1. The Physical and Biological Basis of Radiation Therapy

Wilhelm Conrad Roëntgen

Discovered X rays in 1895
X rays were immediately big news at Columbia

“The College of Physicians and Surgeons is using x-rays to reflect diagrams directly on to the students’ brains, making a more enduring impression than the normal method of learning”

New York Morning Journal, 1896

By 1899 X rays were being used for cancer therapy

1899 1929
Who gets radiotherapy?

HALF

Who gets radiotherapy?

Half of all cancer patients get radiotherapy
Who gets radiotherapy?

Half of all RT patients are treated with curative intent

Half of all RT patients treated with curative intent are cured
RT has both a physical and a biological basis

The goal is always to produce as much cell killing as possible in the tumor, while minimizing damage to normal tissue

Physical Basis of Radiotherapy

- Aim beam at tumor
- Shape beam to conform to the tumor
- Minimize dose to normal tissue
External-beam radiotherapy: 1951

Higher energy beams and aiming at the tumor from more directions, made for better dose distributions
IMRT (intensity modulated radiation therapy)

Continuously changing multi-leaf collimator

The CyberKnife, an x ray machine on the end of a robotic arm
The bottom line in 2007 is that far more normal-tissue dose sparing can be achieved than was previously possible.

Correspondence American Medicine Aug. 15, 1903

The Uses of Radium

Dear Dr. Sowers:

I understand from you that the Röntgen rays, and the rays emitted by radium, have been found to have a marked curative effect upon external cancers, but that the effects upon deep-seated cancers have not thus far proved satisfactory.

It has occurred to me that one reason for the unsatisfactory nature of these latter experiments arises from the fact that the rays have been applied externally, thus having to pass through healthy tissues of various depths in order to reach the cancerous matter.

The Crookes' tube, from which the Röntgen rays are emitted, is of course too bulky to be admitted into the middle of a mass of cancer, but there is no reason why a tiny fragment of radium sealed up in a fine glass tube should not be inserted into the very heart of the cancer, thus acting directly upon the diseased material. Would it not be worth while making experiments along this line?

[signed] Alexander Graham Bell
By late 1903, the first treatment of cervical cancer with radium was reported from New York.

Radioactive seeds are increasingly used for treating prostate cancer.
The Three R’s of Radiotherapy

- Repair
- Reoxygenation
- Repopulation

Repair of DNA damage
Radiation-induced DNA Damage

(a) Intact DNA

(b) Break in a single strand

(c) Two strand breaks far apart

(d) 2 breaks close together opposite

Taking advantage of DNA damage repair

DNA repair is different for tumors (proliferating tissue) compared with late-responding normal tissues (slowly proliferating tissue)

Dividing the treatment into many fractions takes advantage of this, allowing for more repair in late-responding normal tissue than in tumors
The significance of oxygenation:

- Hypoxic cells are more resistant to radiation.

Solution is fractionation:
- Allows reoxygenation between treatments.
Accelerated Repopulation

As the tumor shrinks, the surviving tumor cells proliferate at an accelerated rate

Loss of tumor control as a result of increasing overall treatment time

- 2% per day for head and neck tumors
- 1% per day for cervix, bladder cancers
Biological Basis of Radiotherapy

- Exploit biological differences between tumor and normal tissues
- Minimize effects of hypoxic cells
- Fight accelerated repopulation

From a biological perspective:

Must divide radiotherapy treatment into many separate fractions

- To overcome hypoxia
- For differential response of tumor control and late side effects
From a biological perspective:

Must keep the treatment short
- To counteract accelerated population

Must prolong the treatment
- To limit early side effects

The Physical and Biological Bases of Radiation Therapy

- 1.4 million malignant cancers / yr in the US
- Half of them treated with radiotherapy
- Radiation therapy uses both physics biology to maximize the differential between tumor control and side effects