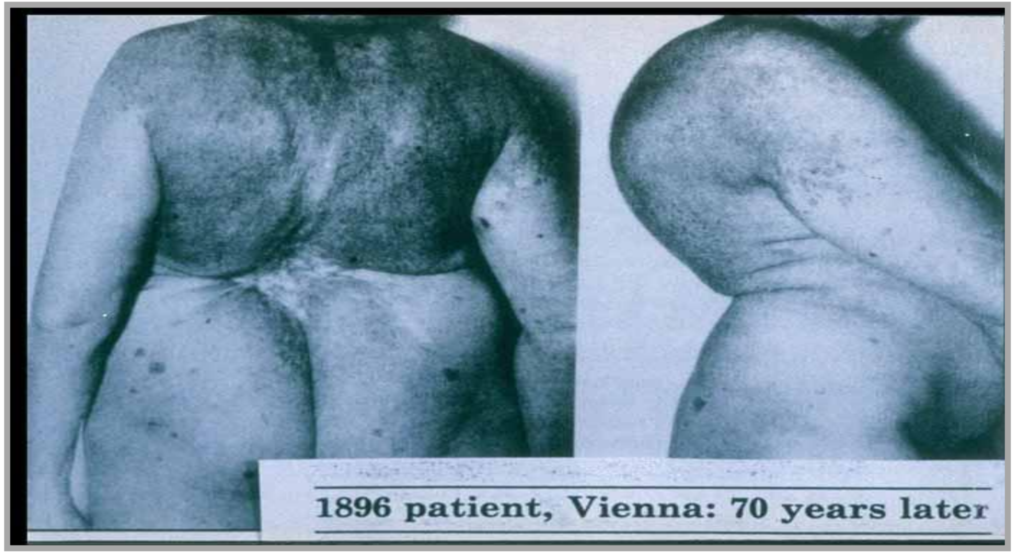
The use of the *x*-ray is, without doubt, a very valuable addition to

First successful treatments 1899



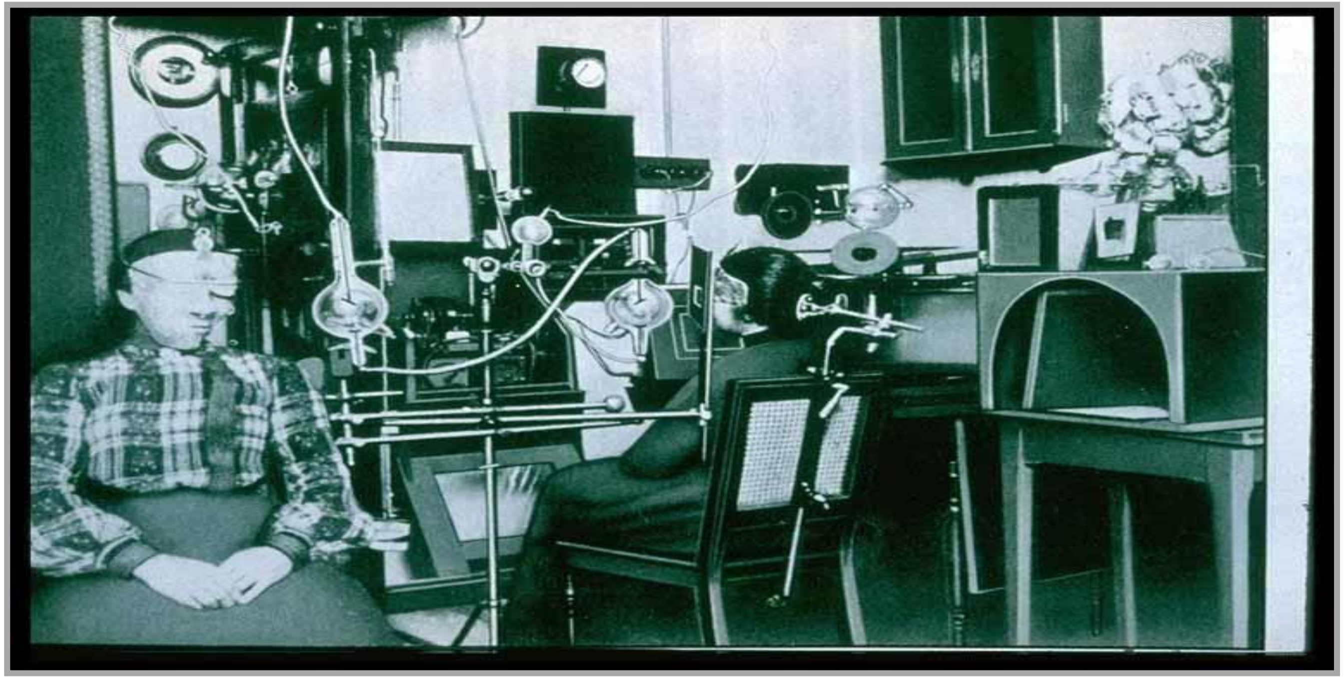
Early cures. In 1899, in Stockholm, Thor Stenbeck initiated the treatment of a 49-year-old woman's basal-cell carcinoma of the skin of the nose (above), delivering over 100 treatments in the course of 9 months. The patient was living and well 30 years later. At the same time, Tage Sjörgen cured a squamous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

