

NEUROSURGERY FOR BRAIN METASTASES

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Introduction

- *Increasing incidence of brain metastases*
- *10%-30% patients with systemic cancer will present brain metastases*
- *Survival still poor*
- *Brain met's outnumber primary brain tumors (10 to 1)*
- *Lung (40-50%), breast (20-30%), melanoma, renal, colorectal, uterine*
- *5% unknown etiology*
- *In case of lungCa: 20%, melanoma and renalCA: 7%, breastCa: 5%*

Introduction

- *Pathophysiology*
 - *Escape from primary tumor and enter systemic circulation*
 - *Migration to target site, extravasation and proliferation*
 - *Only 0,01% of cells will enter circulation and form met's*
 - *Primary tumor cells tendancy to extravasation in watershed zones*
 - *Based on cerebral bloodflow:80% in hemispheres, 15% cerebellum, 5% brainstem*
 - *Blood supply: neovasculature=angiogenesis > aberrant vessels*

Introduction

- *Presentation*
 - *Neurological signs in 2/3 of patients*
 - *Neurological symptoms depend on location*
- *Treatment depends on prognosis*
 - *Recursive Partitioning Analysis (RPA): Class I, II and III (KPS,age,primary)*
(Gaspar et al Int J Radiat Oncol Biol Phys. 1997;37:745-751)
 - *Graded Prognostic Assessment (GPA): 4 criteria (KPS,age,n°met's,extracran)*
(Sperduto et al Int J Radiat Oncol Biol Phys. 2008;70:510-514)
 - *Diagnosis Specific GPA: histology*
(Sperduto et al Int J Radiat Oncol Biol Phys. 2010;77:655-661)

10 FAQs and FACTS(?)

1° what is the role of neurosurgery in brain metastasis?

The use of surgery in brain metastasis is controversial

Other possible treatments:

Radiotherapy

Stereotactic radiosurgery

Chemotherapy

Immune therapy

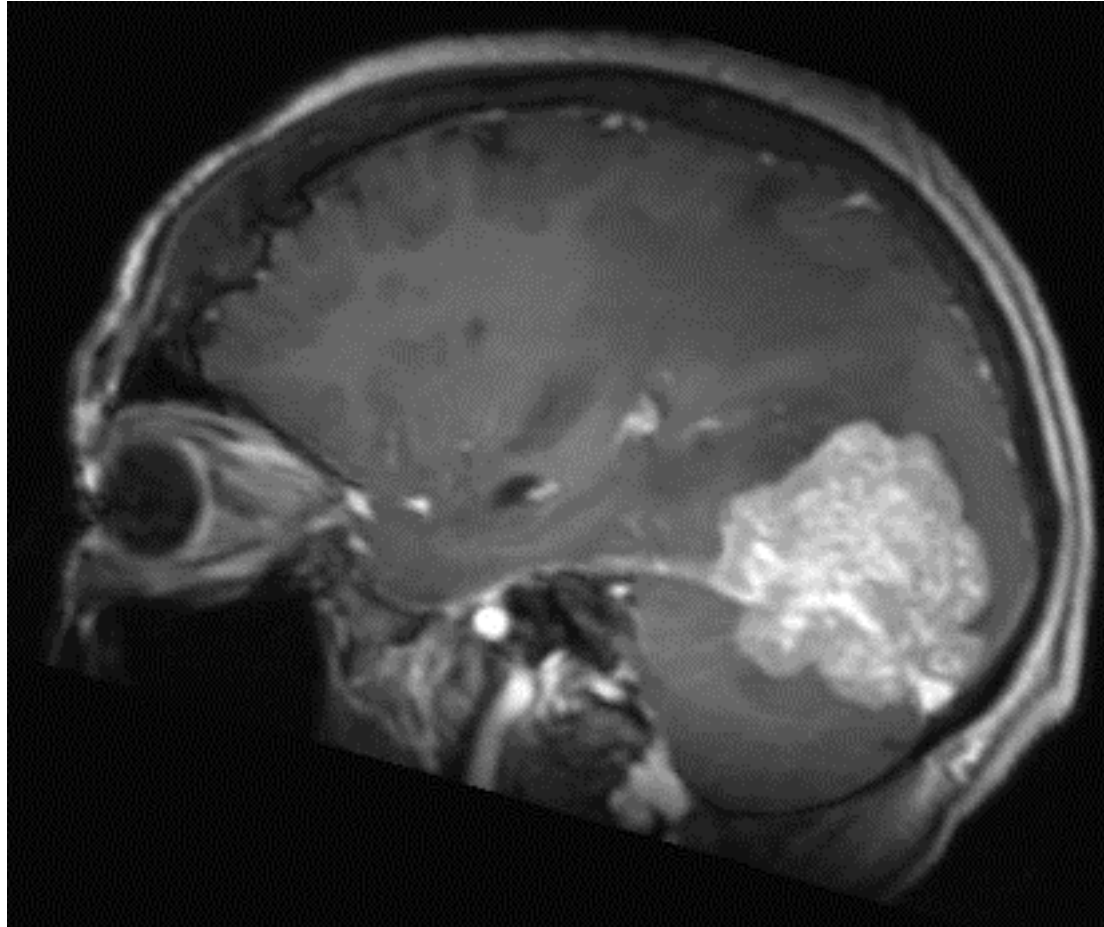
2° What is a strict indication for surgery?

