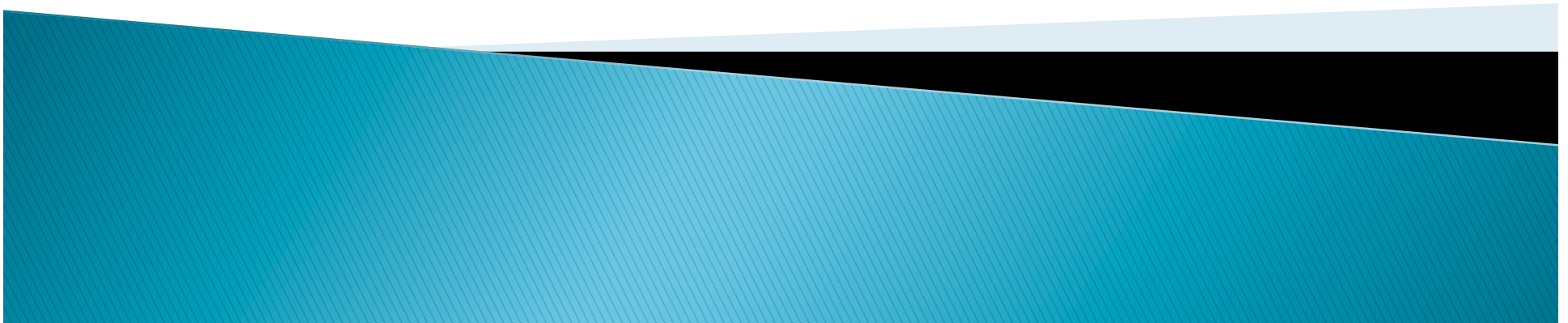


# EVOLUTION OF BRACHYTHERAPY

*PAST AND PRESENT*

*BASIL S. HILARIS, MD, FACR  
PROFESSOR EMERITUS  
NEW YORK MEDICAL COLLEGE*

*RAMPS MEETING  
MAY 15, 2012*



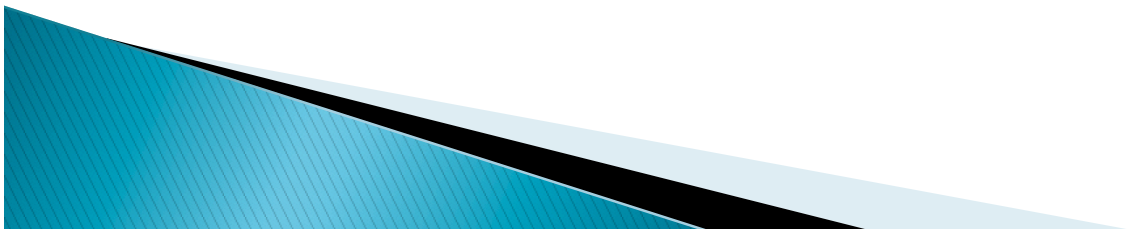
# TWILIGHT OF THE 19<sup>TH</sup> CENTURY

## Physics advances and the discovery of radium

Europe at the end of the 19<sup>th</sup> century was at peace, enjoying an unprecedented prosperity. This made possible a remarkable flowering of arts and sciences.

- ▶ In 1895, W.C. Roentgen discovered a new kind of radiation.
- ▶ In 1896, A. H. Becquerel discovered natural radioactivity.
- ▶ In 1898 the Curies for the first time produced polonium, and soon afterwards radium.

These four scientists were rewarded with some of the first Nobel prizes for their discoveries.



# DISCOVERY OF RADIOACTIVITY



The Curies  
(Pierre, Marie and Irene)

Few days are so significant as

**December 26, 1898**

The day that Marie Curie stated  
at the French Academy of  
Science that:

“ The object of the present work  
is the announcement of  
research which I have been  
carrying on for more than four  
years on radioactive bodies,  
which demonstrated that a  
new element strongly  
radioactive, that is **radium**,  
exists.”

# RATE OF KNOWLEDGE IN MODERN HUMAN HISTORY

- ▶ Modern scientific and technological innovations go through cycles, that include:
  - ***Initial discovery***
  - ***Development-Consolidation***
    - ▶ ***Commercialization***
    - ▶ ***Decline and replacement***
- ▶ This concept will help to understand
- ▶ Brachytherapy's development and evolution.



# CYCLE ONE (1900–1950)

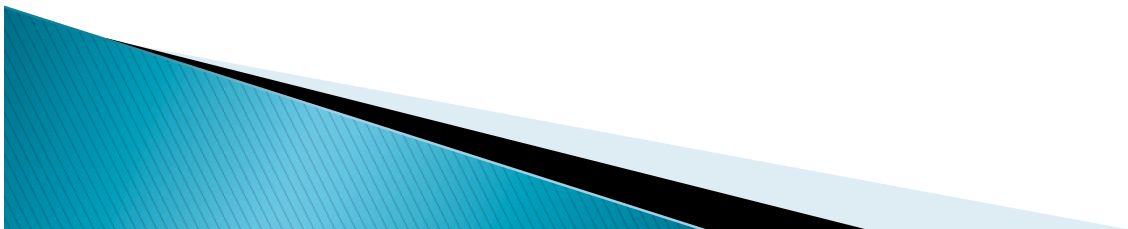
## Early attempts of brachytherapy

*The discovery of radium opened the door for a whole new way of treating cancer and the development of a new specialty. It was Forssell's destiny in 1931 to become the godfather of this new specialty and name it Brachytherapy.*

***The basic foundations of brachytherapy were established during this first period.***

# HIGHLIGHTS OF CYCLE ONE

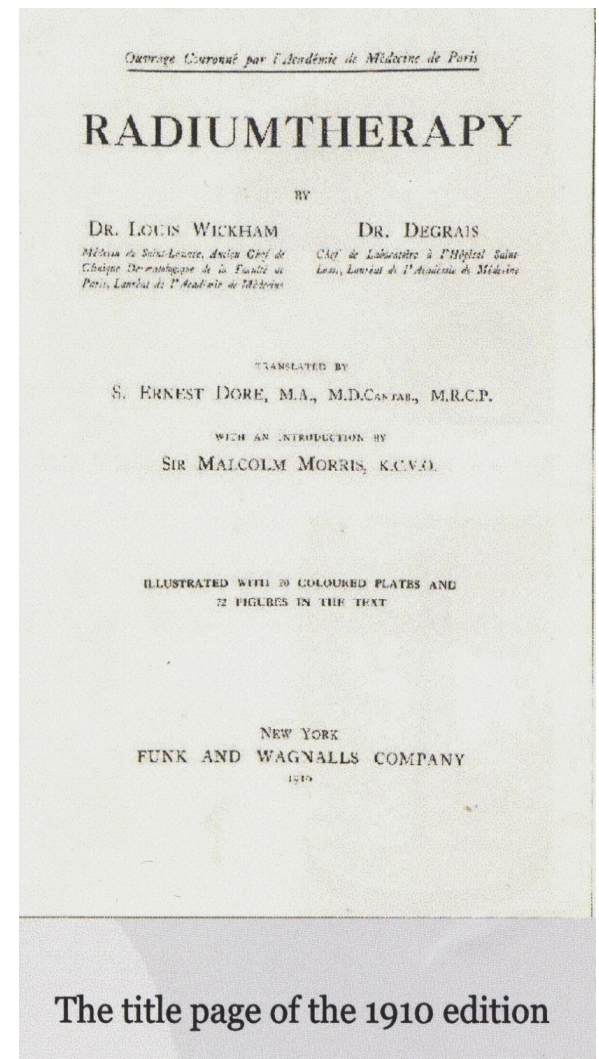
- ▶ Radium therapy Centers were established throughout Europe and North America to treat cancer.
- ▶ Radium techniques were developed for surface, interstitial and intracavitary radiation.
- ▶ Dosage systems were proposed and tested to calculate radiation within the tumor.
- ▶ The role model for brachytherapy was mainly in gynecology, head & neck, and skin cancer
- ▶ Radium price skyrocketed from \$10,000 in 1904 to \$135,000 in 1918.



