

Benefits of Radiation Therapy in the Palliative Cancer Patient

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Overview

- Why we should aim for better palliative radiotherapy treatment
- Bone metastases
 - Rapid response palliative radiotherapy program
- Brain metastases
- Radiotherapy emergencies
 - Malignant spinal cord compression
 - Superior vena cava obstruction

Why better palliative Radiotherapy?

- With better systemic therapy, patients with advanced disease are living longer and management of toxicity and quality of life are important treatment outcomes
- Palliative Radiotherapy
 - Overall Pain Relief 80-90%
 - Average Response Duration is around 6 months
 - Rates of re-irradiation 10-25%

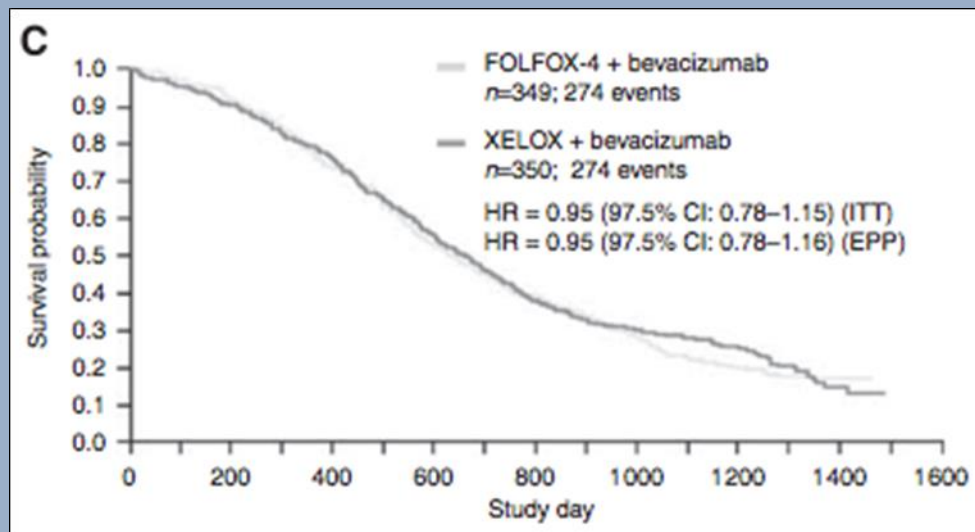
Therefore re-irradiation is becoming a more significant issue in our contemporary era due to improving survival amongst patients with metastatic disease.

- Adelaide Radiotherapy Centre has recently introduced a new protocol to align the management of palliative cases with that offered to curative cases – to ensure quality and best practice patient care outcomes.

Survival rates

- Colorectal Cancer

- Patients with unresectable metastases have median survival exceeding 2 years with modern chemotherapy and biological agents¹ (FOLFOX4, XELOX, Avastin) compared with 5FU alone² (11.5 mths)