- *Single lesion, surgically accessible, no/well controlled systemic, good KPS, neurologically intact, no leptomeningeal infiltration* (Vogelbaum J Clin Oncol. 2006;24:1289-94).
- *Longer survival confirmed by other studies*
(Patchell RA et al. A randomized trial of surgery in the treatment of single metastases to the brain. N Engl J Med. 1990;322:494-500)
(Vecht CJ et al. Treatment of single brain metastasis: Radiotherapy alone or combined with neurosurgery? Ann Neurol. 1993;33:583-90)
- *Functional improvement after surgery has better outcomes in response to adjuvant therapy* (Mut M. Surgical treatment of brain metastasis: A review. Clin Neurol Neurosurg. 2012;114:1-8)

2° What is a strict indication for surgery?

- *Lesions causing significant neurological signs > surgery only option to relief life threatening symptoms*
- *Lesions > 3cm*
- *Lesions causing seizures*
- *Cerebellar lesions often causing brainstem compression/hydrocephalus*
- *Multiple lesions ???*

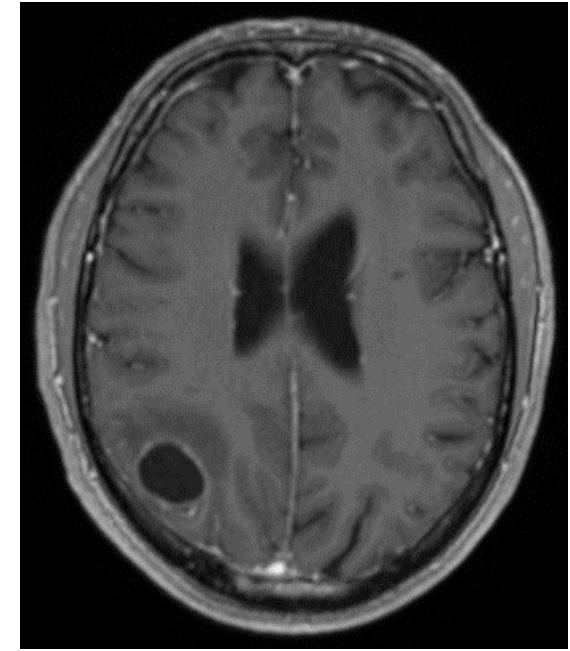
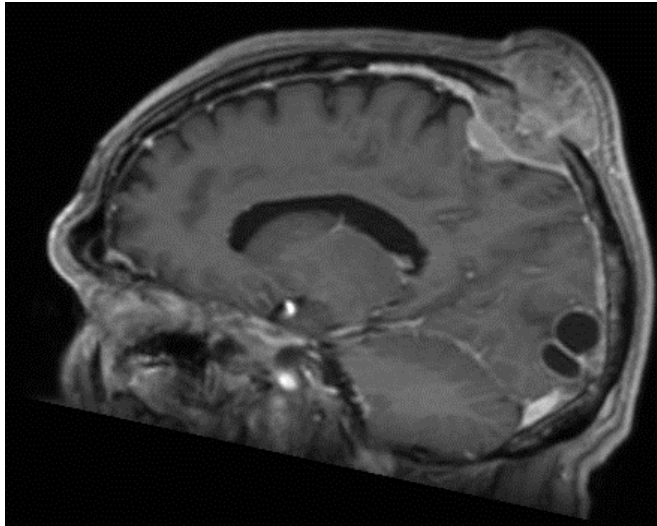
2° What is a strict indication for surgery?



