Palliative Radiotherapy

An Introduction

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Learning Objectives

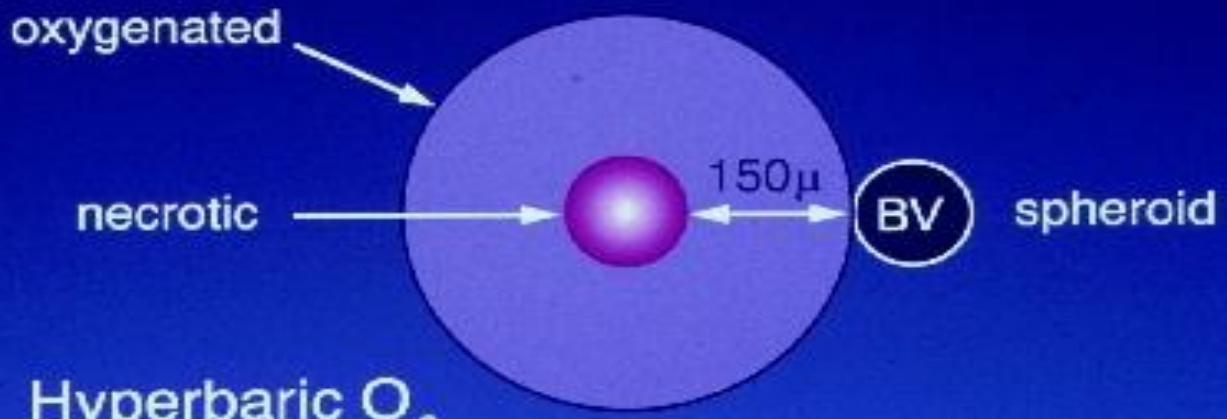
- An understanding of the mechanism of action of Radiation
- The distinction between acute and late side effects of Radiation
- Common clinical presentations
- Treatment strategies

- Radiotherapy 70% all cancer patients
- Radiotherapy 50% palliative patents
- 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

