Radio-isotopes in Radiation Therapy

East TN Health Physics Society
June 2018
Radiation therapy

X-rays were used to cure cancer very soon after their discovery

And rapidly became a standard treatment

First cure of cancer by X-rays
1899 – Basal cell carcinoma
Although side-effects were encountered!
This is a picture of a 70 year old person who was irradiated by Freund at the of age 5 in Austria 1896 for nevus pigmentosus piliferus.
1896 patient, Vienna: 70 years later

[3.12] I am indebted to Prof. H. Vahrson of Giessen for bringing the following to my attention and for providing this English translation from the Strahlentherapie paper by Fuchs and Hofbauer.⁴⁹

Röntgen discovered X-rays on November 8th 1895 and the birth of X-ray therapy was one year later in November 1896. By a rare chance we⁴⁹ are able to report on the late results of this X-ray therapy applied 70 years ago since this irradiated patient has been in our care for the last 10 years. She was born in 1892 with a naevus pigmentosus piliferus which covered the whole surface of the back and was largely symmetrical. Her intelligence was normal. Her parents brought the child to the '1 Öffentliche Kinderkranken-institut' where at that time Freud worked in the dermatological department. Because of the failure of every other therapy which had been attempted, Leopold Freund (1868–1943) made an attempt with X-rays. He later said of his thoughts at the time: 'In June 1896 I read in a Vienna newspaper the joke news that an American engineer who was intensively engaged in X-ray examinations lost his hair because of business. This notice interested me very much.'⁴⁰

The irradiations began on 24 November in the Graphischen Lehr- und Versuchsanstalt in Vienna where already at that time X-ray apparatus was at his disposal. Each irradiation treatment lasted two hours and the first series was given on the neck; the cranial part of the 36 cm long naevus. The first loosening of the hairs was noticed after the tenth treatment. Some days later the irradiated skin was epilated but did not show any alarming alterations. Shortly thereafter a second series of treatments was given, which covered the lower part of the naevus; the skin and the lumbar spine.

To decide the questions as to whether the electric field of the high voltage generator also produced biological effects, this treatment field was protected by an aluminium plate which was positioned in the path of the X-rays: but at the same time, the number of treatments was increased to take into account the loss of radiation dose due to the plate. This explains the considerable overdose in the lumbar region. Some days after the last radiation treatment the hairs were lost but in the following weeks an extended ulcer developed in the region of the lumbar X-ray field. This persisted for about six years and was cured in 1902 but developed a scar. It healed after the application of sea water.

In 1930 another ulcer developed in the region of the old ulceration scar and this was managed with elutions of Zinnkraut (note: This is a plant which was used in 'popular' medicine) and other ineffective agents. Another ulcer developed in 1944, a total of 48 years after the initial X-ray treatment. This was cured after treatment in a waterbed.

Freud gave a last presentation mentioning this patient, in January 1937, at the Society of Physicians in Vienna but did not mention whether she was alive or dead. It was therefore a big surprise to us⁴⁹ when in 1956 an elderly woman entered our Institute and declared herself to be the child who had been irradiated 60 years earlier by Freud. She was 64 years old at this time and presented because of osteoporosis of the vertebral column in combination with back pain. Examination showed kyphosis of the thoracic spine with curvature in the lumbar region. The entire skin of the back was hairless and covered by small hyperkeratotic changes. In the lumbar region a scar was found and the skin surrounding the scar showed atrophy. No damage was found to inner organs beneath the skin and we assumed therefore that the radiation was of a very soft quality.

Because of the historic interest in this patient she was asked to attend for follow-up at the age of 75 years and apart from back pain was found to be in good health. The X-ray ulcer is cured, as seen in the photographs. The osteoporosis is not thought to be radiation related but due to an ageing process. She told us that menarche occurred at the age of 13 years and that her only son is now 48 years old and in good health, as is her 13 year old grandson.
Initially more non-cancerous diseases were treated that cancer (still popular in Europe)
RT mainly performed with Linear Accelerators
Radio-isotopes therapy