Extraordinary follow-up

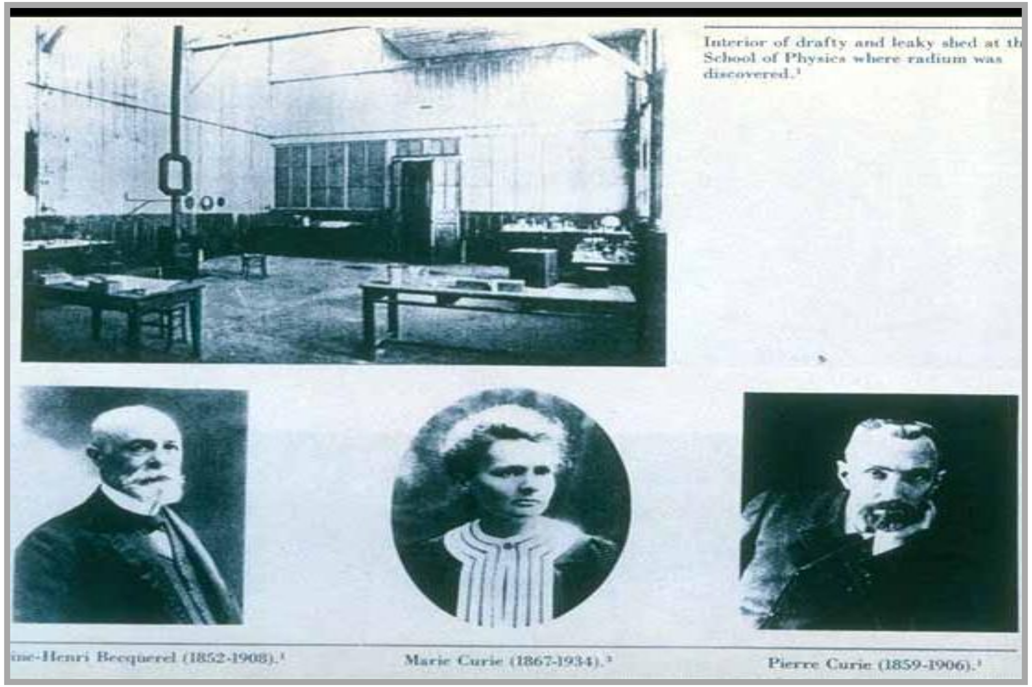


In November 1896, Leopold Freund in Vienna irradiated a 4 -year-old girl with an extensive dorsal hairy nevus. Although the immediate result was a painful moist radioepidermatitis, permanent regression followed. The young woman led a normal life, bearing a healthy son. Photographs taken at 74 years of age, however, reveal lumbar skin scarring, kyphoses, keratoses, and sequelar osteoporosis.

