



# **PRINCESS MARGARET CANCER CENTRE CLINICAL PRACTICE GUIDELINES**

## **CENTRAL NERVOUS SYSTEM**

### **BRAIN METASTASES**

# CNS Site Group – Brain Metastases

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# Brain Metastases

## 1. Introduction

- brain metastases from all primary sites
- commonest primary sites include lung, breast, colon, melanoma, renal
- commonest cause of intracranial mass
- may occur in up to 45% of cancer patients

This document is intended for use by members of the Central Nervous System site group of the Princess Margaret Hospital/University Health Network.

The guidelines in this document are meant as a guide only, and are not meant to be prescriptive. There exists a multitude of individual factors, prognostic factors and peculiarities in any individual case, and for that reason the ultimate decision as to the management of any individual patient is at the discretion of the staff physician in charge of that particular patient's care.

## 2. Prevention

- prophylactic cranial RT for newly diagnosed patients with limited stage small cell lung cancer has been shown to significantly reduce subsequent incidence of brain metastases

## 3. Screening and Early Detection

- baseline MRI of brain of all newly diagnosed patients with small cell and non-small cell lung cancer and melanoma
- baseline MRI of brain of all patients with small cell and non-small cell lung cancer and melanoma at time of systemic progression

## 4. Diagnosis and Pathology

- presence of brain metastases is M1.

## 5. Management

### 5.1 Management Algorithms

- major prognostic factors include age, performance status, extent of extra-cranial metastatic disease, state of primary tumour (controlled or not)
- all cases are reviewed at tumour board by a multidisciplinary team (neurosurgery, radiation oncology, neuro-oncology, neuropathology, neuroradiology) for a recommendation on further management
- dexamethasone is a useful symptomatic measure in most patients
- the standard of care for patients with brain metastases is currently in a state of flux
- surgery and stereotactic radiotherapy has been shown to be associated with a survival advantage for a single brain metastasis compared to WBRT alone
- the addition of WBRT after resection of a single brain metastasis has been associated with a decrease in local recurrence, decrease in distal brain failure, but no increase in survival
- radiosurgery to 1-4 brain metastases following WBRT has been associated with an increase in local tumor control over WBRT only
- the addition of WBRT in addition to SRS has been associated with an increase of local control and a decrease in distal brain failure over SRS alone
- the addition of WBRT in addition to SRS has not been associated with an increase in survival, but is associated with increased cognitive toxicity
- SRS of the surgical cavity has been shown to have reasonably good local control

- and results in less cognitive decline in comparison to WBRT
- various fractionation schemes have not been demonstrated to have a survival advantage of one over the other (20 Gy/5, 30 Gy/10, 40 Gy/15, 40 Gy/20, 50 Gy/20)
- all decisions made for patients with brain metastases incorporate their age, performance status, state of extra-cranial disease and state of primary tumour, and recommendations below may be altered by these factors
- presence of meningeal carcinomatosis is a contra-indication for SRS

#### **Single brain metastasis**

- surgery if lesion is large (> 3.0 cm), associated with mass effect, and in a surgically accessible area of the brain
- SRS if lesion is not associated with mass effect, or located in a deeper or surgically inaccessible area of the brain
- following surgery, SRS to surgical cavity

#### **1-5 brain metastases**

- SRS alone generally preferred over WBRT given lower toxicity
- surgical resection of an individual mass if necessary

#### **> 5-10 brain metastases**

- Decision about SRS vs. WBRT is made according to multiple factors, in particular the performance status (ECOG 0-3) and life expectancy (> 3 months) of the patient.

#### **> 10 brain metastases**

- Generally speaking, WBRT is recommended

#### **Single Fraction vs. Hypofractionated SRS**

- Single fraction radiosurgery may be considered for any brain metastasis < 3cm in maximum dimension, however the preferred maximum dimension lesion volume for single fraction SRS is 4 cc (~ 2 cm in maximum diameter).
- The preferred method of SRS for lesions >4 cc is hypofractionated SRS using the ICON frameless system
- For hypofractionated SRS using the ICON frameless system, a 1 mm CTV is added
- The ICON frameless system can also be used to deliver single fraction SRS, however the minimum lesion diameter for the ICON frameless system is 1 cm

#### **Post-operative surgical cavity**

- SRS doses based on cavity volume. For all but small cavities (<4 cc), hypofractionated SRS using ICON is preferred
- 2 mm CTV added to cavity for frame based SRS to cavity, if using frameless SRS, then 1 mm CTV and 1 mm PTV
- if cavity is too large, can consider either WBRT or partial brain IMRT (25-30 Gy in 5 fractions).