1. Cassidy *et al.* NO16966 trial BJC 2011
2. Advanced CRC Meta-Analysis JCO 1992

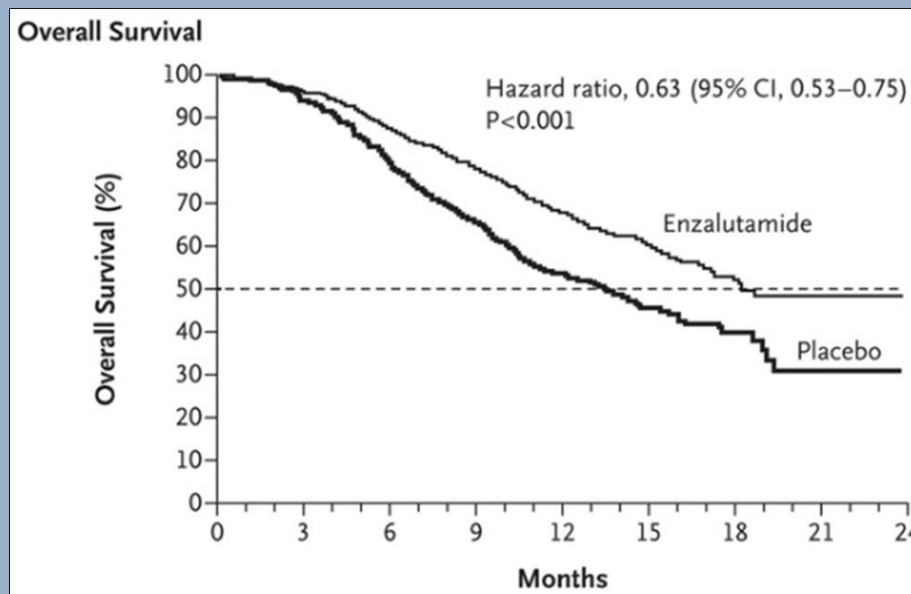
Survival rates

- Breast Cancer
 - Patients with metastases have median survivals approaching 2 years for a 5 year interval 2000-2004 with modern chemotherapy, hormonal and immunotherapy compared with 10 months when only more limited options were available for the 1985-1990 period³
 - Median survival can exceed many years depending on hormone receptor status, Her 2 status and location of metastases (bone versus visceral)

3. M Sundquist *et al.* Katnor Sweden EBCC 2010

Survival rates

- Prostate Cancer
 - Patients with metastases have median survivals approaching 6 years with hormonal therapy and chemotherapy (taxanes)
- Enzalutamide AFFIRM
 - Median OS improved from 13 to 18 months



Palliative radiotherapy

Traditionally large doses were delivered via simple beam arrangements – this restricted our ability to deliver re-irradiation.

A traditional PA Plan of 30.00Gy @ D5cm

- Peak dose of 33Gy to Spinal Cord with EQD₂ 44Gy
- Plus poor coverage of target volume

Palliative radiotherapy

This severely restricts our ability or willingness to RE-IRRADIATE as we approach the limits of the critical normal tissue tolerance.

This will DENY patients the opportunity to have further benefit from radiotherapy with 50-80% deriving pain relief with re-irradiation.