Brachytherapy  Systemic therapy  Teletherapy
Brachytherapy

<table>
<thead>
<tr>
<th>Isotope</th>
<th>Average(^a) photon energy (MeV)</th>
<th>Half-life</th>
<th>HVL in lead (mm)</th>
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<tbody>
<tr>
<td>Co-60</td>
<td>1.25</td>
<td>5.26 a</td>
<td>11</td>
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<tr>
<td>Cs-137</td>
<td>0.66</td>
<td>30 a</td>
<td>6.5</td>
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<tr>
<td>Au-198</td>
<td>0.41</td>
<td>2.7 d</td>
<td>2.5</td>
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<tr>
<td>Ir-192</td>
<td>0.38</td>
<td>73.8 d</td>
<td>3</td>
</tr>
<tr>
<td>I-125</td>
<td>0.028</td>
<td>60 d</td>
<td>0.02</td>
</tr>
<tr>
<td>Pd-103</td>
<td>0.021</td>
<td>17 d</td>
<td>0.01</td>
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</table>
Photon-Emitting Radionuclides: $^{226}\text{Ra}$

Radium’s appearance is almost pure white, but it readily oxidizes on exposure to air, turning black.
Radium plaque treatment

First cure of cancer by radium plaque - 1922
Photon-Emitting Radionuclides: $^{137}\text{Cs}$

Fig. 1.1 Diagrammatic representation of a caesium-137 tube similar to an Amersham 'J-Type' tube.
Photon-Emitting Radionuclides: $^{192}\text{Ir}$
Partial breast HDR brachytherapy
Lung HDR brachytherapy
Photon-Emitting Permanent Implants

$^{198}\text{Au}$

- Half Life: 2.7 d
- Emission: 0.412 MeV
- HVL: 2.5 mm Pb

$^{125}\text{I}$

- Half Life: 59.4 d
- Emission: 0.028 MeV*
- HVL: 0.025 mm Pb

$^{103}\text{Pd}$

- Half Life: 17.0 d
- Emission: 0.021 MeV*
- HVL: 0.008 mm Pb

*average energy
Beta-Emitting Radionuclides: $^{90}\text{Sr}$

Strontium mass: 88.907747

$^{90}\text{Sr}$

T$_{1/2}$ = 28.78 y

Yttrium mass: 88.907183

$^{90}\text{Y}$

99.9995 %

T$_{1/2}$ = 64 h

Zirconium mass: 89.904700

$^{90}\text{Zr}$

2$^+$ 2162.3 keV

0$^+$ 1756.7 keV

0$^+$
Systemic Radiation Therapy

- Radiation can also be delivered by an injection
  - Metastron ($^{89}$Strontium), Quadramet ($^{153}$Samarium) and Xofigo ($^{223}$Radium) are radioactive isotopes absorbed primarily by cancer cells
    - Used for treating bone metastases
  - RAIT ($^{131}$Iodine)
    - Radioactive isotopes may be attached to an antibody targeted at tumor cells
    - Zevalin, Bexxar for Lymphomas
  - Radioactive “beads” may be used to treat primary or metastatic liver cancer
    - Y$^{90}$-Microspheres
Radium Dial Painters (ca.1924)

Dial painters at their desks. Note open trays of luminized dials – tightly packed workers!

Photo courtesy of Drs. Finkel & Miller (Argonne Radium Study) – used to trace workers.

**Xofigo**

**$^{223}\text{Ra}$**

- **Primary alpha**
  - 95.3% $\alpha$ (5–7.5 MeV)
  - 3.6% $\beta$ (0.45-.492 MeV)
  - 1.1% $\gamma$ (0.01-1.2 MeV)

- 11.4 day half life

- Range = 100 $\mu$m ~ 10 cell diameters (limiting damage to absorption site)

- **Treatment**
  - Dose (uCi) = 1.49 Weight (kg)
  - Once a month for six months

- Treatment helps extend life by more than 30%

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**Overall Survival**

![Graph showing overall survival comparison between Treatment and Placebo groups.](image)
Xofigo \( ^{223}\text{Ra} \)

- **Distribution after injection**
  - \( ^{223}\text{Ra} \) rapidly cleared from blood primarily into bone or excreted into intestine

- **Blood:**
  - Fifteen minutes following injection ~ 20% remains in the blood.
  - At 4 hours following injection ~ 4% remains in the blood.
  - At 24 hours following injection ~ 1% remains in the blood.

- **Bone and Intestine:**
  - At 10 minutes following injection, radioactivity is observed in bone and in the intestines.
  - At 4 hours following injection ~ 61% remains in the bone.
  - At 4 hours following injection ~ 49% remains in the intestine.
  - No significant uptake was seen in other organs such as heart, liver, kidneys, urinary bladder, and spleen at 4 hours post-injection.