#### **Recurrent brain metastases after prior WBRT**

- 1-10 mets, SRS is recommended
- > 10 mets, repeat WBRT 25 Gy/10
- if prophylactic WBRT at 25 Gy/10 had previously been given for small cell carcinoma of lung, then conventional dose WBRT can be given (ie. 20 Gy/5 or 30 Gy/10)
- if recurrence is within a prior surgical site, or large (> 4cc), then hypofractionated SRS can be performed

#### **Recurrent brain metastases after prior SRS**

- Depending on rate of progression (interval between prior SRS to recurrence) and other factors, if 1-10 mets, repeat SRS is considered
- > 10 mets, WBRT

- if recurrence is within a surgical cavity, or large (> 3 cm), then hypofractionated SRS can be done

### **5.2 Surgery**

- surgery can be done at initial presentation or at time of brain metastases recurrence
- surgery is always considered in possible cases of radiation necrosis following SRS in lesions that are associated with significant mass effect in surgically accessible areas

### **5.3 Medical Therapy**

- in patients with melanoma which possess the BRAF mutation, upfront management with BRAF inhibitors is a useful approach as the response rate may be as high as 80% and the median duration of response is approx. 6 months
- for EGFR non-small cell carcinoma of lung with brain metastases, patient may be treated with EGFR agonists only with q3monthly MRI surveillance, reserving treatment with RT until evidence of intracranial progression. Typically this strategy is reserved for lesions less than 1-2 cm in greatest dimension and not in eloquent areas or the brainstem.
- for ALK+ non-small cell carcinoma of lung with brain metastases, patient may be treated with ALK agonists only with q3monthly MRI surveillance, reserving treatment with RT until evidence of intracranial progression. Typically this strategy is reserved for lesions less than 1-2 cm in greatest dimension and not in eloquent areas or the brainstem.

### **5.4 Radiation Therapy**

#### **Fractionated WBRT**

- immobilization: thermoplastic U/S frame
- imaging: CT brain
- GTV: whole brain
- CTV: none
- PTV: 1 cm beyond cranial bone
- technique: opposed lateral pair for WBRT
- Dose: initial WBRT 20 Gy/5 fractions or 30 Gy/10 fractions  
recurrent WBRT 25 Gy/10 fractions

#### **Focal IMRT**

- immobilization: thermoplastic U/S frame
- imaging: CT brain, MRI brain T1 gad, T2
- GTV: surgical cavity and enhancing disease
- CTV: 5-10 mm respecting anatomic boundaries
- PTV: 3 mm
- technique: IMRT
- Dose: 25-35 Gy/5 fractions

#### **Radiosurgery (SRS)**

- done on Gamma Knife unit at our centre
- immobilization: Leksell stereotactic frame or Mask
- imaging: CT, MRI T1 gad, T2
- GTV = enhancing tumour

- CTV: none except for 1 mm for surgical cavities treated with or without frame
- PTV: 1mm for all frameless SRS

- Dose (single fraction, intact lesions):

< 4 cc	21 Gy (unless < 1.0 cm in maximum diameter, in which case 15 Gy is acceptable, provided the dose is prescribed to 60% IDL or less)
4-8cc	18 Gy
8-20cc	15 Gy
Brainstem mets	15 Gy

dose between 2 adjacent metastases < 13 Gy  
 surgical cavities <4cc (CTV) can also be targeted with a single fraction of 21 Gy

- Dose (hypofractionated, intact lesions):

<4 cc	27 Gy in 3 fractions
>4-10 cc	24 Gy in 3 fractions
>10-20 cc	21 Gy in 3 fractions
>20 cc	35 Gy in 5 fractions
Brainstem mets	21 Gy in 3 fractions

- Dose (hypofractionated, surgical cavity)

< 8cc	27 Gy in 3 fractions
>8-20 cc	24 Gy in 3 fractions
>20-65 cc	21 Gy in 3 fractions
>65 cc	35 Gy in 5 fractions

## 6. Oncology Nursing Practice

Refer to [general oncology nursing practices](#)

## 7. Supportive Care

### 7.1 Patient Education

#### Driving

- advised not to drive until stable disease on imaging and/or seizure free for one year

#### Seizures

- education about seizures
- what to do when a seizure occurs
- how to take seizure medications
- possible side effects of seizure medications
- avoid heights, taking baths or swimming alone

#### Raised Intracranial Pressure: Steroids

- symptoms of raised intracranial pressure
- side effects of steroids
- titration of steroids for optimal dose

#### When to call multidisciplinary team

- change in seizure pattern
- new or progressive neurologic loss
- symptoms of raised intracranial pressure

#### ***7.2 Psychosocial Care***

- assess family finances
- assess for possible disability applications
- assess possible depression/anxiety
- presence or absence of drug program, apply for provincial assistance if necessary
- possible need for assistive devices or services in the home

#### ***7.3 Symptom Management***

- seizures
- raised intracranial pressure
- neurologic loss
- visual loss
- depression

- psychosis
- anger issues
- poor memory

#### ***7.4 Clinical Nutrition***

- recommend normal diet as per recommendations of Canadian Cancer Society
- diabetic diet if elevation of blood glucose secondary to steroids

#### ***7.5 Palliative Care***

- make referral in cases of progressive disease for which there is no further active therapy recommended
- management of uncontrolled symptoms

#### ***7.6 Rehabilitation***

- in cases of neurologic loss, assess for possible rehabilitation OT/PT
- assess for supportive devices in the home

### **8. Follow-up Care**

- q3 monthly with MRI of brain