Palliative radiotherapy

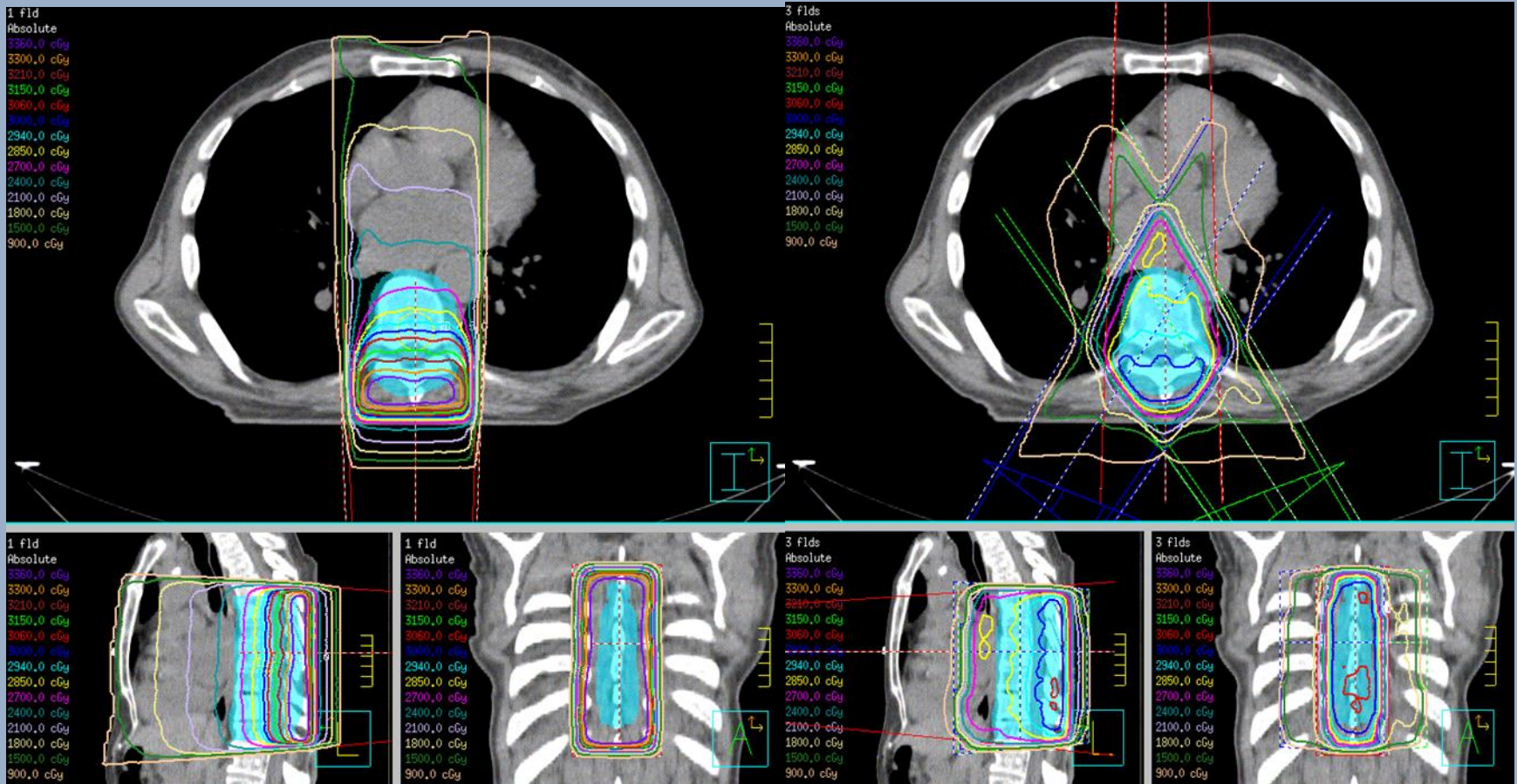
Using a conformal planning and treatment approach aligning palliative treatment with treatment given to radical cases, the total dose and dose per fraction is kept at or below our prescription and we achieve far better coverage of our target volume.