## 1906-BIOLOGICAL LABORATORY OF RADIUM OF PARIS

▪ The first “Radium Institute” in the world was founded by **L. Wickham (1861 - 1913)** and **P. Degrais (1874-1942)** with **Henri Dominici (1867-1919)**, as the first clinical director. They perfected the techniques and dosimetry of radium especially in cancer of the cervix; demonstrated the different biological effects of the various qualities of radium; initiated filtration; and introduced the principle of cross-firing.

The Laboratory closed in early 1914, in the beginning of WWI.



The title page of the 1910 edition

# 1910-RADIUMHEMMET IN STOCKHOLM

(Literally “Radium Home”)

The Stockholm school founded *by G. Forssell*, (E. Berven, J. Heyman, M. Strandqvist, R. Sievert, R. Thoraesus), made significant contributions:

- Treatment of cancer of the uterus (**Stockholm technique**);
- Time-dose fractionation ( **Strandqvist curve**);
- Radiation protection issues (**Sievert chamber**; **Thoraesus x-ray filter**, **Free-air ionization chamber**, etc)

In 1979, the unit of equivalent dose was named after Sievert (Sv).



Dr Gosta Forssell (around 1910)  
1876-1950



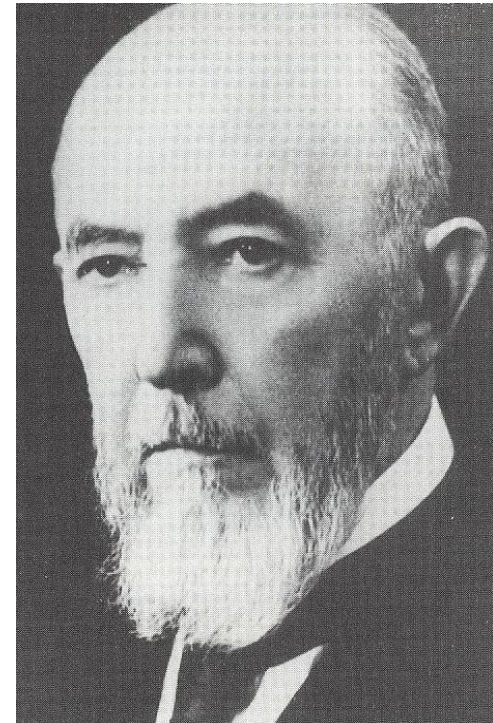
# 1912-RADIUM INSTITUTE OF PARIS

*The renowned Pasteur Institute and the University of Paris founded the Radium Institute in 1912.*

*It was divided into the **CURIE PAVILION** under Marie Curie and the **PASTEUR PAVILION** under Claude Regaud.*

*Regaud and his school (**A. Lacassagne, Monod, H. Coutard**) exerted an enormous influence on cancer research.*

- *They emphasized the experimental side of radiology, particularly “**radiobiology**” a term introduced by Regaud .*
- *Established optimal dose rules and the concepts of protraction and fractionation.*
- *Developed principles and treatment techniques for cancer of the cervix (**Paris technique**) .*



Claude Regaud  
1870–1940

## 1933-HOLT RADIUM INSTITUTE OF MANCHESTER

*Holt Radium Institute was founded in 1933 by the fusion of two much older hospitals, the **Christie Hospital** and the **Radium Institute in Manchester**.*

**Ralston Patterson**, built a team of physicists and clinicians (his wife **Edith**, **Margaret Tod**, **W. J. Meredith** and **Herbert Parker**), who brought the Holt Radium Institute to the forefront of therapeutic radiology. Some of the school's contributions are:

- ▶ Standardized treatment for the same type of tumor
- Introduced randomization of patients for scientific comparison **by clinical trials**
- Introduced rules for interstitial radium implantation with dose tables which allowed more accurate dosimetry (**Paterson-Parker tables**)
- A radium system for intracavitary treatment of cancer of the cervix (**Manchester System**); and the introduction of points A & B for dose specification in roentgen units.



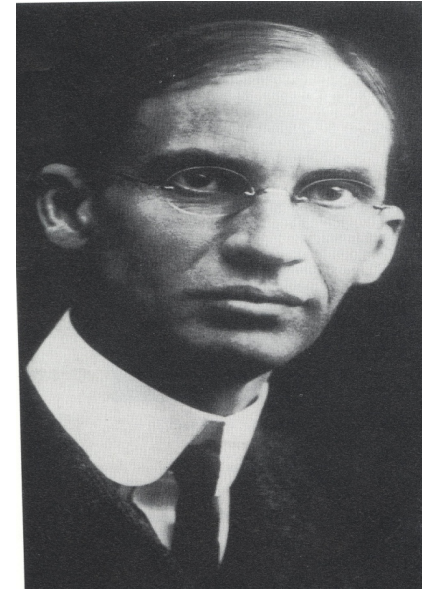
Ralston Paterson  
1897-1961

## 1915-MEMORIAL HOSPITAL OF NEW YORK

In 1915, James Ewing, professor of Pathology at Cornell University Medical College became the first director of MH, transforming it from a General Hospital into a leading Cancer Hospital (**Memorial Hospital for Cancer and Allied Diseases**, known informally as the *Radium Hospital* or *The Bastille*.)