Clinical treatments: early uses of RX in EBRT

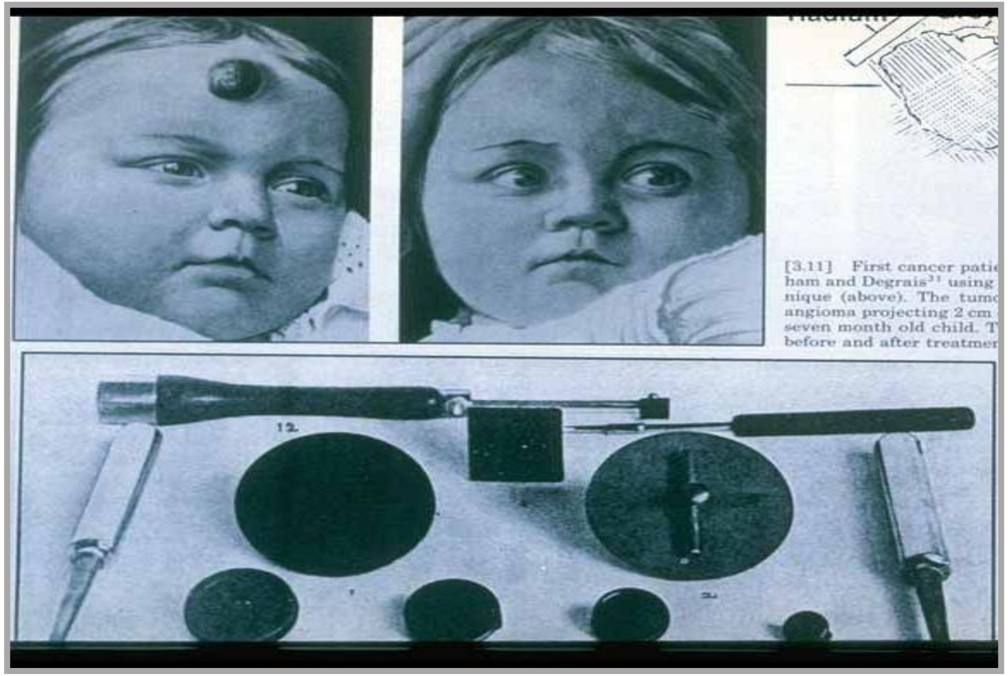


The “Paris” triangle



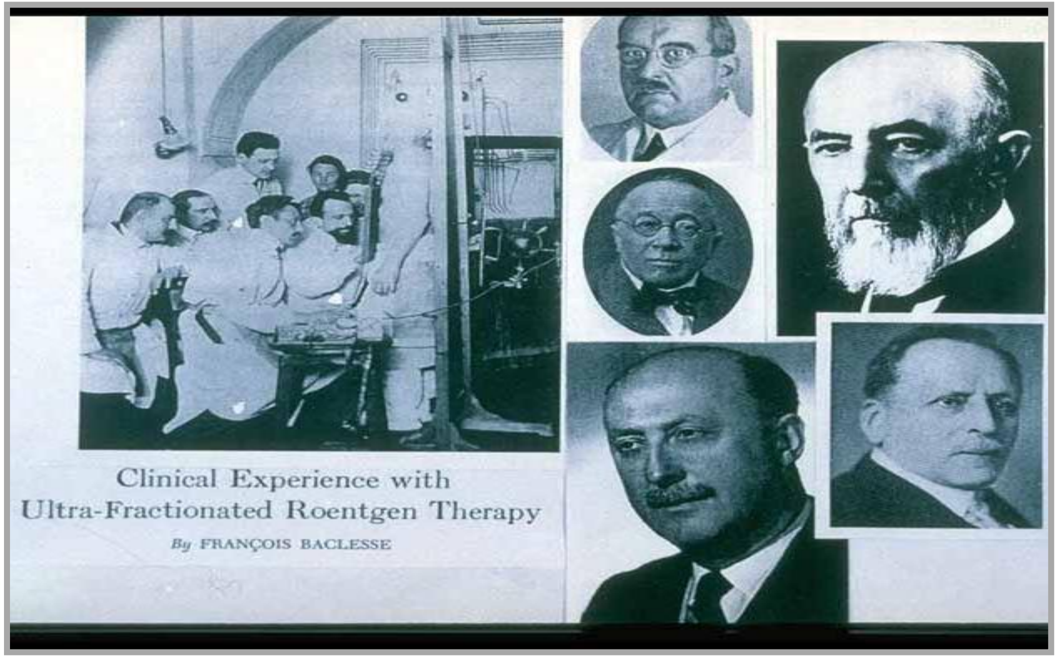
Radioactivity and radium. Parisian physicist Antoine Henri Becquerel's 1896 discovery of natural radiations emanating from uranium salts piqued the interest of Marie and Pierre Curie. Working in primitive conditions and using an alley and shed for research facilities, the Curies worked to isolate the 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 accident, Marie continued her researches and won a second Nobel Prize in 1911. She died of aplastic anemia in 1934.

Radium Treatments



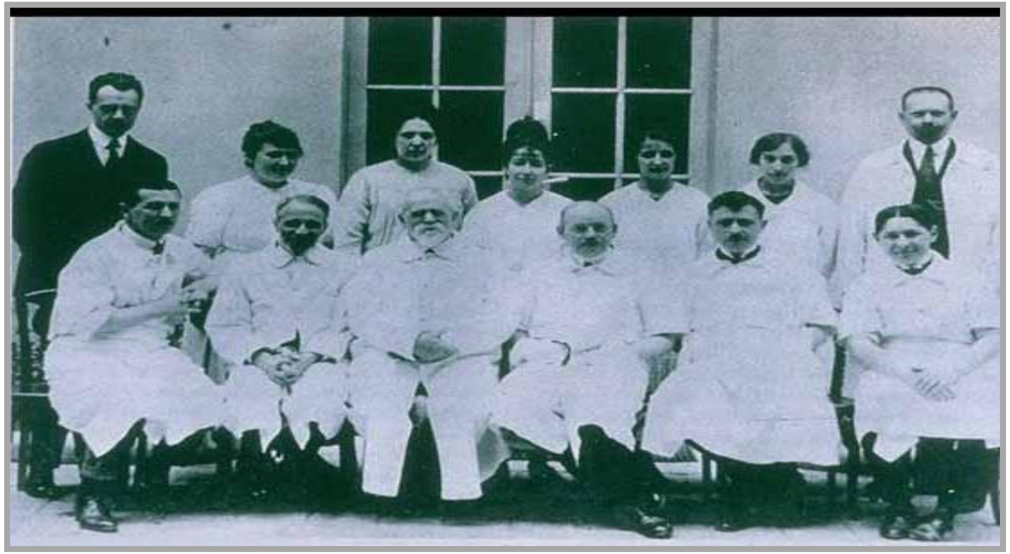
Early radium treatment. The painstaking process of extracting minute amounts of radium from tons of ore made the element extraordinarily rare and expensive in these earliest years. The Curies loaned small amounts to various Paris physicians, including Louis Wickham and Paul Desgrais who in 1907 treated 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.