A conformal plan of 30Gy

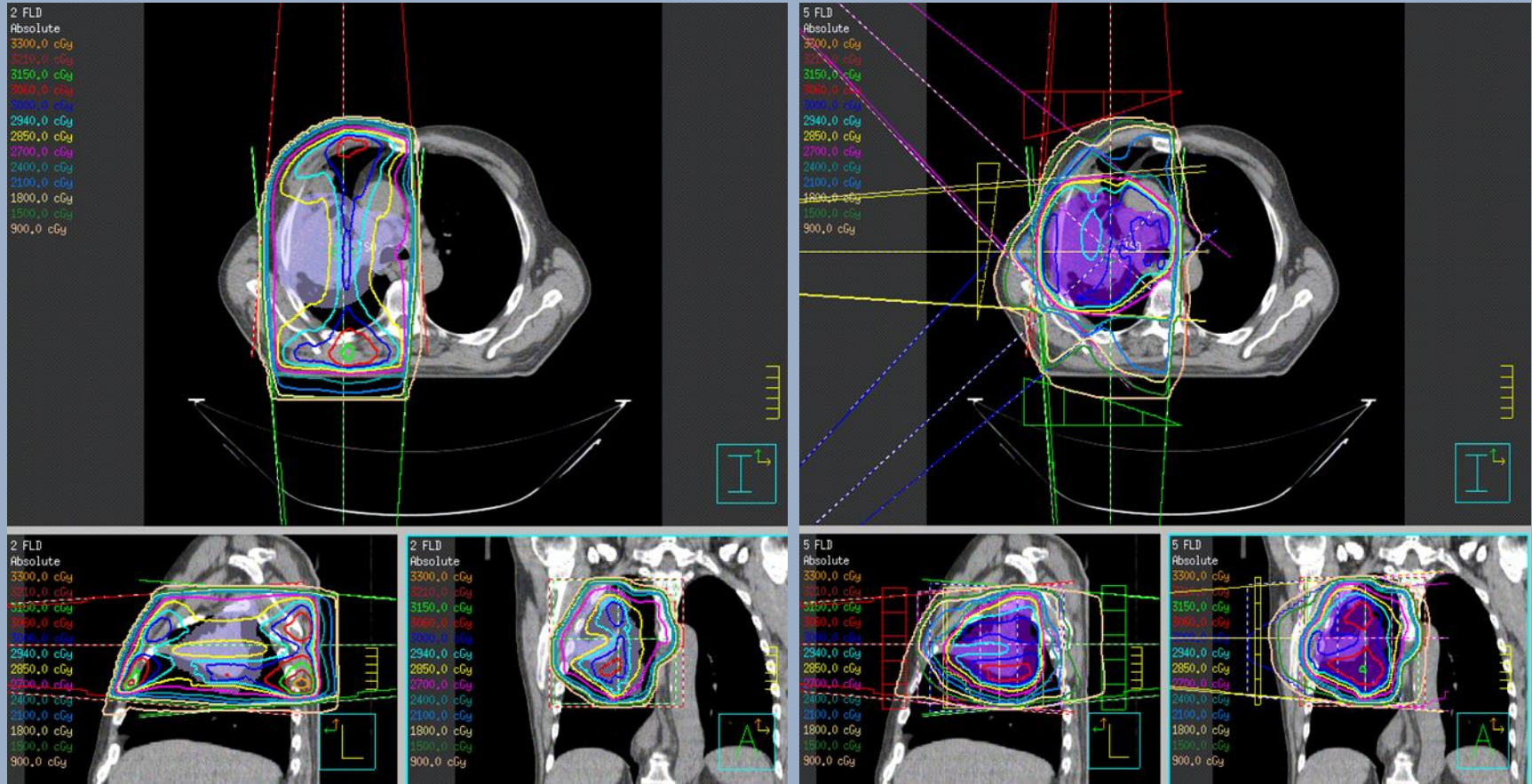
- Peak dose of 30Gy to spinal Cord with EQD2 of 36Gy
- Improved coverage/control of symptoms and decreased acute and late toxicities

In general, better management of the high dose region, including absolute value (the hot spot) and location (avoid OARs) is now required for every palliative plan.

