PRINCESS MARGARET CANCER CENTRE
CLINICAL PRACTICE GUIDELINES

CENTRAL NERVOUS SYSTEM

BRAIN METASTASES
1. INTRODUCTION 3

2. PREVENTION 3

3. SCREENING AND EARLY DETECTION 3

4. DIAGNOSIS AND PATHOLOGY 3

5. MANAGEMENT 3

   5.1 MANAGEMENT ALGORITHMS 3
   5.2 SURGERY 5
   5.3 CHEMOTHERAPY 5
   5.4 RADIATION THERAPY 4

6. ONCOLOGY NURSING PRACTICE 6

7. SUPPORTIVE CARE 6

   7.1 PATIENT EDUCATION 6
   7.2 PSYCHOSOCIAL CARE 6
   7.3 SYMPTOM MANAGEMENT 6
   7.4 CLINICAL NUTRITION 7
   7.5 PALLIATIVE CARE 7
   7.6 REHABILITATION 7

8. FOLLOW-UP CARE 7
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 WBRT has been shown to be associated with a survival advantage when a single brain metastasis has been excised over 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 1-3 brain metastases following WBRT has been associated with an increase in local intracranial 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
• SRS of the surgical cavity has been shown to have reasonably good local control in uncontrolled studies
• 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)
• the decision to give or withhold WBRT following SRS would be based on the information that adding WBRT increases local control and decreases distal brain failures but suffers from the possible cognitive consequences of WBRT, particularly on short term memory, and this may be more pronounced in older patients: this must be balanced by the possible neurologic consequences of recurrent disease in brain when withholding WBRT
• 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 (> 2-2.5 cm), associated with mass effect, and in a surgically accessible area of the brain
• SRS if lesion is small (< 3 cm) and located in a deeper or surgically inaccessible area of the brain
• following surgery, SRS to surgical cavity or whole brain RT as the usual options
• WBRT alone would be an option if the metastasis is quite small (< 1 cm)

**1-4 brain metastases**
• SRS alone with or without WBRT would be considered as options
• surgical resection of an individual largish mass in an accessible area could be considered as part of the management
• WBRT alone would be an option if the metastases are quite small (< 1 cm)

**> 4-6 brain metastases**
• WBRT is our usual recommendation

**Post-operative surgical cavity**
• SRS to various doses based on volume of cavity
• 2 mm CTV added to cavity
• if cavity too large or has dural extension, then can consider either WBRT or partial brain IMRT

**Recurrent brain metastases after prior WBRT**
• 1-6 mets, SRS, all lesions < 3 cm
• > 6 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 if infiltrative around a prior surgical site, or large (> 3 cm), then focal IMRT 30 Gy/5 fractions or hypofractionated SRS in 3 fractions can be done

**Recurrent brain metastases after prior SRS**
• 1-6 mets, SRS, all lesions < 3 cm
• > 6 mets, WBRT
• if recurrence if infiltrative around a prior surgical site, or large (> 3 cm), then focal IMRT 25 to 30 Gy/5 fractions or hypofractionated SRS in 3 fractions can be done

5.2 Surgery
• surgery for lesions > 2.5 cm in surgically accessible areas is a preferred approach in patients with up to several metastases
• 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 vemurafenib is a useful approach as the response rate may be as high as 80% and the median duration of response is approx. 6 months
• there are many other BRAF inhibitors in development, so the list of possible drugs will increase
• 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
• 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

5.4 Radiation Therapy
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
• PTV: 3-5 mm
• technique: IMRT
• Dose: 30 Gy/5

Radiosurgery (SRS)
• done on Gamma Knife unit at our centre
• for tumours smaller than 3 cm with no intrinsic abnormal brain stem signal on MRI T2 or flair exam
• immobilization: Leksell stereotactic frame
• imaging: CT, MRI T1 gad, T2
• GTV = enhancing tumour
• CTV: none for non-operated mets, but 2 mm for surgical cavities
• PTV: none
• dose:
  < 4 cm$^3$  21 Gy
  4-10 cm$^3$  18 Gy
  > 10-20 cm$^3$  15 Gy
  intrinsic brain stem metastases – 15 Gy
  dose between 2 adjacent metastases < 13 Gy

6. Oncology Nursing Practice

Refer to general oncology nursing practices

7. Supportive Care

7.1 Patient Education

Driving
• possible restriction

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