Theories about fractionation ?



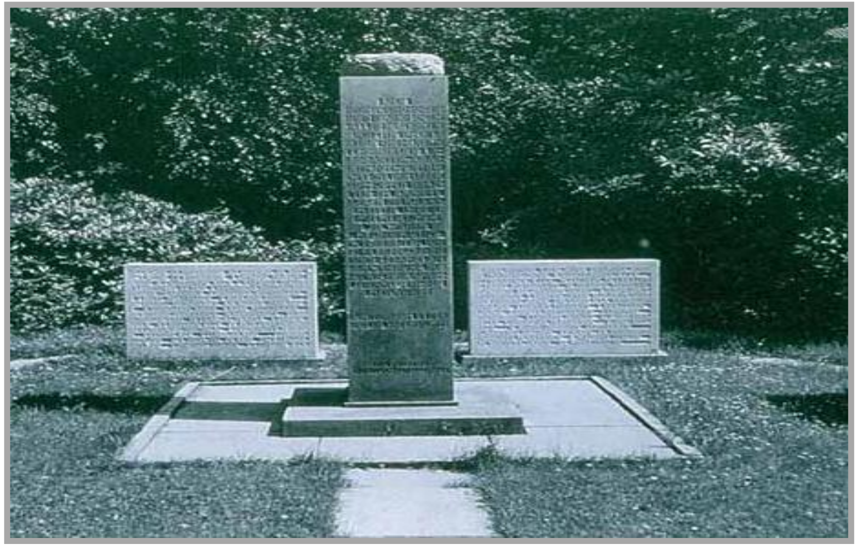
Divergent theories. Baclesse (center, bottom) summarized two opposing dose methods. Wintz (center, top) and Holzknecht (at fluoroscope) advocated the delivery of the largest possible dose in the shortest possible time. Others, like Leopold Freund (right, bottom) and Claudius Regaud (right, top) favored 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

Multidisciplinary approach



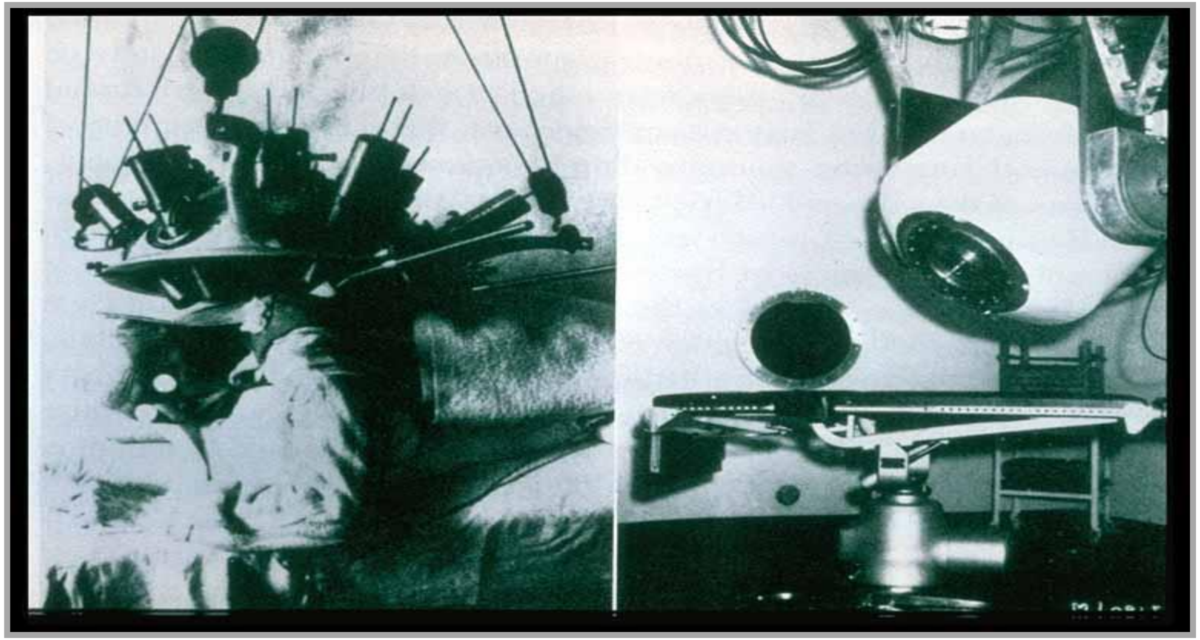
Beclere at the Radium Institute, 1927. Early academic centers enhanced radiodiagnosis, X-ray therapy, and radium therapy with basic research in biology, pathology, and physics. At the university of Paris, educator and innovator Antoine Beclere created a team approach among techs, lab workers, clerical staff, and engineers under the guidance of prominent clinicians, including (left to right, seated): Henri Coutard, Justin Jolly, Beclere, Octave Monod, Georges Richard, and Alfonso Esguerra. The support team stands behind