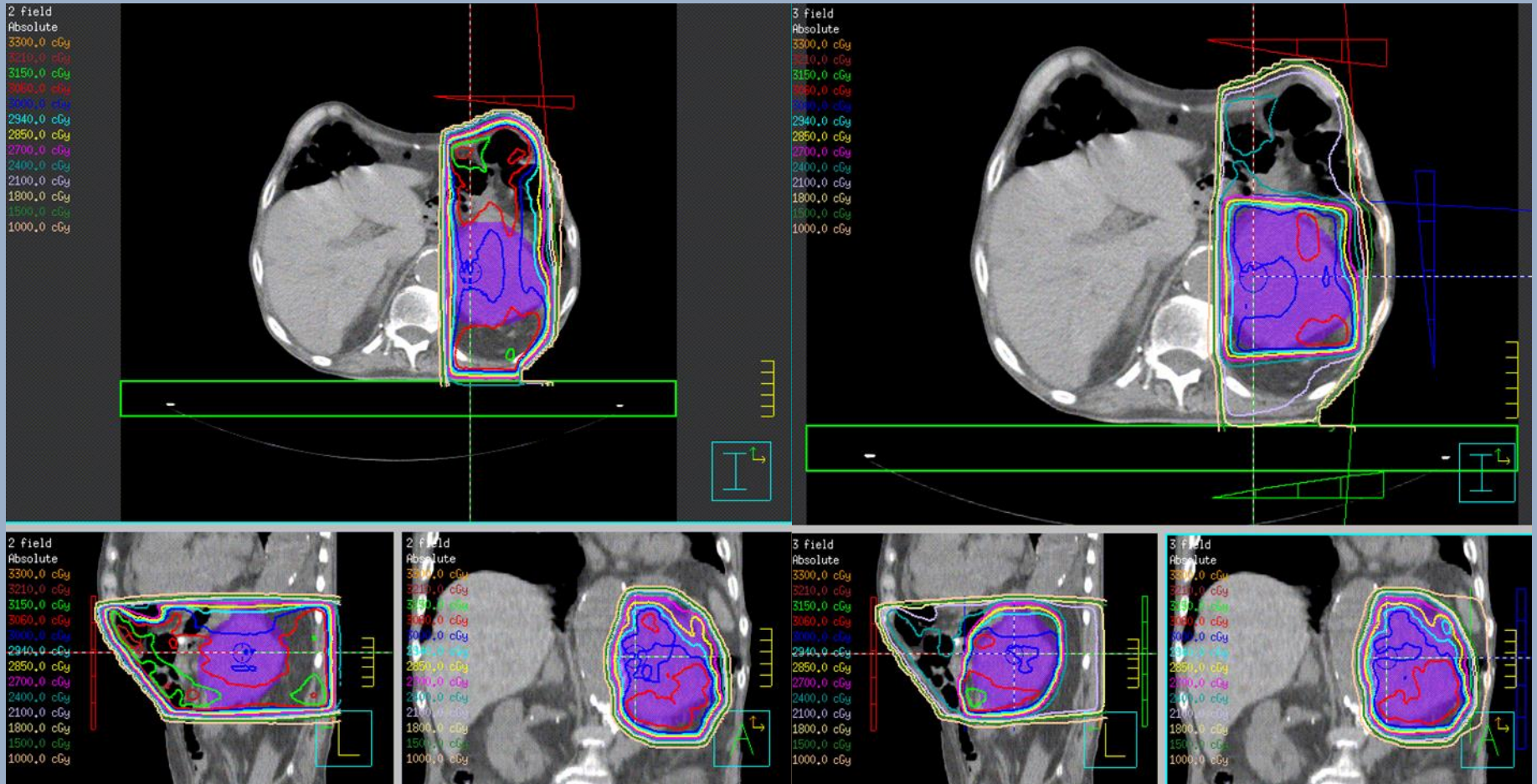
Examples: 2D vs 3D Conformality



Examples: 2D vs 3D Conformality



Examples: 2D vs 3D Conformality



Burden of bone metastases

- Bone metastases are the most common cause of cancer-related pain
- 60-80% of patients with advanced cancer will develop bony metastases
- >70% of patients with bone metastases are symptomatic
- Bony metastases account for 20% of all radiotherapy treatments
- In addition to pain, skeletal complications from bone metastases include:
 - Pathological fractures (10-30% long bone mets)
 - Spinal cord/cauda equina compression (5-10%)

Role of palliative RTx for bone mets

- Aims of palliative radiotherapy for bone metastases:
 - Relieve pain
 - Delay/prevent skeletal complications
 - Improve/preserve function and QOL
- Radiotherapy is one of the most effective treatments for cancer pain
 - 70-80% response rate to palliative RTx for painful bone mets

Bone mets

- Mechanism of analgesic effects of RTx not completely understood:
 - Inhibition of release of chemical pain mediators
 - Tumor shrinkage and recalcification of bone lesions
- Onset of response within 2-4 wks in 80% patients
- Median duration of pain relief varies b/w 3 - 6mths
- Common side effects include:
 - Fatigue
 - Pain flare: 10 - 40 %; usually within first 5 days after RTx
 - Nausea/vomiting: 10-17%
 - Others are site dependent: eg mucositis, diarrhoea