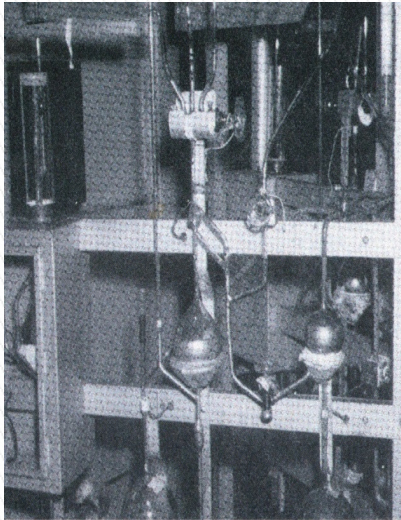


The "old" Memorial Hospital (1884-1939)

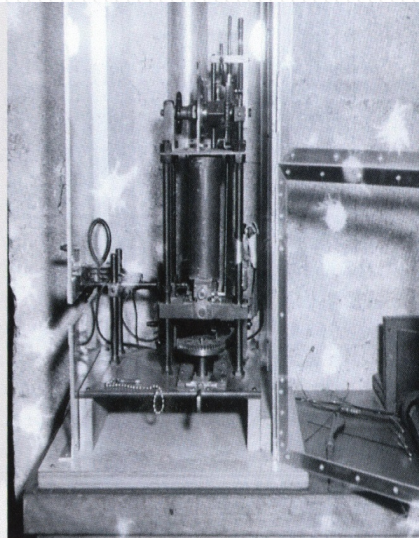


Henry Janeway was appointed as the first Director of the newly created Radium Department

# MEMORIAL HOSPITAL OF NEW YORK



The pumping apparatus which produced the gold (radon) seeds



The seeds were sorted according to their activity with this semiautomatic apparatus



In 1915, William Duane, Professor of Physics at Harvard University, installed a model of his radium extraction and purification plant at MH to produce radon seeds for therapeutic use.

In 1915, Henry Janeway appointed Gioacchino Failla in charge of the radon plant, and in 1919 as director of the new Physics Department. The same year Edith Quimby joined as Failla's assistant.

## ***1916-AMERICAN RADIUM SOCIETY (ARS)***

- ▶ On October 26, 1916, in Philadelphia, a new association, the American Radium Society was established **by oncologic surgeons, gynecologists, radiologists and pathologists concerned with the treatment of cancer.**
- ▶ The aims of the society were declared to be **“the promotion of the scientific study of radium, its physical properties, and its therapeutic application.”**
- ▶ **The ARS was a model of interdisciplinary collaboration from its inception.**
- ▶ William Aikins (1859-1924) of Toronto, was elected as the first President.

# Opportunistic uses of Radium

Given the chance people will often misuse technology and create an enormous amount of mischief. This was the case with radium too! Radium was used in creams, shampoos, toothpastes or as a beverage, to prolong life and prevent aging!



## 1934-AMERICAN BOARD of RADIOLOGY (ABR)

The ABR was formed through the efforts of ARS, ACR, and RSNA and incorporated in Washington in January 1934 “to protect the public from irresponsible practices and to preserve the dignity of qualified professionals”. Since its inception in 1934 the ABR has issued more than 65,950 certificates in several subspecialties, that at times were very confusing.

- ▶ Since 1994 the certificates are issued, in Diagnostic Radiology (and various subspecialties), Radiation Oncology and Radiological Physics, time limited (10 years) requiring recertification.

# Recognition of Radiation Hazards

In the 40's and 50's, health professionals and public, began to recognize and be concerned with many aspects related to the use of radium, such as:

- ❑ Harmful effects of radium exposure
- ❑ Frequent radium accidents resulting in disastrous effects
  - ❑ Radium source construction and integrity issues
  - ❑ Laborious radium dose calculations

Lost radium sources frequently ended up in incinerators, trash water or down drains, but one missing source was located inside a pig!





# CYCLE ONE CONCLUSIONS

- ❑ During this period radium work was done in several “Radium Therapy” centers in Europe and North America.
- ❑ Radium based techniques were developed for surface, interstitial and intracavitary irradiation.
- ❑ Radiation physics departments were established that steadily contributed to the science of radiation therapy and specifically brachytherapy.
- ❑ Various dosimetry systems were developed to calculate radiation dosages and distribution of radioactive sources, including the Paterson–Parker System in Europe and the Quimby System in the United States.
- ❑ *By the end of the first half of the 20<sup>th</sup> century, however, spectacular technical developments in the field of external beam therapy; significant improvements in surgical techniques and anesthesia; and professional concern regarding the harmful effects of radium exposure*

**Resulted in a declining interest for Brachytherapy and a marked decline in its utilization.**

# CYCLE TWO (1950-PRESENT)

## Brachytherapy's Renaissance

Many radiation workers felt that the disadvantages of radium required the investigation of alternative radionuclides for clinical use, that became possible only with the development of nuclear reactors. Production of artificial radionuclides resulted in a variety of commercially available sources for brachytherapy.

**By the 1980's, radium and radon had been almost completely replaced by sources such as Cesium-137, Cobalt-60, Iodine-125 and Iridium-192.**

# ***TWO EXCEPTIONAL PEOPLE AT MH***

Many of the modern brachytherapy concepts and techniques were developed at MSKCC because of the efforts of these two scientists; and had a major impact on the practice of brachytherapy in North America and the rest of the World.

## **In Brachytherapy**



*Ulrich Henschke, MD, PhD*

## **In Medical Physics**



Dr. John Laughlin, chairman of the department of Medical Physics, MSKCC

# HIGHLIGHTS OF THE SECOND PERIOD

Research and *development of artificial radionuclides as alternative to radium and afterloading techniques*

Development and clinical applications initiated during this period mainly at MSKCC include:

- Iridium-192 sources
- Manual afterloading
- HDR Remote Afterloading
  - Low energy sources
- Computerized dosimetry

They will be discussed in more details in the following slides



# AMERICAN ASSOCIATION OF PHYSICISTS IN MEDICINE (AAPM)

CHICAGO, NOVEMBER 17, 1958

- ▶ *Many physicists in biology and medicine, among them [W.K. Sinclair](#), [J.S. Laughlin](#), and [G.D. Adams](#), felt that had no professional identity and that a national organization might speak for the profession in a louder voice than all individuals singly.*
- ▶ *[Gail Adams](#) was the first President, and the initial annual meeting was held near the time of RSNA meeting in Chicago in November.*

***This was the beginning of a remarkably strong educational, scientific, research , and professional association as we witness it today.***

# ARTIFICIAL RADIONUCLIDES

- ▶ *The development of nuclear reactors allowed the production and investigation of several safer radionuclides as alternative to radium, among them:*

