Palliative Radiotherapy

An Introduction
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Learning Objectives

• An understanding of the mechanism of action of Radiation
• The distinction between acute and late side effects of Radiation
• Common clinical presentations
• Treatment strategies
• Radiotherapy 70% all cancer patients
• Radiotherapy 50% palliative patients
• Consistently high response rates
• Often not considered early in the terminal stages of disease.
Cellular Effects

- X-rays and Gamma rays
- Damage cellular DNA
- Base deletions, single and double strand breaks
- Differences in repair capacity tumour v normal tissue
Reoxygenation

- Oxygenated
- Necrotic

Hyperbaric O₂
Radiosensitizers
High LET
Fractionation

Increases the Therapeutic ratio of radiation

- Log S
- normal tissue
- tumour
- Time

0
Normal Tissue Effects

**Acute (within 6 weeks)**
- Due to the anti proliferative effect of radiation
- Occur during the treatment or within 2 weeks of completion
- Treatment is symptomatic and expectant
- Mechanical shearing is important
- Recovery usually takes place within 2 weeks of completion of treatment.
- There is a lag phase between completion of treatment and re proliferation.
- Proportional to total dose received

**Late (after 6 months)**
- Due to the small vessel obliteration due to the radiation
- This causes local anoxia and the development of new blood vessel formation and fibrosis.
- Extent related not to the total dose but to the fraction size
- Can cause serious permanent disability
- Frequently does not occur for many (10+) years post treatment.
Radiation Carcinogenesis

• Rare complication of radiation
• Two peaks of incidence
• 12 – 14 years Leukaemia
• 20 years plus solid tumours
• Related to low does and very high dose treatments
Delivery Systems

• External Beam - Superficial
  - Orthovoltage
  - Megavoltage
  - Electrons

• Intracavity (Caesium)

• Interstitial (Iridium)

• Internal (Iodine, Strontium)
Palliative Radiotherapy

- Aim - Reduction of symptoms with minimal acute radiation reaction
- Low dose
- Large fraction
- Short treatment time (1-2 weeks)
Radiotherapy for Bone Pain

• External-beam radiotherapy provides excellent palliation in metastatic bone pain.

• The treatment of choice in majority of these patients.

• A wide range of single and multifraction schedules are used.

• No clear evidence of a dose-response for RT and bone-pain relief.
Radiotherapy for Bone Pain

• The sole object is to decrease or eliminate the distressing symptom - **PAIN**.

• The treatment should employ

  - the simplest fractionation schedule

  - maximum relief

  - minimum morbidity & cost
Radiotherapy for Bone Pain

- Major workload for any Radiation Oncology Department
  - 40-50% of all treatments
  - 15-25% of all new radiotherapy courses

500-600 new cases of bone pain in Auckland each year
Radiotherapy for Bone Pain

- Auckland data for 1998
  - Total no. of treatment courses for bone pain - 696
  - Single fraction - 246 (35.4%)
  - 4 fractions - 52 (7.5%)
  - 5 fractions - 321 (46%)
  - >5 fractions - 77 (11.1%)
## Radiotherapy for Bone Pain

- **RTOG Study (1982)**

  **Solitary metastasis**
  - 20 Gy/1 wk.
  - 30 Gy/2 wk.
  - 40.5 Gy/3 wk.

  (266 pt. - 146pt.)

- **Multiple metastasis**
  - 15 Gy/1 wk.
  - 20 Gy/1 wk.
  - 25 Gy/1 wk.

  (750 pt. - 613pt.)
Radiotherapy for Bone Pain

- RTOG Study (1982)
  - 90% experienced some pain relief.
  - 54% achieved complete pain relief.
  - Median duration of complete relief 12wk.
  - Primary site & primary pain scores were prognostic factors.
Radiotherapy for Bone Pain

RTOG Study (1982)

• Low-dose, short-course schedules were as effective as high-dose protracted schedules.

• Higher incidence of fractures at the treatment site in the 40.5 Gy group.
Radiotherapy for Bone Pain

• Reanalysis of the RTOG study (1985) by Blitzer. ‘I have reanalysed the data using different techniques.’

* Different endpoints (accounting for retreatment and the use of narcotics)

* Protracted dose-fractionation schedules are more effective than short course schedules.
Radiotherapy for Bone Pain

- The Royal Marsden Hospital Trial (1986)
  - Single fraction - 8 Gy (140 pt.)
  - Multiple fraction - 30 Gy/2 wk. (148 pt.)

  Pain assessment by the patients.

Follow up - 3 months
Radiotherapy for Bone Pain

The RMH Trial (1986)

• No significant differences in speed of onset or duration of pain relief between two regimens.

• Pain relief was independent of histology of primary tumour.
Radiotherapy for Bone Pain

- The Royal Marsden Hospital Trial (1992)
  - 4Gy single dose (137 pt.)
  - 8Gy single dose (133 pt.)

* At 4 wk actual response rates were 69% (8Gy) and 44% (4Gy), but no differences in complete response or duration of responses.

*8Gy gives higher probability of pain relief than 4Gy.
Radiotherapy for Bone Pain


  20Gy in 5 f (51pt.) vs. 30Gy in 15f (49pt.)

  *No significant differences in frequency, duration of pain relief, improvement of mobility, recalcification and frequency of pathological fractures.
Radiotherapy for Bone Pain


4Gy (109 pt.), 6Gy (108 pt.), 8Gy (110 pt.)