Bone mets

- For patients with uncomplicated bony mets experiencing distressing pain, poor mobility/performance status and limited life-expectancies, a single fraction will be more convenient/acceptable and cost-effective.
 - * Uncomplicated bony metastases - absence of:
 - neuropathic pain
 - large soft tissue masses
 - impending/actual pathological fracture or cord compression
- RTx generally involves a series of appointments:
 - Initial clinic consultation
 - Radiotherapy simulation/planning
 - Radiotherapy treatment: Single fraction or 5-10 fractions

Rapid Response Palliative Radiotherapy (RRPR) Program

- Aims of the RRPR program for bone metastases:
 - Provide quick/easy access for referring doctors
 - Reduce waiting times for:
 - Initial consultation,
 - Simulation/planning
 - Start of treatment
 - Reduce the number of visits required before delivery of treatment
 - Improve the underutilization of palliative RTx for bone mets, esp in rural populations

Rapid Response Palliative Radiotherapy (RRPR) Program

Patient Suitability:

- Public and private patients
- Symptomatic bony metastases requiring palliation

Nb. Actual/impending cord compression: RTx emergency – NOT for RRPR Clinic

Referral Process:

- Direct referral to the RRPR Clinic
- Standardized RRPR Clinic referral form
 - Ensure availability of all necessary patient investigations/info
 - Facilitate prebooking of planning and treatment start date

Brain mets

- Approx 25% of patients with systemic cancers – possible increase due to more effective local and systemic control (most chemo doesn't cross blood brain barrier)
- Most common – breast, lung, colorectal, melanoma
- Confers poor prognosis with MS of 4-5mths and 1yr OS 10%
 - no treatment – 1mth
 - Steroids – 2mths
 - RTx - 4-6mths
 - Surg+RTx – 8-12mths
- General prognostic factors
 - Age, performance status, status of extracranial disease, disease free interval, size of mets, mass effect, histology

Whole Brain Radiotherapy (WBRT)

- The main goal of WBRT
 - Improve neurologic deficits caused by the metastases and surrounding oedema
 - Prevent any further deterioration of neurologic function.
- The extent of improvement after WBRT is directly related to the time from diagnosis to radiation therapy, and early treatment is generally associated with a better outcome.

WBRT

- WBRT is the treatment of choice for
 - Patients with single or multiple brain metastases not amenable to surgery or radiosurgery
- Complete and partial responses have been reported in approximately 60% of patients, with symptom improvement that is in part attributable to concomitant steroids.
- Tumour volume reduction after WBRT is associated with prolonged survival and better neurocognitive function preservation.

Indications for WBRT

- Histological or radiological evidence of metastatic disease involving the brain
- Multiple brain metastases or solitary metastasis unsuitable for surgical resection
- ECOG 0-2 (KPS of >70 ~ equates to ECOG 0-1)
- No prior cranial radiotherapy
- Stereotactic radiotherapy may be considered in patients with 1-3 brain metastases who have controlled extra-cranial disease

Side Effects of WBRT

- **Short term side effects during or within a few weeks of finishing radiotherapy (usually temporary)**
 - Alopecia
 - Fatigue
 - Skin erythema and desquamation
 - Headaches
 - Nausea and/or Vomiting
 - Neurological deficits
- **Sub acute**
 - Somnolence
- **Long term side effects that may be permanent**
 - Cerebrovascular disease
 - Cognitive impairment
 - Fatigue

Stereotactic Radiosurgery

- May be considered in 1-3 mets and in eloquent or deep areas where surgery not feasible
- Lesion <4cm
- >1cm from optic apparatus
- Newer frameless techniques making it more convenient and less resource intensive for treatment