**Gold-198 (1947)**

**Cobalt-60 (1948)**

**Iridium-192 (1954)**

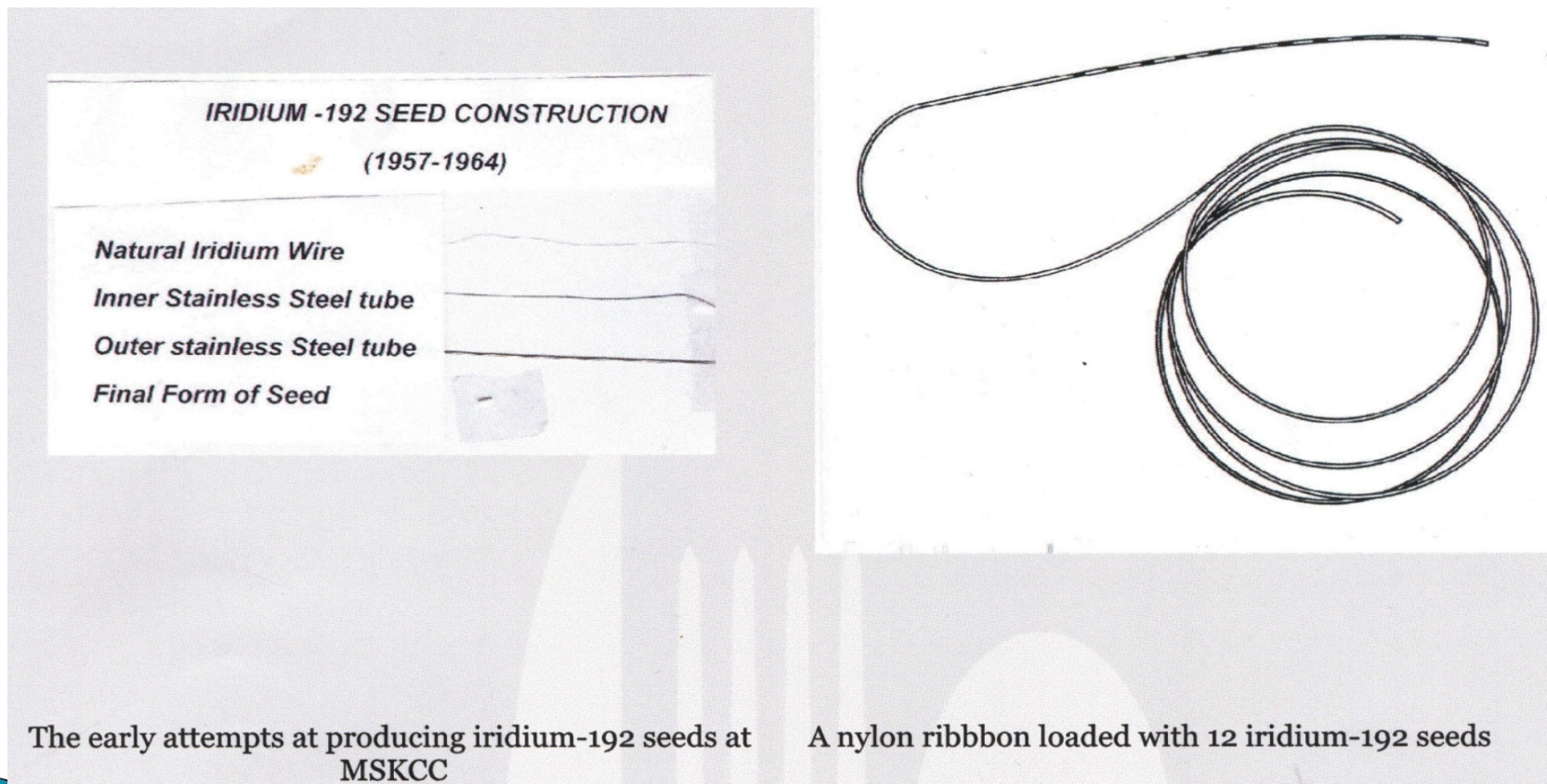
**Yttrium-90 (1956)**

**Cesium-137 (1957)**

- ▶ *Dr Henschke introduced Gold-198 seeds in 1954 at Ohio State University and Iridium-192 wires/seeds in 1955 at MSKCC, as substitutes for radium needles and/or radon seeds.*
- ▶ *This represented an improvement over the use of radium and radon sources but **radiation exposure still remained a major problem.***

# FIRST ATTEMPTS TO PRODUCE IR-192 SEEDS AT MSKCC (1957-1964)

Iridium-192 seeds were investigated because of their  
**Lower energy, Longer half-life and Large cross section**



# COMPUTERIZED DOSIMETRY

- ▶ **1957- First report on computerized implant-** *The application of automatic computation methods to implant dosimetry was presented by Richard Nelson and Mary Lou Meurk (MSKCC)*
- ▶ **1962- First application of computer dosimetry in conjunction with iridium-192 afterloading,-** *W. Siler (MSKCC)*
- ▶ **By 1971, applications of computers in radiation therapy, included:**
  - ***Dose-time computations,***
  - ***Treatment planning for internal sources and for external beams,***
  - ***Teaching,***
  - ***Automation of machine control ,and***
  - ***Logging and retrieval of patients' chart data.***

▪

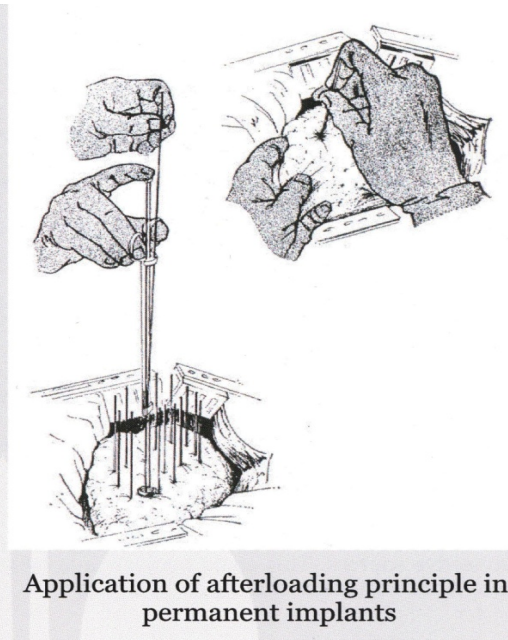
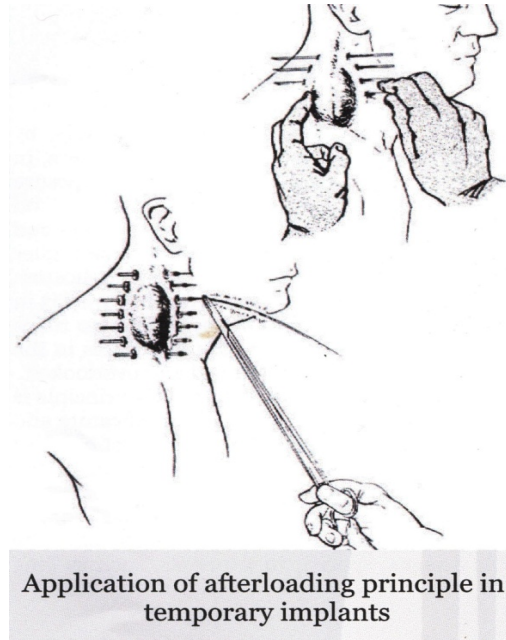


# MANUAL AFTERLOADING

Manual afterloading was introduced, developed and refined in the late 50's by Henschke, first at Ohio State University and then at MSKCC, in an attempt to:

**Decrease radiation exposure to physicians, nurses, and other health workers of the institution, during a brachytherapy procedure .**