3° Are multiple lesions amenable for surgery?

- *Individual decision making*
- *In case of poor response rate to chemo/radiotherapy*
- *Multiple lesions > 3cm*
- *3-5 lesions*
- *Single session surgery*
- *Can be technically challenging*

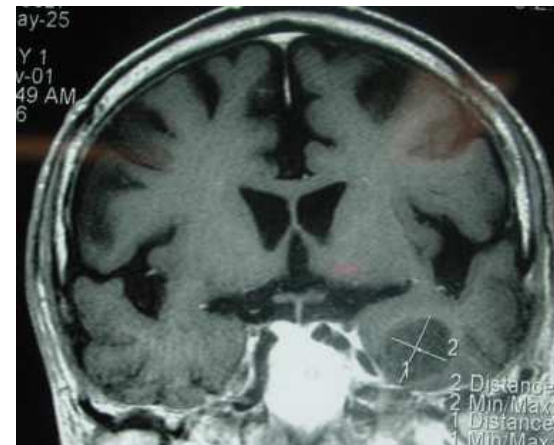
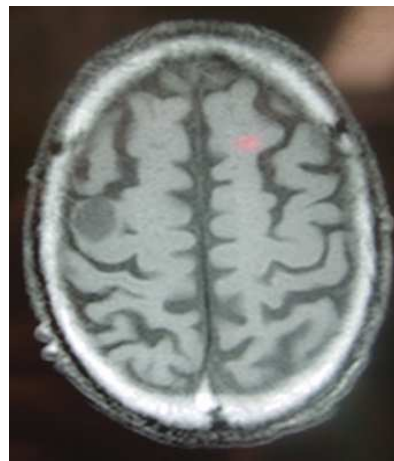
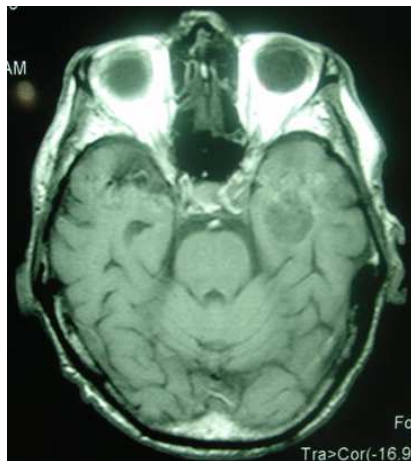
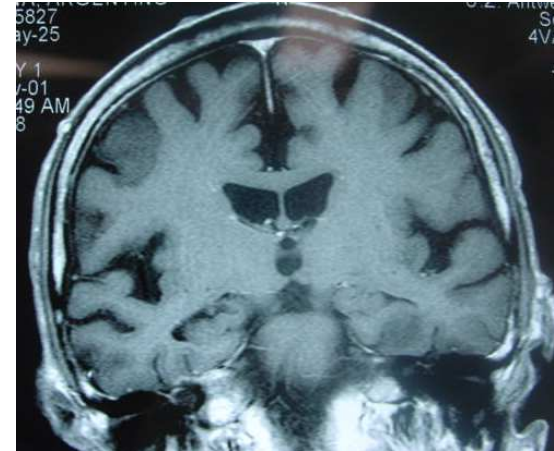
3° Are multiple lesions amenable for surgery?