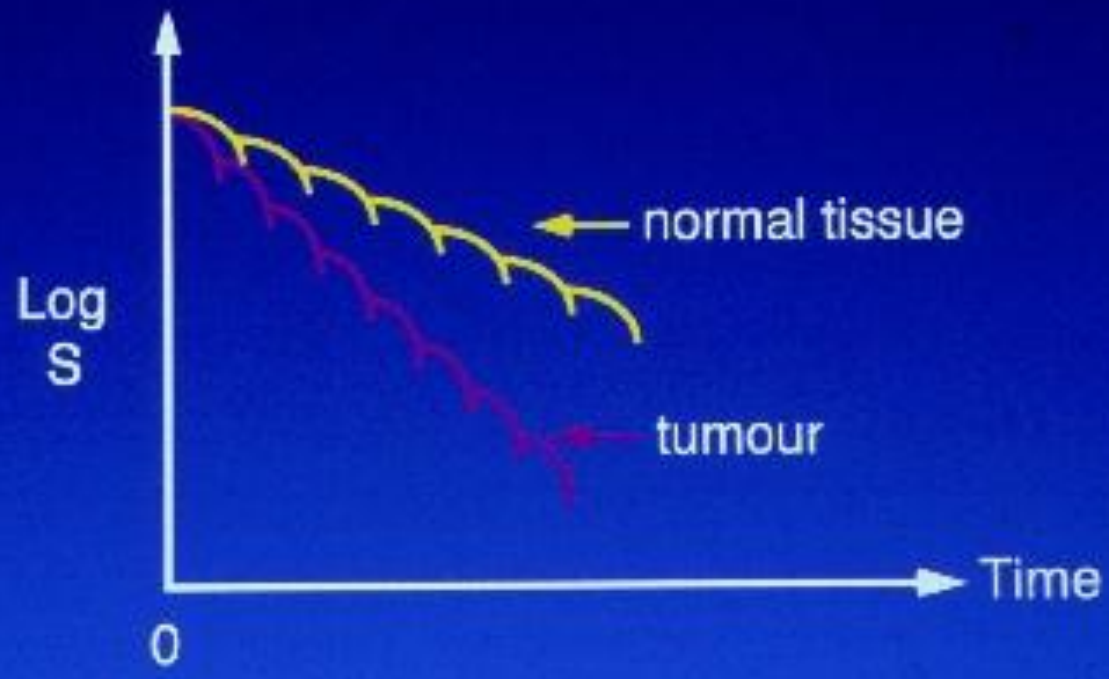
Reoxygenation



Hyperbaric O_2
Radiosensitizers
High LET

Fractionation

Increases the Therapeutic ratio of radiation



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.
(266 pt. - 146pt.)	- 30 Gy/2 wk.
	- 40.5 Gy/3 wk.
Multiple metastasis	- 15 Gy/1 wk.
(750 pt. - 613pt.)	- 20 Gy/1 wk.
	- 25 Gy/ 1 wk.

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

- Rapid course radiation therapy vs. more standard treatment: A randomised trial for bone metastases. Niewald et al (1996)

  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

- A randomized trial of three single dose radiation therapy regimen in the treatment of metastatic bone pain. Jeremic et al (1998)

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

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

*No difference between the 3 groups in duration of response and retreatment rate.

Radiotherapy for Bone Pain

- Randomised trial of single dose versus fractionated palliative radiotherapy of bone metastases. Nielsen et al 1998.

  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.

Single fraction	Multifraction
(8GY)	(20Gy/5f or 30GY/10f)
383 pt.	378 pt.

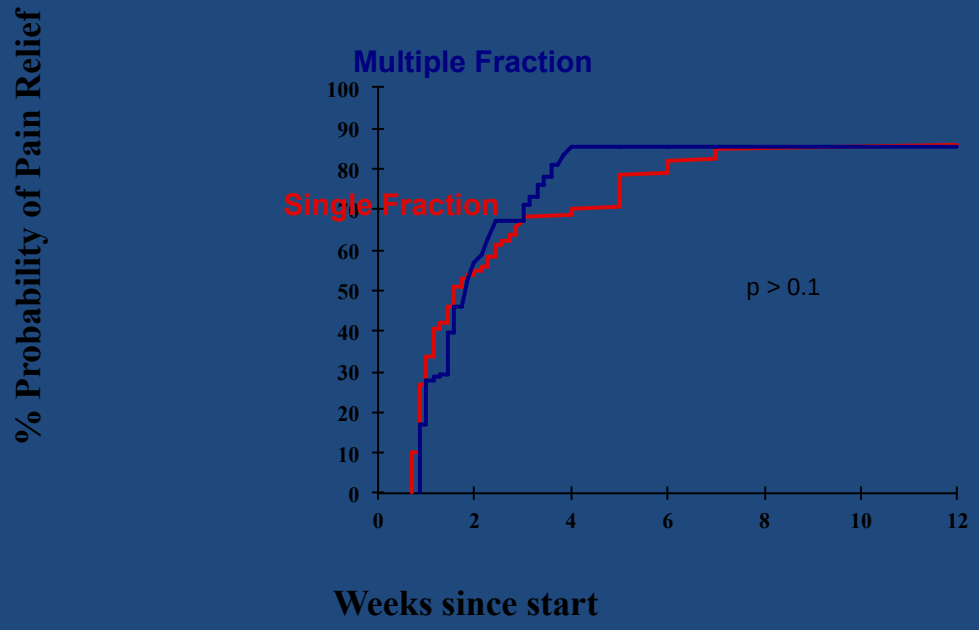
- 78% & 78% - some pain relief
- 57% & 58% - complete response