Malignant Spinal cord/Cauda equina Compression (MSCC)

- Actual cord compression = radiological compression of dural sac AND clinical features
 - Back pain
 - Motor deficits
 - Sensory abnormalities
 - Sphincter dysfunction
- Impending cord compression = radiological evidence of cord compression but without neurological deficits

MSCC - Epidemiology

- 5-10% of all cancer Pts
- Common malignancies
 - Prostate, Breast, Lung
 - Others: myeloma/plasmacytoma, NHL
- 20% are first presentations of the malignancy
- 1/3 have multilevel disease

MSCC - Investigations

1. Confirm MSCC and nature/extent

- MRI WHOLE spine with Gad: Gold standard

2. Obtain histological diagnosis

- Favourable histo
- Intent of Rx
- Type of Rx

3. Staging

- Prognosis
- No known malignancy
 - Primary
 - Another site for Bx

MSCC Treatment - Surgery

- Generally accepted indications:
 - Instability
 - Bony compression
 - Progression on/after RTx
 - No histo Dx
- if single level compression

MSCC Treatment - Surgery

- Direct decompressive surgery/Postop RTx superior to RTx alone
- Patchell et al (NEJM 2005; 366: 643)
 - Multi-institutional RCT; N=101
 - Stopped early
 - Med survival: Surg/RTx 126 days
RTx alone 100 days (p=0.03)

MSCC Treatment - Radiotherapy

- RTx main Rx modality for most Pts
- Intent: Palliative (most)
 - Improving pain, maintaining function/delaying progression, ± improving function
- Timing: Upfront RTx started within 24hrs
 - the longer the duration of Sx, esp motor, the poorer the outcomes

MSCC Treatment - Radiotherapy

- Strongest PF for functional outcome is preRx ambulatory status
- 20-30% of nonambulatory Pts will regain ambulation with RTx alone

PreRTx Ambulation	PostRTx Ambulation
Ambulatory	90%
Assisted ambulation	60%
Nonambulatory paraparesis	< 40%*
Paraplegic	< 10%*

MSCC Treatment - Radiotherapy

- Only ~ 15% regain sphincter control/ continence
- Strongest PF for survival is also preRx ambulatory status

PreRTx Ambulation	Median Survival
Ambulatory	6 - 12 mths
Nonambulatory	2 - 4 mths

MSCC Treatment - Radiotherapy

- Est. survival < 4-6 mths: Short course
 - Equally effective for functional outcome
 - More convenient/less distressing for Pt
 - Despite apparent higher rate of in-field recurrences, re-irradiation safer
- Est. survival > 4-6 mths: Longer course
 - Apparent lower rate of in-field recurrences (but more difficult to re-irradiate)
 - Better bone recalcification (several mths; prospective German study cf single 8 Gy)

Malignant Superior Vena Caval Obstruction (SVCO)

- Invasion or external compression of SVC by disease involving:
 - Rt lung, LNs, mediastinal disease
 - \pm thrombosis within SVC
- SVCO causes venous collaterals to form
 - rate determines rate of onset of Sx/signs

SVCO - Epidemiology

- Malignancy most common cause (80-85%)
 - Others: Infection, Thrombosis (\pm catheter related)
- 2 most common malig causes (\sim 95% cases):
 - Lung Ca: Most common
 - \sim 5% of lung Ca Pts
 - SCLC: 20% will develop SVCO (central)
 - Lymphoma:
 - \sim 5% of lymphoma Pts
 - NHL > HL

SVCO - Investigations

- EMERGENCY Rx if STRIDOROUS
 - indicative of central airway obstruction by tumor
- Otherwise most cases now emphasis is on:
 - accurate but prompt diagnosis of the underlying malignancy
 - allows the most appropriate Rx to be given in a timely manner

Conclusion

- More conformal palliative treatment will hopefully decrease toxicities of treatment and allow more retreatment if necessary leading to improved quality of life

Thank you