- **Elimination:**
  - Fecal excretion is the major route of elimination from the body. At 48 hours after injection, the cumulative fecal excretion is ~ 13% (range 0 - 34%), and the cumulative urine excretion is ~ 2% (range 1 - 5%).

- **No restriction regarding contact with other people upon release**
- **Follow good hygiene to minimize dose to family**
- **Use condom and ensure female partner uses highly effective birth control**
RAIT radioiodine therapy

- Tx for differentiated thyroid cancer post surgery
- Capsule form Iodine-131 dissolves in the stomach travel systemically throughout the body absorbed by thyroid tissue remains
- ~ 100 mCi
Y-90 microsphere (Therasphere)

Hepatic vein carries blood from the liver on to the heart with levels of food adjusted

Liver

Blood arrives at the liver from two sources:

1. Hepatic portal vein carries blood containing digested food from the intestines to the liver
2. Hepatic artery brings oxygenated blood to the liver
Y-90 microsphere treatment
Teletherapy Gamma Knife
How is conformity accomplished?
Accuracy & Precision

Neither A or P

P but not A

A but not P

A & P
Hallmarks of Radiosurgery

- High Penumbra is system dependent
  - How sharp is the beam edge

![Graph showing Penumbra widths for 4mm, 8mm and 16mm collimators for an iso-center.](image)
Helmet Penumbra

The broader the field, the larger the overlapping volumes
60Co Sources
Video Overview
Leksell Gamma Knife® Perfexion™

- Collimator system built into unit (inner cylinder)
  - 3 collimator sizes: 4-, 8- and 16-mm
- Sources move on sectors above collimator (outer cylinder)
- Patient positioning via precise couch movements
- Fully automated - no manual patient positioning or source/collimator adjustment
### Rings:

<table>
<thead>
<tr>
<th>Ring Number</th>
<th>Number of Sources</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>48</td>
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<tr>
<td>2</td>
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<tr>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>5</td>
<td>34</td>
</tr>
</tbody>
</table>
Perfexion vs. C Collimator
Radiation Beam Collimation

- Color coded ring with spring loaded bearings for easy mounting
- Central body
- Stationary Collimator
- Collimator Helmet
- Final Collimator
- Bushing assembly
- Final Collimator channel
- Unit center point
- Beam diameter

[Image of radiation beam collimation system with labeled parts]
Stereotactic Frame
Diagnostic Imaging

- MRI, CT, Angiogram
- Images registered in Leksell coordinate system via fiducial box
GK Planning
GK Planning
GK Planning
Acoustic Neuroma

Pre 6 months post 2 years post

Courtesy: Douglas Kondziolka, MD, MSc, FRCS, University of Pittsburgh, USA
Arteriovenous Malformation

Pre Gamma Knife Surgery

2 years post Gamma Knife Surgery

Courtesy: Douglas Kondziolka, MD, MSc, FRCS, University of Pittsburgh, USA
The patient presented is a 37 year old female treated with the Gamma Knife for 4.0cc AVM on Nov 11, 1995. The treatment was 23 Gy to the 50% isodose. The follow-up was Oct 25, 1999 and showed complete obliteration. The patient remains well.

Courtesy: Aizik Wolf, M.D., Sam Coy, Ph.D., Miami Neuroscience Center, Coral Gables, Florida
NCCN Guidelines Central Nervous System Cancers – Brain Metastases

80% in cerebral hemispheres
5% in brainstem
15% in cerebellum

Presenting signs and symptoms include headache, seizures, & neurologic impairment
Metastasis

10 months post

Pre

Courtesy: Aizik Wolf, MD, Miami Neuroscience Center, USA
Trigeminal Neuralgia

Dose plan 6 months post

Courtesy: Douglas Kondziolka, MD, MSc, FRSC, University of Pittsburgh, USA
Functional disorder

Figure A
Handwriting sample from a 76 year old woman with longstanding essential tremor before Gamma Knife Surgery.

Figure B
The left Gamma Knife thalamotomy could be seen 4 months later after a max. dose of 140 Gy delivered with a single 4mm isocenter.

Figure C
Handwriting sample four months after Gamma Knife Surgery showed that her tremor had resolved.

Courtesy: L. Dade Lunsford, M.D., and Douglas Kondziolka M.D., University of Pittsburgh, USA
Metastasis Ex 2013-08-19
Metastasis Ex 2013-09-04
Conclusion

- Majority of radiation therapy performed with Linear Accelerators
- Radio isotopes do have a role and it seems to be expanding