The three sketches below show the characteristic steps of afterloading

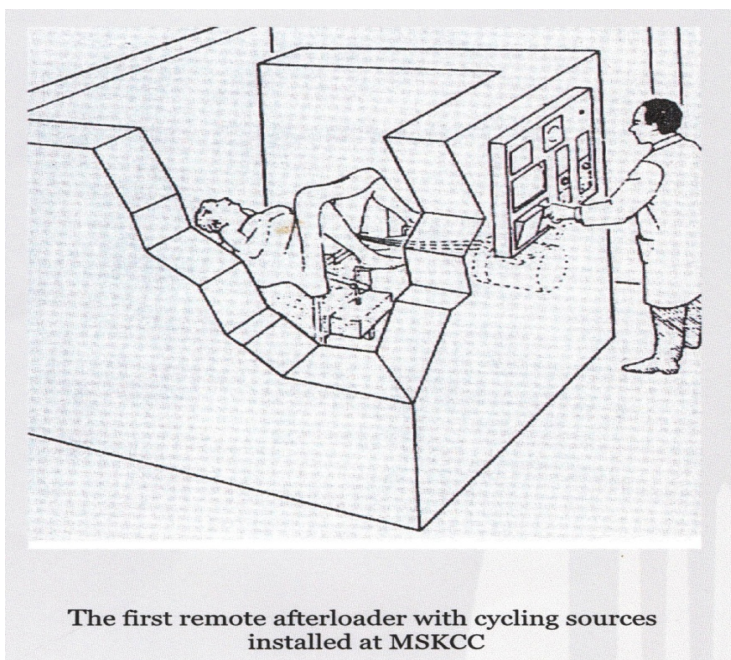


**This concept was presented for the first time at the 10<sup>TH</sup> International Congress of Radiology, in Montreal in 1962.**

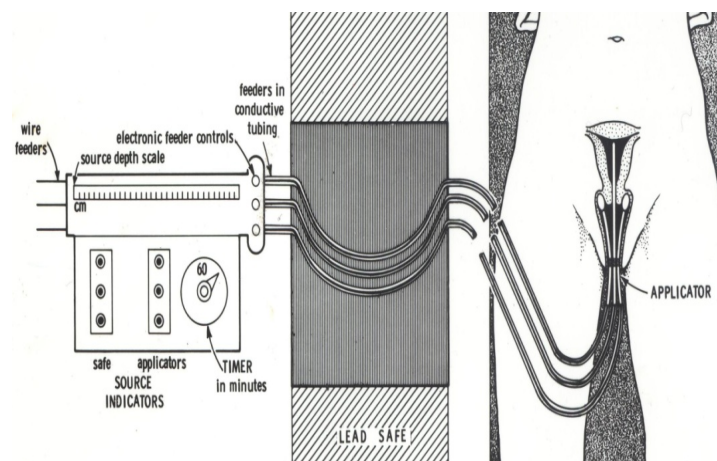
# HDR REMOTE AFTERLOADING

Remote afterloading, using small cobalt sources of high activity, moving back and forth to simulate sources of different longer active length, was proposed in 1964 (Radiology, 1964), to:

**Eliminate radiation hazards to health personnel,  
Avoid long hospitalization, and  
Decrease patient discomfort**



The first remote afterloader with cycling sources installed at MSKCC



Control panel

**This HDR Remote Afterloader remained in use at MSKCC, from its installation in 1964 until 1979, when it was replaced by a commercial unit.**

# INVESTIGATION OF LOW ENERGY RADIONUCLIDES AT MSKCC (1966-1967)

Investigation of low energy radionuclides (**Iodine-125, Cesium-131, and Xenon-133**) was undertaken in 1966, to explore the possibility of further decreasing radiation exposure. From this experience we concluded that: **I-125 sources were a promising substitute for high energy sources; and radiation exposure to personnel was reduced considerably.**

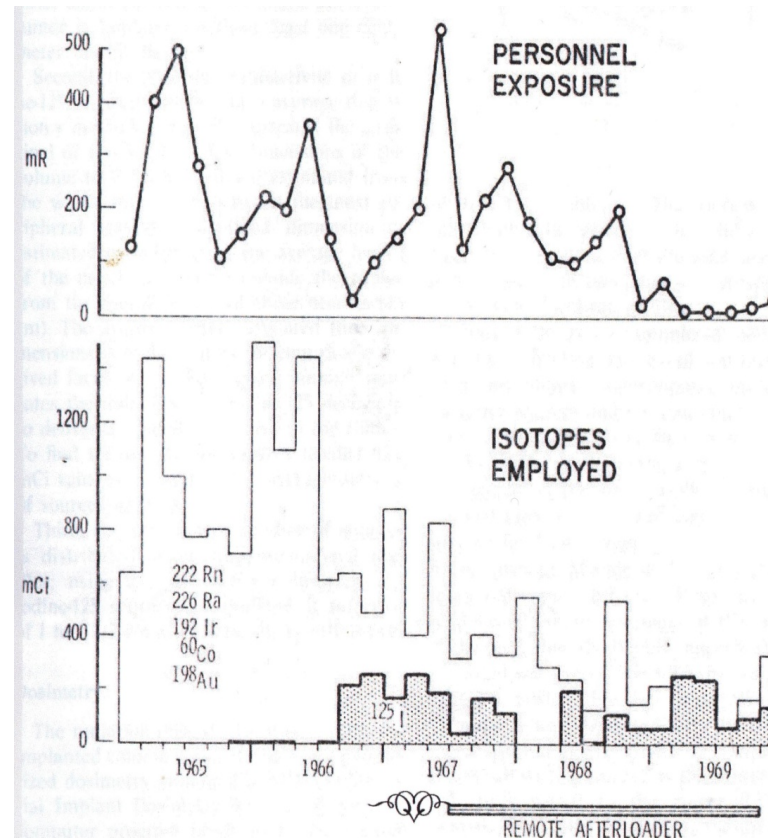
COMPREHENSIVE PROGRESS REPORT  
COVERING THE PERIOD MAY 16, 1966 - AUGUST 31, 1967  
CONTRACT NO. PH 86-66-132

or: Memorial Hospital for Cancer and Allied Diseases  
444 East 68th Street  
New York, New York 10021

Performance: New York, New York

Investigate Low Energy "Seeds" for Permanent Interstitial Implants in Cancer Treatment, and to Measure the Reduction of Unnecessary Radiation from This Use

PUBLIC HEALTH SERVICE  
NATIONAL CENTER FOR  
RADIOLOGICAL HEALTH  
1901 Chapman Avenue  
Rockville, Maryland 20852