Memorial to radiation martyrs



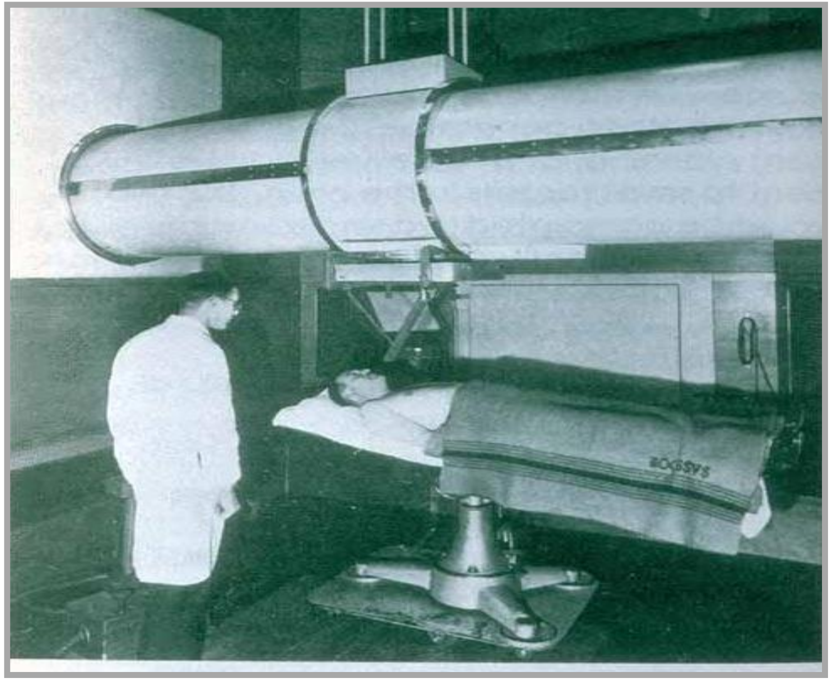
Memorial to radiation martyrs, Sankt Georg Hospital, Hamburg. The central stele, dedicated in 1936, contained the names of 159 physicians, scientists, and others who had died as a result of working with X-rays and radium. Hermann Holthusen had suggested the idea for the contemplative garden, and at the dedication Beclere noted that the martyrs had been "devoted to the same mission: to fight disease and suffering, at the peril of their own lives, with the help of the marvelous weapon put into their hands by Roentgen 200 names have been added since 1936

Radium Bombs



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. **Today's TeleCobaltherapy**

First accelerators



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.

