

**Hong Kong Hospital Authority** 

## **Convention 2018**

### Stereotactic Radiosurgery in Brain Metastases -Development of the New Treatment Paradigm in HA, Patients Profiles and Their Clinical Outcomes

8 May 2018

Dr Frank CS Wong,

**Clinical Oncology, Tuen Mun Hospital** 





<sup>1</sup>Horton J, et al. Am J Roent Rad Ther Nucl Med 1971;3:334 <sup>2</sup>Wong FCS et al. J HK Coll Radiol 2005;8:87-92



## Brain metastasis: After 1990



\*Surgery vs SRS: No large randomised studies

<sup>3</sup>Patchell RA, et al. N Engl J Med 1990; 322:494-500

<sup>4</sup>Kondziolka D, et al. Int J Radiat Oncol Biol Phys 1999;45: 427–434

	Surgery	SRS
Advantage	• Can treat >4cm	Non-invasive
	Histology	<ul> <li>Can treat N&gt;2</li> </ul>
	• Re-operation (local recurrence) is feasible	<ul> <li>'Feasible' to treat deeply seated area (e.g. brainstem)</li> </ul>
Limitation	• Usu N<=2	• <4cm, Usu N <4
	Surgical risk	(N.B. N=10 is now 'feasible')
	<ul> <li>Deeply seated; close to critical area (e.g. motor cortex)</li> </ul>	<ul> <li>Not close to critical structure</li> </ul>
		Risk of radionecrosis
		• Difficult in re-treatment
		<ul> <li>No histology</li> </ul>



# **Focal Treatment: Selection**

1. Performance status

Recursive Partitioning Analysis (RPA)<sup>5</sup>

**KPS>=70**, <65, No extraCNS



(Survival 2.3mos vs 4.2 mos vs 7.1mos)

- Number and Size of brain met, Location (adjacent critical organ)
   → Need an MRI
- 3. Can't treat systemic progression  $\rightarrow$  Need a PET

<sup>5</sup>Gaspar et al IJROBP 1997



## Brain metastasis: After 2000



<sup>6</sup>Peters S, et al. N Engl J Med 2017; 377:829-838

WBRT Vs Focal Treatment Vs Systemic treatment



## WBRT

#### **Problem (1): Late side effects of WBRT**



Global health status

Cognitive functioning<sup>7</sup>

<sup>7</sup>EORTC 22952-26001, JCO 31:65-72, 2013



## WBRT

#### **Problem (2): Patient Selection**



QUARTZ study<sup>8</sup>: Nonsmall cell lung cancer with brain met, unsuitable for either OT or SRS

<sup>8</sup>Mulvenna P, et al. Lancet 2016; 388: 2004–14



# **WBRT : Current Trend**

- Avoid WBRT in patients with survival > 6-9 months
- 2. Avoid WBRT in patients with survival < 8 wks
- 3. WBRT may be indicated for intermediate risk group, and if no effective systemic Rx to prevent CNS progression



# **Focal therapy**

## Problem (1) New brain met

WBRT: Reduce intracranial recurrence (18% v 70%)<sup>9</sup>

Current Trend:

- Poor risk: No WBRT and no focal therapy
- Intermediate risk: (>3 9 mos): add WBRT
- Survival >6-9 mos: Omit WBRT, Close monitoring (MRI) and re-focal Tx
- Systemic Rx (?? pass blood-brain-barrier)

<sup>9</sup>Patchell RA, et al. JAMA 280:1485-1489, 1998



# **Focal therapy**

### **Problem (2) Local failure (surgical bed)**

# Current trend: SRS boost instead of WBRT in good risk

NCCTG N107C/CEC·3<sup>10</sup>: WBRT vs SRS boost of surgical bed

- Cognitive deterioration at 6 mos: 85% vs 52%
- 6-month surgical bed control: 87.1% vs 80.4%
- Overall survival: 11.6mosvs12.2 mos

<sup>10</sup>Brown PD, et al. Lancet Oncol 2017; 18: 1049–60



# **Focal therapy**

#### **Problem (3) Systemic failure**

- Add systemic Tx



<sup>11</sup>Lam TC, et al. Abstract, International SRS Society Meeting 2015



# **Systemic Treatment**

Problem (1) Inferior CNS control (blood-brain-barrier)

- Need focal Tx or WBRT (if no effective systemic Rx to control CNS involvement)
- New generation (e.g. EGFR or ALK inhibitor)
   Research topic: still need WBRT or focal Tx?



# **Systemic Treatment**

## **Problem (2) Drug resistance**

- Ultimate failure (brain met or systemic) even if good initial response
- Better consider focal Tx if oligometastasis



## **Brain metastasis: Treatment Paradigm**

Brain metastasis

> Whole brain RT

#### Terminal care



#### Brain metastasis: New treatment paradigm





# Case 1 M/58 Sudden left hemiparesis MRI 4/2008 CXR 4/2008





#### What would you advice?

# Case 1 M/58 Sudden left hemiparesis

M/58

MRI 4/2008

CXR 4/2008

What would you advice?

Assess KPS MRI Staging (PET) and Biopsy





#### Case 1 M/58 Good KPS

#### **Solitary brain met + Solitary lung mass**

- 1. Whole brain RT, then hospice care
- 2. Whole brain RT, then systemic treatment
- 3. Molecular test, targeted therapy or chemotherapy or immunotherapy
- 4. Surgery for brain met and lung tumour +/- systemic
   Tx
- 5. SRS (+/- whole brain RT) for brain met and SBRT for primary lung tumour +/- systemic Tx
- 6. Others

What would you suggest?

#### M/58 Good KPS Case 1

#### Solitary brain met + Solitary lung mass

- 1. Whole brain RT, then hospice care
- 2. Whole brain RT, then systemic treatment
- 3. Molecular test, targeted therapy or chemotherapy or immunotherapy (??)
- 4. Surgery for brain met and lung tumour

#### +/- Systemic Tx

5. SRS (+/- whole brain RT) for brain met and SBRT for primary lung tumour +/- systemic Tx

#### Case 1 M/58 Good KPS

#### **Solitary brain met + Solitary lung mass**

- Craniotomy and excision 4/2008: metastatic adenoCA
- Right upper lobectomy 5/2008: AdenoCA, pT1N2
- Pt declined postop systemic treatment
- Last FU Dec 2017: no evidence of recurrence; normal life

#### Case 1 M/58 Good KPS

#### **Solitary brain met + Solitary lung mass**

- Craniotomy and excision 4/2008: metastatic adenoCA
- Right upper lobectomy 5/2008: AdenoCA, pT1N2
- Pt declined postop systemic treatment
- Last FU Dec 2017: no evidence of recurrence; normal life

Oligometastasis

## Case 2

2008 (age 28)

CA left breast with surgery; completed adjuvant chemoRT and Herceptin 2013 (Age/33) c/o persistent headache CT brain: large cystic brain met

What would you advise?



## Case 2

2008: CA breast with OT, chemoRT, herceptin

- 2013: Large brain met
- Good KPS
- MRI: Large solitary brain met
- PET: Isolated brain met

No distant failure

**Blood brain barrrier** 



## Case 2

2008: CA breast with OT, chemoRT, herceptin

2013: Large solitary brain met; craniotomy and excision, then WBRT with IMRT boost of surgical bed

Systemic treatment: Capecitabine + Lapatinib

Remained well x 4 years

12/2017 MRI: New brain met

Ultimate drug resistance