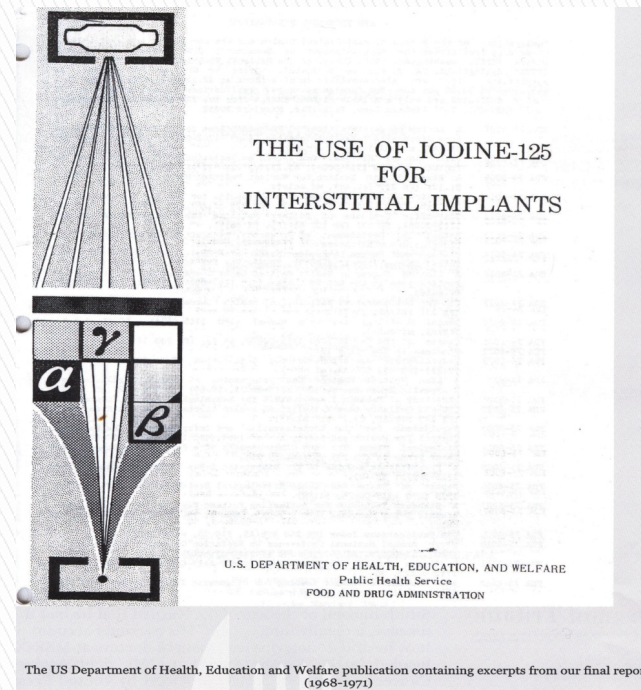
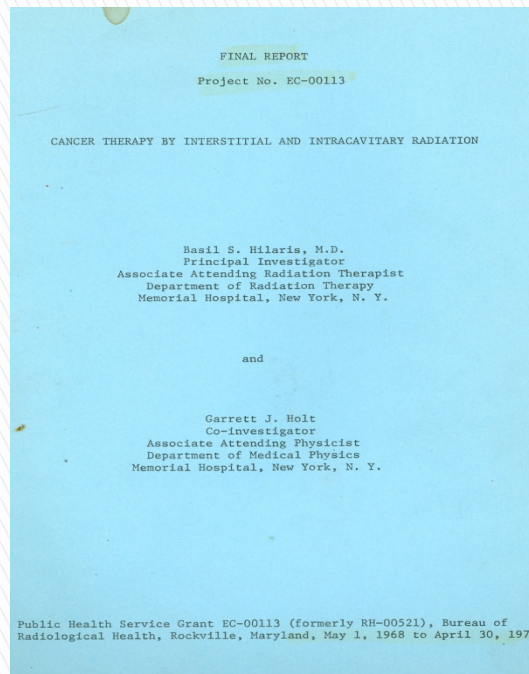


# INVESTIGATION OF IODINE-125 AND HDR REMOTE AFTERLOADING AT MSKCC (1968-1971)

A more comprehensive investigation was conducted by Jean St Germain, Garrett Holt and Basil Hilaris in 1968. We investigated radiation protection issues; seed design, construction, calibration and dosimetric issues; and obtained clinical experience with I-125 (in 234 pts) and HDR remote afterloading (in 196 pts).

**The USDHEW response was as follows:**

**“The section on Iodine-125 appears to be significant for brachytherapy; The section on HDR remote afterloading is not, because the traditional techniques with radium are already well established and very effective”.**



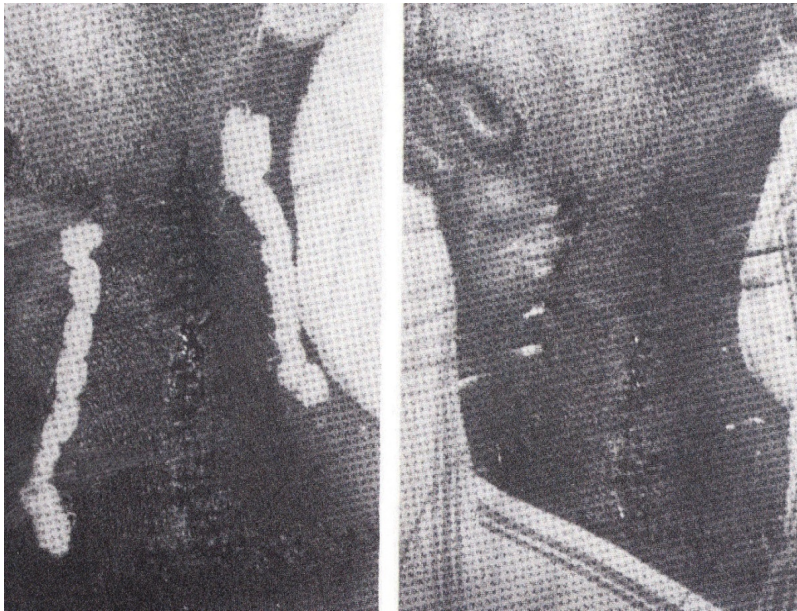
# The Working Team in the 70's



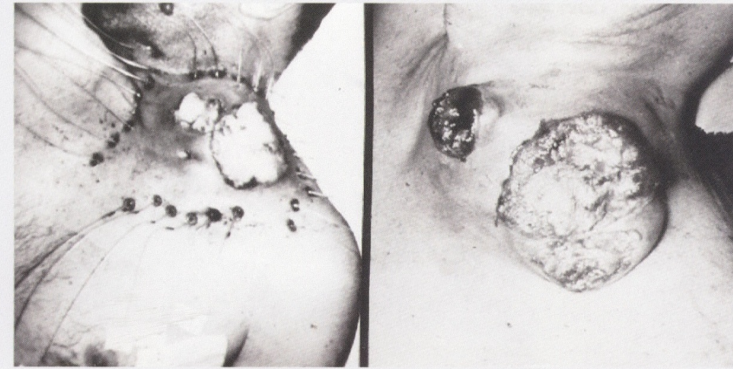
Dr. Lowell Anderson, Jean St Germain, Dr. Basil Hilaris and Dr.J.H. Kim

# AFTERLOADING IN H&N CANCER

*The role of brachytherapy in H&N cancer was reestablished after the introduction of afterloading techniques and artificial radionuclides.*



*The first postoperative afterloading H +N implant, using Gold-198 seeds, was performed by Henschke at Ohio State University in 1953.*



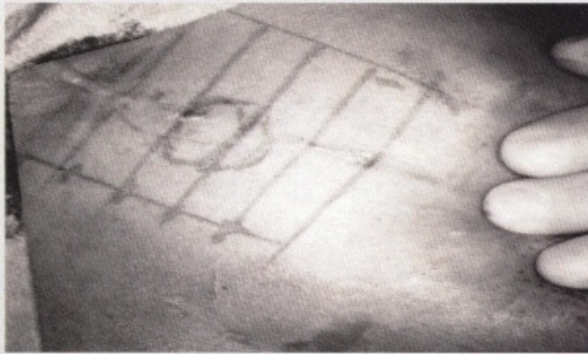
Right: a mass measuring 8x6x5 cm Left: a two plane implant preformed



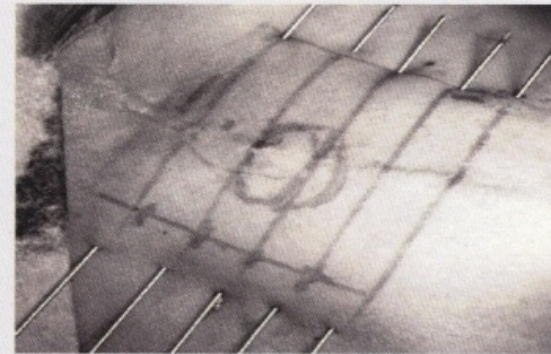
Left: x-ray of the two plane implant. Right: 10 years later: no evidence of cancer, but severe late skin change.