*Significantly higher overall response rates for 6&8Gy when compared with 4Gy

*No difference between the 3 groups in duration of response and retreatment rate.
Radiotherapy for Bone Pain

  8Gy single f  versus  20Gy in 5 f

* No significant differences in pain relief up to 6 months post-treatment.
Radiotherapy Bone Pain Trial

8Gy single fraction radiotherapy for the treatment of metastatic skeletal pain: randomised comparison with a multifraction schedule over 12 months of patient follow up.

<table>
<thead>
<tr>
<th>Single fraction</th>
<th>Multifraction</th>
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<td>(8GY)</td>
<td>(20GY/5f or 30GY/10f)</td>
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• 78% & 78% - some pain relief

• 57% & 58% - complete response

* No statistically significant differences between the groups
Radiotherapy Bone Pain Trial

• No differences in the time to first improvement in pain, time to complete pain relief or time to first increase in pain upto 12 months, nor in the analgesic used.

• No significant differences in the incidence of nausea, vomiting, spinal cord compression or pathological fracture.

• Retreatment was twice as common after 8Gy - evidence suggests clinician bias.
Time to Pain Control

Weeks since start

% Probability of Pain Relief

Multiple Fraction

Single Fraction

$p > 0.1$
Radiotherapy for Bone Pain

• Conclusions
  * No clear evidence of a dose-response relationship for radiotherapy and bone pain relief.
  * Single fractions appear as effective as multi-fraction regimens.
  * A single fraction of 8Gy appears as safe and effective as a multifraction regimen for the palliation of metastatic bone pain for at least 12 months.
  * All trials have a spread of variables (primary tumour types, site of bone lesions and bone defects, pain scores, treatment techniques, frequency of re-treatment and methods of calculation of benefits).
  * The greater convenience and lower cost make 8GY single fraction the treatment of choice for the majority of patients.
Hemi - body Radiation

- Under used
- Multiple sites of disease
- Multiple sites of pain
- Poorly localized
- Wide field (upper / lower)
- 600cGy - 800 cGy
- Single treatment
Hemi - body Side Effects

- Nausea
- Vomiting
- Diarrhoea
- Bone marrow suppression
- Pneumonitis
Hemi - body Indication

- Prostate cancer
- Breast Cancer
- Myeloma
- Disseminated cancer (all types should be considered)
Hemi-body: Onset of Pain Relief

Cumulative Percentage

Days after treatment

- Hemibody irradiation
- Local radiotherapy
Method of Action

• Not clear

• Tumour cell kill

• Local effects -? supporting tissues
  ? humoral factors
  ? osteoblast / osteoclast interactions
Internal Radiation

- Strontium 89
- Phosphorus 32
- Iodine 131
- Simple outpatient intravenous injection
- Radiation protection
- Prostate cancer, breast cancer, lymphoproliferative disorders
Malignant
Extra Dural Spinal Cord Compression
The Problem

5% of all patients with cancer.
20% of patients with axial bone metastases
Commonest - NSCLC & SCLC
    - Breast Cancer
    - Myeloma
    - Prostate
Results of Treatment (Findlay)

- Average Survival 4 months
- No difference between Surgery + XRT Vs XRT alone
- 80 - 90% Spinal cord compression can be treated by XRT
- Pain control achieved in 80%
- 90% of Ambulatory patients remain ambulatory
- 50% Paretic become ambulatory
- 0 - 10% Plegic become ambulatory
Aims of Treatment

• Palliative
• Maintenance / restoration of spinal stability
• Restoration and maintenance of Mobility/ continence
• Pain Control
Ideal Treatment

- Short
- Low Side effect
- Simple
- Effective
Dexamethasone

- Good evidence to support the use of high dose Dexamethasone 96 mg/day
- Inconclusive for 16 mg/day
- Steroids may not be indicated in patients who are ambulatory and not paretic.
Radiotherapy

- 5 articles (RTOG, ACR,)
- No evidence to support the use of more than 20 Gy 5#
- Patients other than those paraplegic for > 24 hrs should receive immediate XRT
- For paraplegic patients where the aim is pain control 8 - 10 Gy single fraction
- For paraplegic patients with no pain irradiation may not be indicated
Rehabilitation

- Fully ambulant (WHO 0 - 2) Nil

- Moderately impaired (WHO 3) Intensive rehabilitation

- Severely impaired (WHO 4+) Assume wheelchair / bed bound for the future.
Brain Metastasis
Results of Treatment

• 50% Patients with radiosensitive tumours respond to XRT

• Average survival 3 - 5 months

(WHO 4 and 5 - 4 Weeks)
Aims of Treatment

• Palliative
• Maintenance independence
• Pain Control
Ideal Treatment

• Short
• Low Side effect
• Simple
• Effective
Literature Review

• Generally disappointing concentration on Radiosurgery.

• Two good trials:

  RTOG Brain mets trial 1980 (20 - 40 Gy various # schemes. 20 Gy 5# equivalent to all else
  RCR Brain mets trial 12 GY in 2# Vs 30Gy in 10# no difference seen
• Radiotherapy 70% all cancer patients
• Radiotherapy 50% palliative patients
• Consistently high response rates
• Often not considered early in the terminal stages of disease.