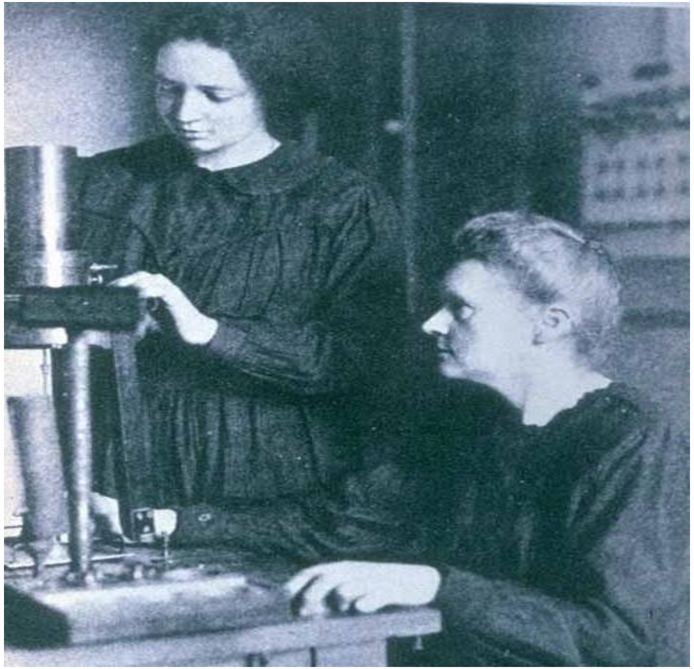
Developing Brachytherapy

Brachytherapy. Different schools of thought on dosimetry and technique were represented at specific institutions. Memorial Hospital: Gioacchino Failla and Edith Quimby (top, right and center) promoted patient shielding, protection, and education. Manchester: Herbert Parker (top, left), Ralston Patterson (bottom, 2nd from left), and John Meredith (bottom, left) derived dosimetry laws, improved supervoltage protection, and originated the rep/rem. Paris system of Regaud, represented here by Juliette Baud (bottom, center), Jean Pierquin (bottom, 2nd from right), and George Richard (far right). Not pictured is the Stockholm school of Strandqvist, Forssell, and Berven

Role of research in Radiation Oncology

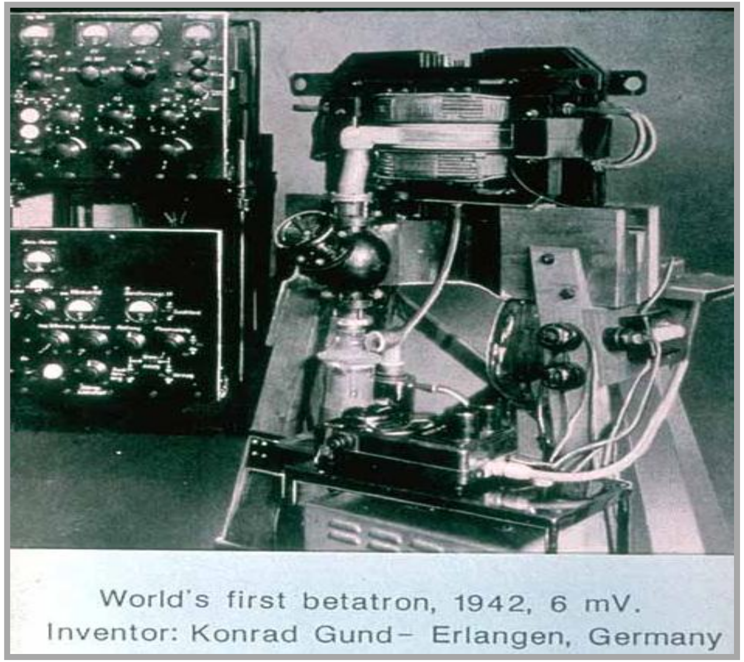
Physicists, photons, particles, and accelerators. Both theory and research formed the basis of modern day radiation therapy. Gioacchino Failla visits H.L. Gray (above), both pioneers in measuring dosage, dose distributions, particle interactions, and protection. Below (left to right) T.S. Walton, influenced by Ernest Rutherford and John Cockroft, built a high- voltage transformer accelerator to produce protons, setting the stage for particle accelerators.

Artificial Radioactivity



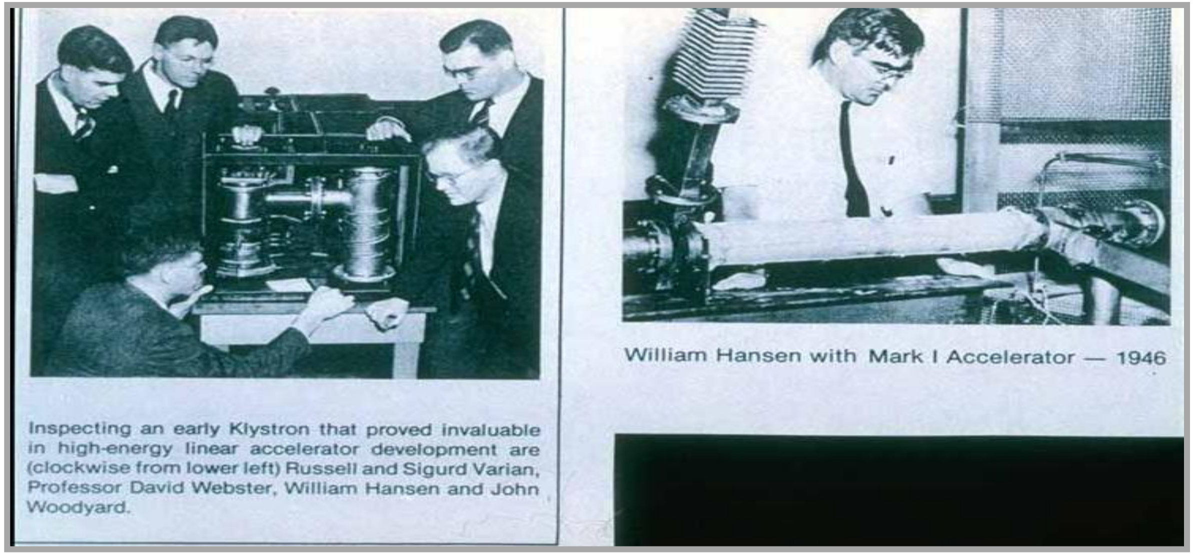
Artificial radioactivity. Irene Joliot-Curie, seen here with her mother, bombarded aluminum, magnesium, and boron with radiation, causing lingering positron emissions even after the original source was removed. Her modest report in Nature (1934) suggested the possibility that a "new element" or radioisotope had formed. Lawrence was soon producing cyclotron-generated radioisotopes, heralding the practical start of nuclear medicine and therapy.