# ***AFTERLOADING IN BREAST CANCER***

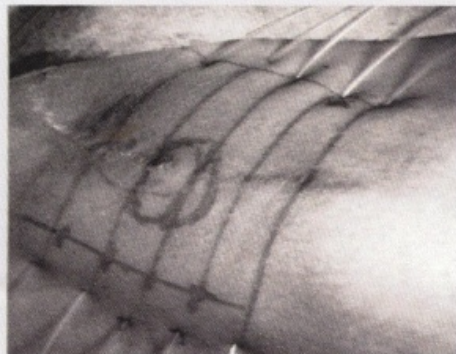
- ▶ *Manual afterloading of Ir-192 in conjunction with conservative surgery ((lumpectomy) revived interest in brachytherapy.*



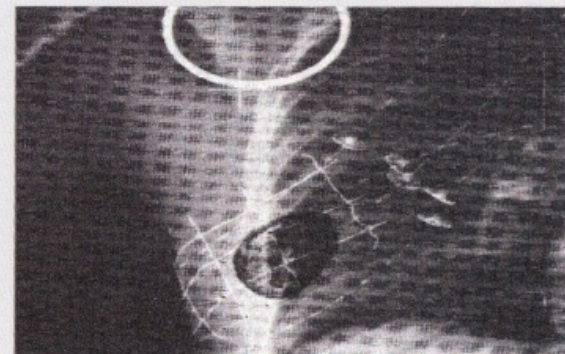
**(A) original breast implant technique**



**(B) original breast implant technique**



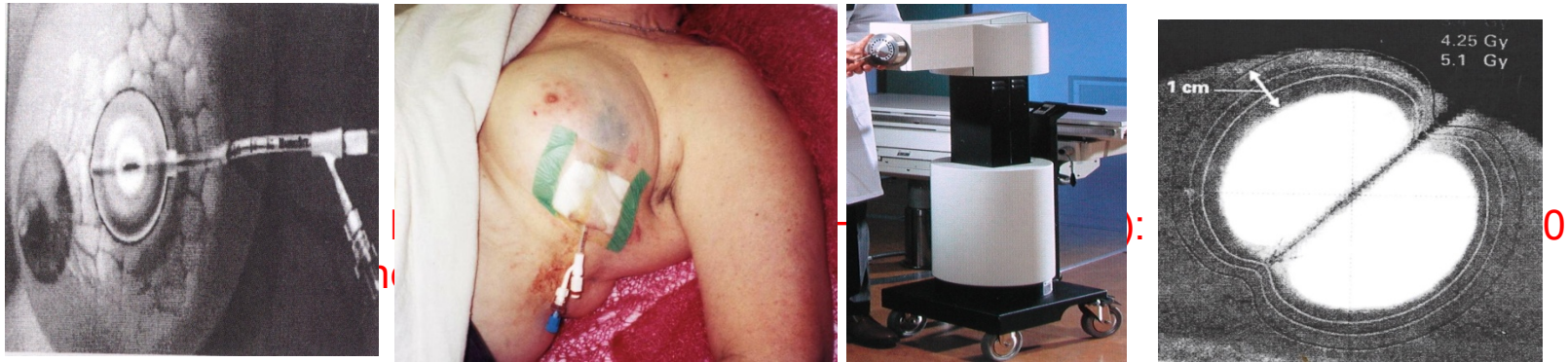
**(C) original breast implant technique**



**(D) original breast implant technique**

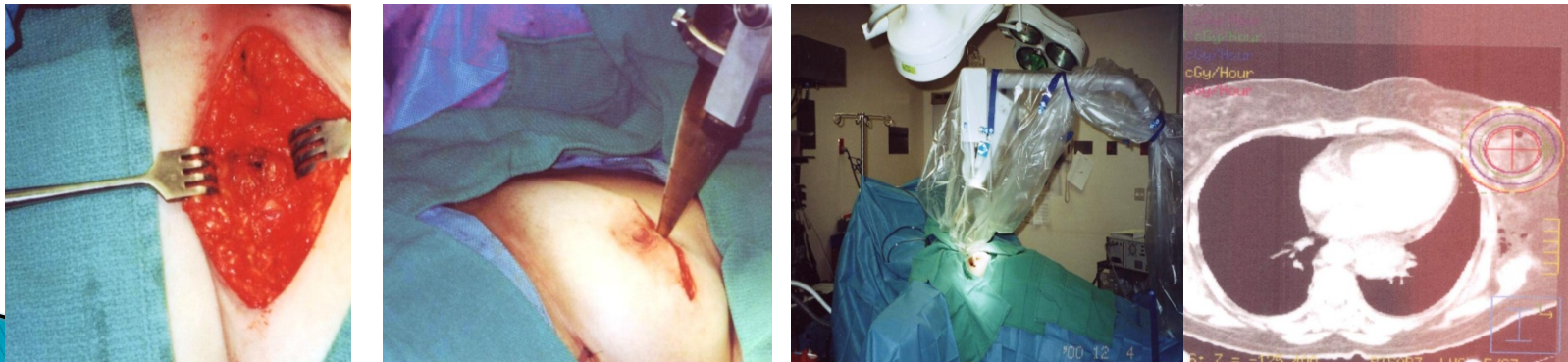
# MODERN AFTELOADING TECHNIQUES IN BREAST CANCER

- ▶ ACCELERATED PARTIAL BREAST IRRADIATION (APBI)
- ▶ (a total dose of 34 Gy, twice a day x 5 days on an outpatient basis)



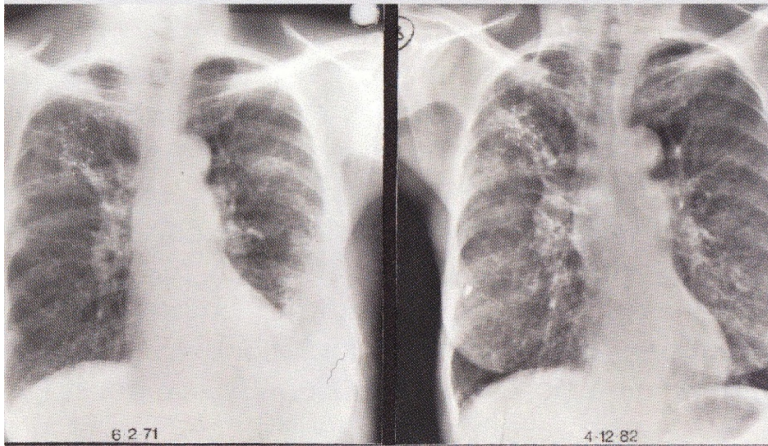
## INTRAOPERATIVE BREAST RADIATION THERAPY (IORT)

- ▶ (a single dose of 10–20 Gy is delivered in 30 minutes)