* 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



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

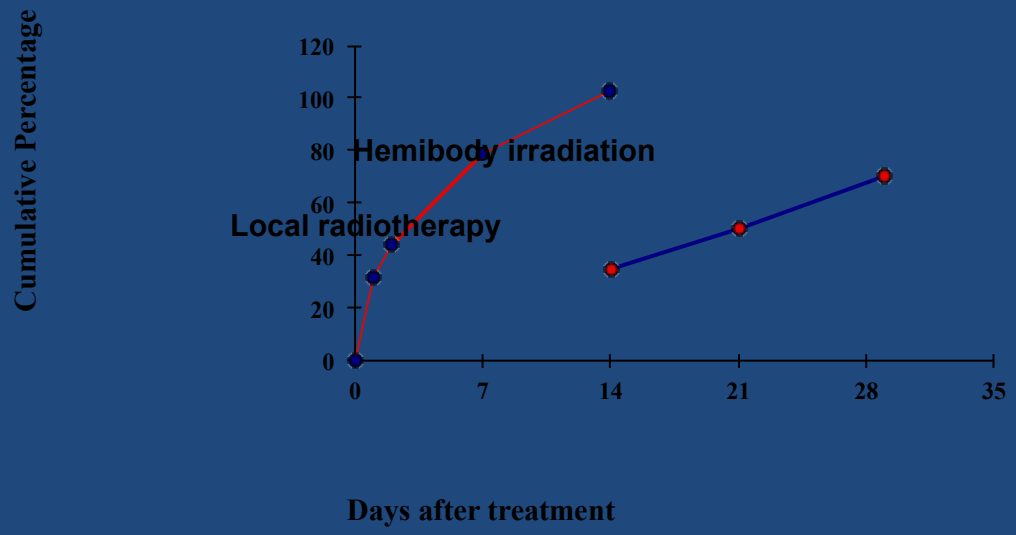
Hemi - body Side Effects

- 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



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

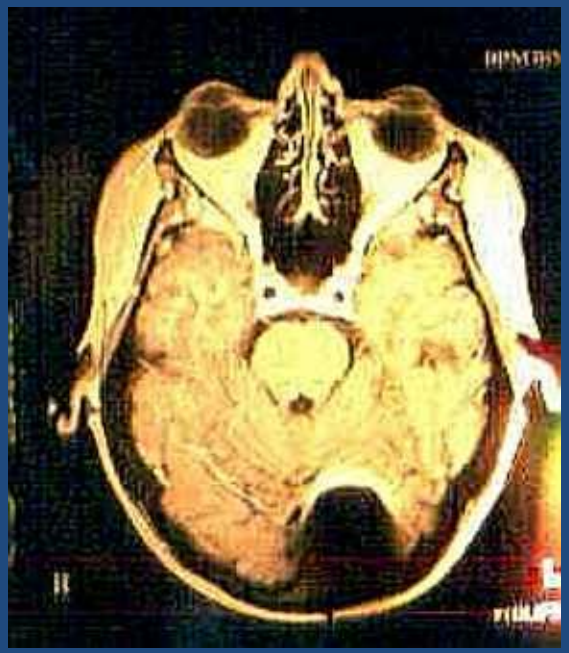
- Severely impaired (WHO 4+) Assume wheelchair / bed bound for the future.

Brain Metastasis

Results of Treatment

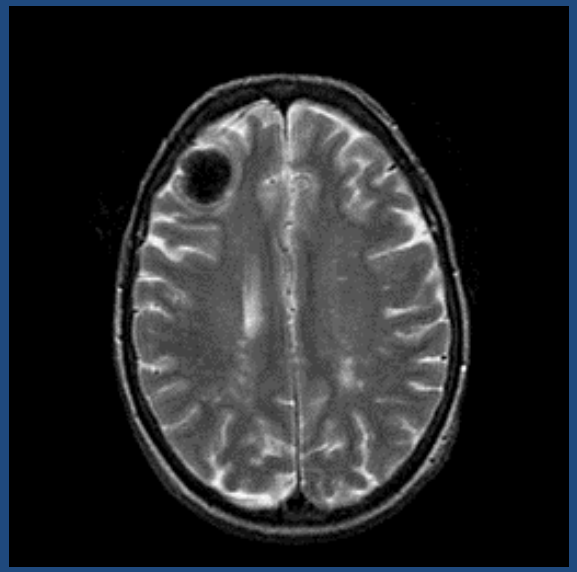
- 50% Patients with radiosensitive tumours respond to XRT
- Average survival 3 - 5 months

(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 patents
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