Clinical Betatrons



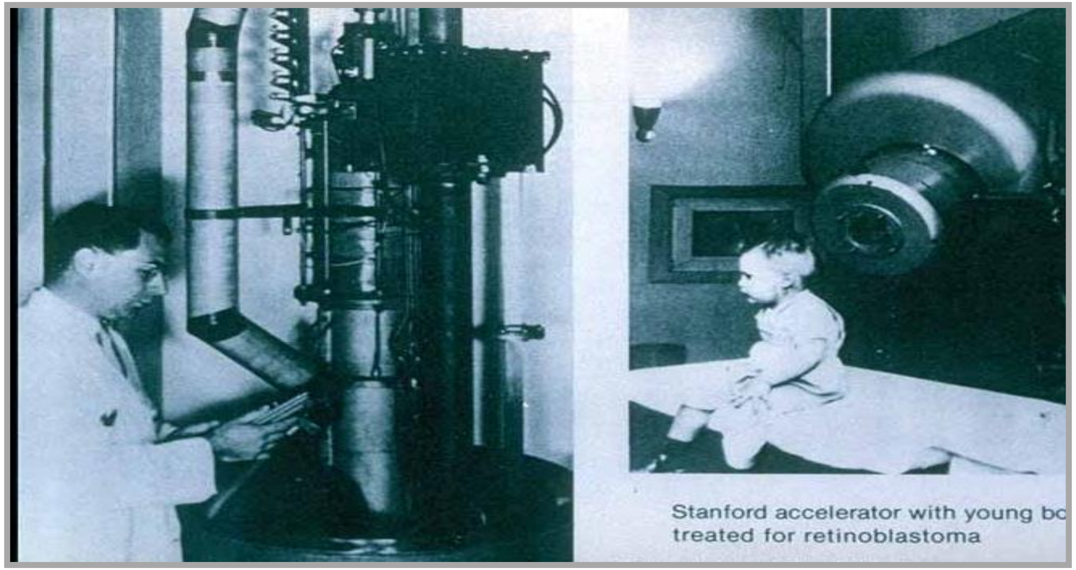
First betatron in clinical use, Konrad Gund, 1942. Although Kerst first developed the betatron in the U.S., it saw its first clinical application by Gund, using this machine in Germany during the war

Linear accelerators: Stanford



Varian klystron accelerator project. Shown here on the left are key members of the Stanford research team for high-energy linear accelerator development (clockwise from lower left): Russell Varian, Sigurd Varian, Professor David Webster, William Hansen, and John Woodyard (who suggested using a wave-guide). On the right is Hansen with his prototype unit, the Mark I accelerator, ca. 1946, which incorporated the Varian brothers' ideas for microwave technology.