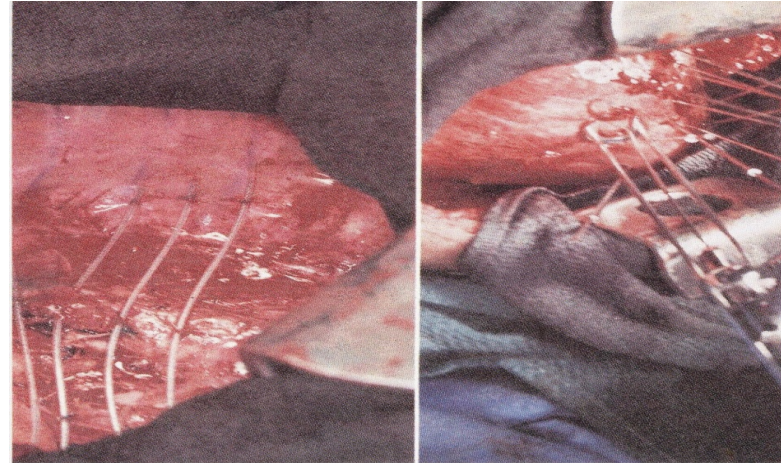




# AFTERLOADING IN LUNG CANCER



Example of permanent I-125 implant



Example of temporary Ir-192 implant

- The largest experience with permanent I-125 and temporary Ir-192 implants (in over 1000 pts) was accumulated at MSKCC during the 60's to 80's. The long term results for selected patients with limited pulmonary reserve who could not tolerate resection (stage I and II) were promising with an overall 5-year survival of 32%.
  - ***The availability of newer techniques, including IMRT, improved dosimetry, and the integration of chemotherapy have almost completely replaced BRT today.***

# AFTERLOADING IN PROSTATE CANCER

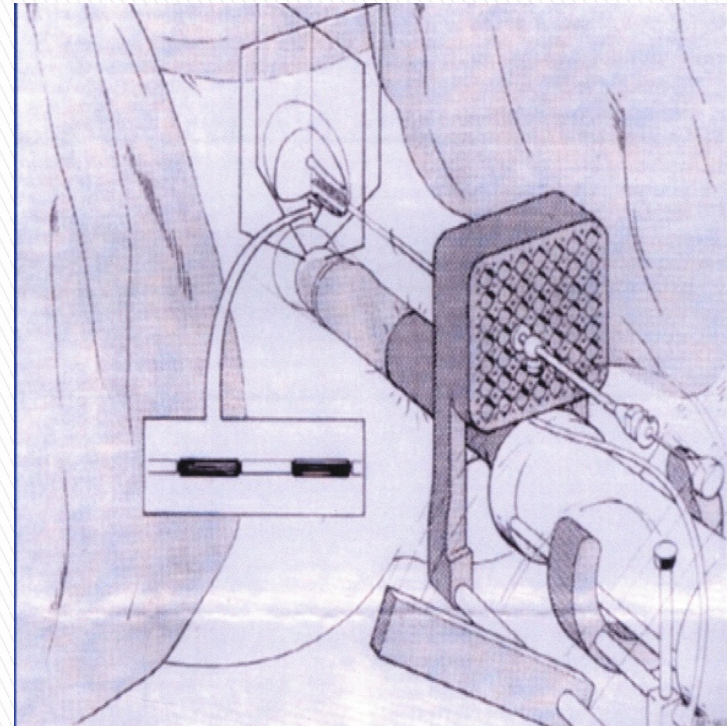
*In 1969 the Urology and Brachytherapy service at MSKCC began a collaborative study to investigate I-125 in conjunction with pelvic lymphadenectomy for the treatment of cancer of the prostate, as an alternative to radical prostatectomy. Several hundred patients were treated and the following conclusions were drawn from this experience*

- *Patients with positive nodes would soon develop distant (bone) metastases.*
- *Small tumors, localized to prostate were optimal candidates.*
- *Tumors that were treated to a minimum of 160 Gy were better controlled, than tumors receiving a lesser dose.*



# Modern afterloading techniques in prostate cancer

- ▶ *The original retropubic manual afterloading technique was difficult to learn and misapplications were frequent resulting in its decline by the early 80's.*
- ▶ *The adaptation of the transperineal approach in 1987, in combination with transrectal ultrasound, CT or US pretreatment planning optimization and prefabricated templates resulted in the reestablishment of brachytherapy (**Manual or HDR**) in the treatment of cancer of the prostate.*



Modern manual afterloading technique

## 1979-BRACHYTHERAPY SERVICE AT MSKCC

The first modern BRT service in the USA was established on July 1<sup>st</sup>, 1979 at MSKCC. Many members of the service had subsequently very successful careers. You will recognize the following names:

- ▶ **Dr D. Nori**
- ▶ **(NYH),**
- ▶ **Dr B. Vikram**
- ▶ **(IAEA & NCI),**
- ▶ **Dr. S. Nag,**
- ▶ **Dr. A. Martinez,**
- ▶ **Dr. L. Harrison**
- ▶ **(President of ASTRO),**
- ▶ **Dr. M. Zelefsky**
- ▶ **(editor of Brachytherapy Journal  
Chief of Brachytherapy Service)**



From left: Sitting: Drs. H Brenner, B. Hilaris, D. Nori. Standing: Drs A.Tankenbaum, L. Linares, a surgical resident, Dr D. Greenblatt

# AMERICAN BRACHYTHERAPY SOCIETY

- ▶ In 1978 Syed and sixty–seven other physicians founded the **Endocurietherapy Society** in California.
- ▶ By 1985, the membership had grown to 395 practicing radiation oncologists, medical physicists and radiation biologists throughout the United States.
- ▶ In 1997 the society was renamed **American Brachytherapy Society**. Today the society is broadly accepted with a significant increase in its membership and the quality of its members; significant clinical and research contributions; and successful efforts in continuing education by the establishment of “schools” in head & neck, breast and Gyn brachytherapy

# CYCLE TWO CONCLUSIONS

## THE SECOND 50 YEARS OF BRACHYTHERAPY

- ▶ Modern brachytherapy, properly applied, contributed to improved treatment techniques and advanced the cause of cancer control.
- ▶ New radionuclides with lower energy, commercially produced HDR units, optimization of BRT planning, and ultrasound/CT based real-time planning became available.
- ▶ Computer technology and the resulting ability to produce very accurate three dimensional radiation dose distributions within the patient; and standardization of brachytherapy techniques, allowed for more uniform practice and better use of integrated treatments.
  - ▶ **This success story of brachytherapy was driven**
- ▶ **By extensive technological developments; the increased number of physicians and physicists practicing brachytherapy, and the interest generated in other ontological specialties. And it is reflected in the considerable brachytherapy literature; the formation of the American Brachytherapy Society; and its dedicated Brachytherapy Journal.**

# CYCLE THREE

## THE SPECIALTY'S FUTURE

Today brachytherapy and medicine in general, face several impending risks, threatening its practice, such as:

- **Constant warnings** about radiation overdoses, lack of safeguards, and software flows, resulting in more stringent regulation of medical radiation.
- **A fast-rising cost curve** which must be dealt within our specialty.
- **An uncertain political outlook;** it appears that treatment decisions in the future will be made by protocols with several layers of midlevel administrators.

Some steps can be taken right away, such as

- Becoming more proactive in medical education.
- Continue to minimize the invasiveness of brachytherapy procedures and
- Reassessing risks, vs. benefits vs. cost

**It is my strong belief, that Brachytherapy because of solidly developed medical and technical foundations, is the most suitable medical specialty for the implementation of the rapidly advancing technology including biotechnology, and even nanotechnology.**