Stanford Linac

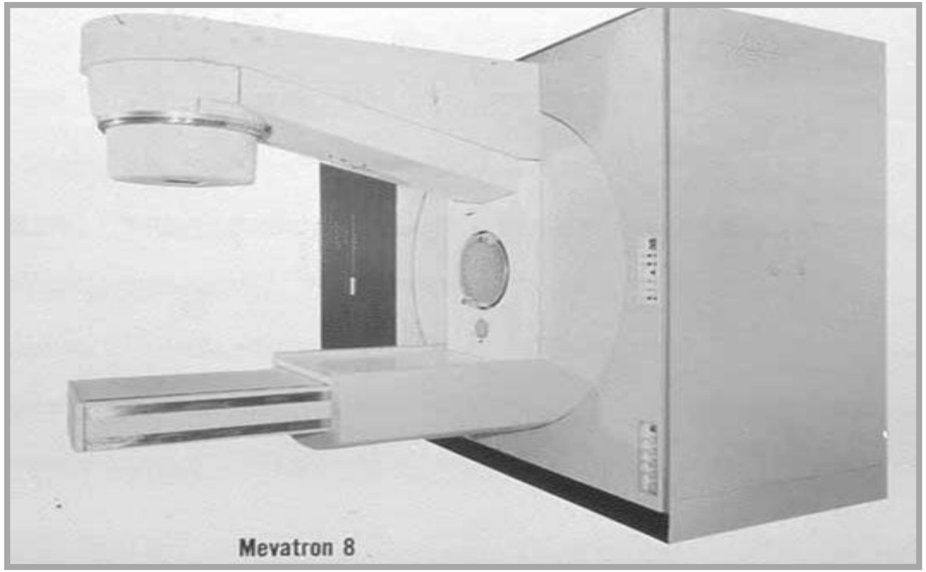


Henry Kaplan, 6 MV Stanford linac and first treatment, 1956. Henry Kaplan, the founding father of the linac in the U.S., is seen at left next to his first installed 6 MV medical linac in late 1955. The first patient, a boy with retinoblastoma (right) was treated in January 1956. Forty years later the boy remains disease free and retains his vision. Kaplan's legacy includes a search for new technologies in cancer therapy, with care toward exacting standards for use.

Modern linac design: The gantry

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

Dual Energies



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

Historical review of Radiation Therapy Physics.

- 1896- X-Rays – Radiodiagnostic, Therapy, Industry
- 1896 – Natural radioactivity: Brachytherapy, Teletherapy, Industry
- 1896 – first treatments
- 1900 – clinical reports of cured patients
- 1900-1920 – Research and clinical schools
- 1900-1910 fractionation effect well know.
- 1920 – External Beam radiation therapy: Radium bomb
- 1920-1930.- Registered deads from radiation source management. (~150)
- 1920 –1930: ICRU and ICRP
- 1930-1940 X-ray techniques and energy effect used in clinics
- 1942 – First Betatron in clinical uses
- 1942-1950 Linac technology development
- ~1950-56 First Linac treatments.

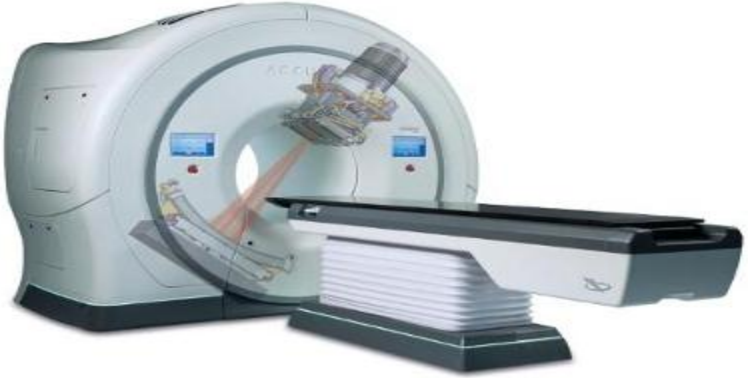
From 1966 - 2007

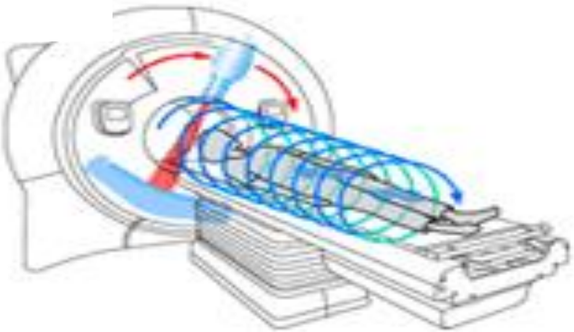
•2-3 photon energies, 6 electron
•Improved filters and beam lines
•Reduced design
•Multileaf Collimators
•Imaging lines
•2 sources concept
•Digital Controls
•SW, SW, SW…..

So: today's linac is an imaging machine with sophisticated treatment capacities

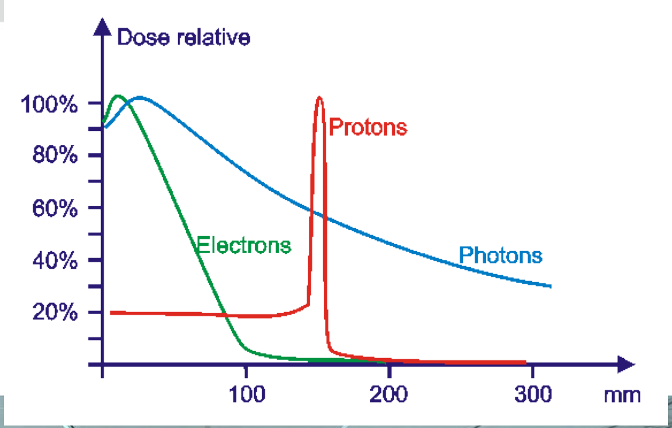
Modern era, incorporate robots

Helical CT plus Helical RT





Particle therapy, IGPT and IMPT



MRI plus LINAC