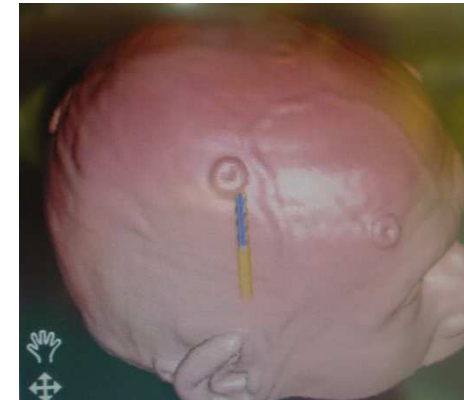
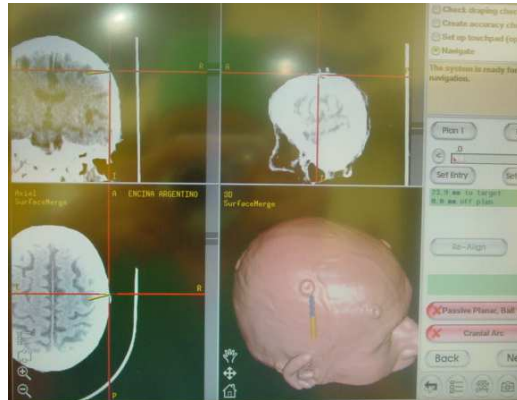
4° Does surgical technique make the difference?

- *Tools: neuronavigation, neuromonitoring, wake up anesthesia*
- *En bloc resection results in 1,7 times lower recurrence rate compared to piecemeal resection* (Patel TR, Management of brain metastases: Surgery, radiation, or both? Hematol Oncol Clin North Am. 2012;26:933-47)
- *Especially in posterior fossa* (Ahn JH et al. Risk for leptomeningeal seeding after resection for brain metastases: Implication of tumor location with mode of resection. J Neurosurg. 2012;116:984-93)
- *Additional white matter resection?* (Yoo H et al. Reduced local recurrence of a single brain metastasis through microscopic total resection. J Neurosurg. 2009;110:730-6)

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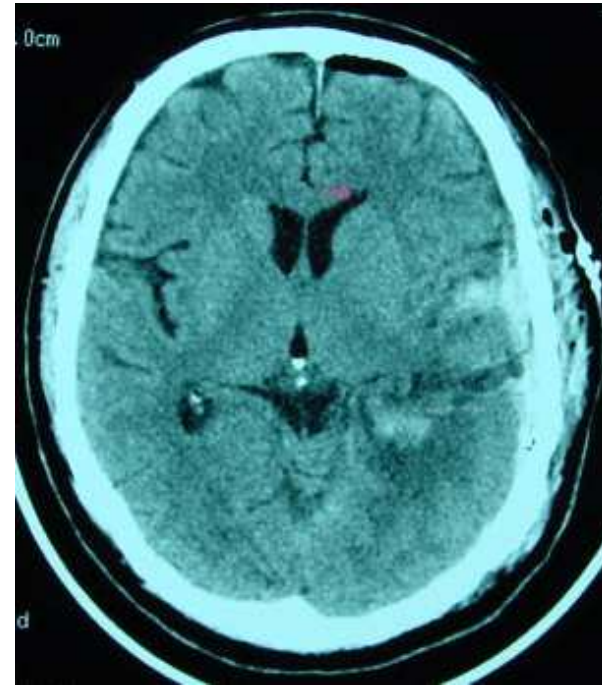
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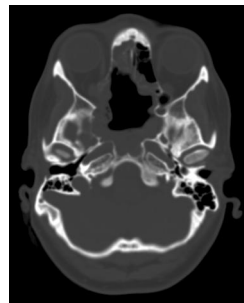
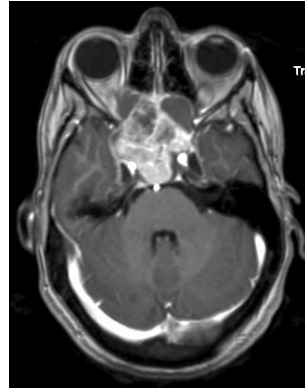
5° Does the location influence surgical decision making?

- *Superficial lesions*
- *Microsurgical techniques*
 - *Transsulcal approaches*
- *Skull base techniques*
 - *Transpetrous, transoral...*
- *Alternative approaches*
 - *Supracerebellar transtentorial*
 - *Ventriculoscopic*

5° Does the location influence surgical decision making?



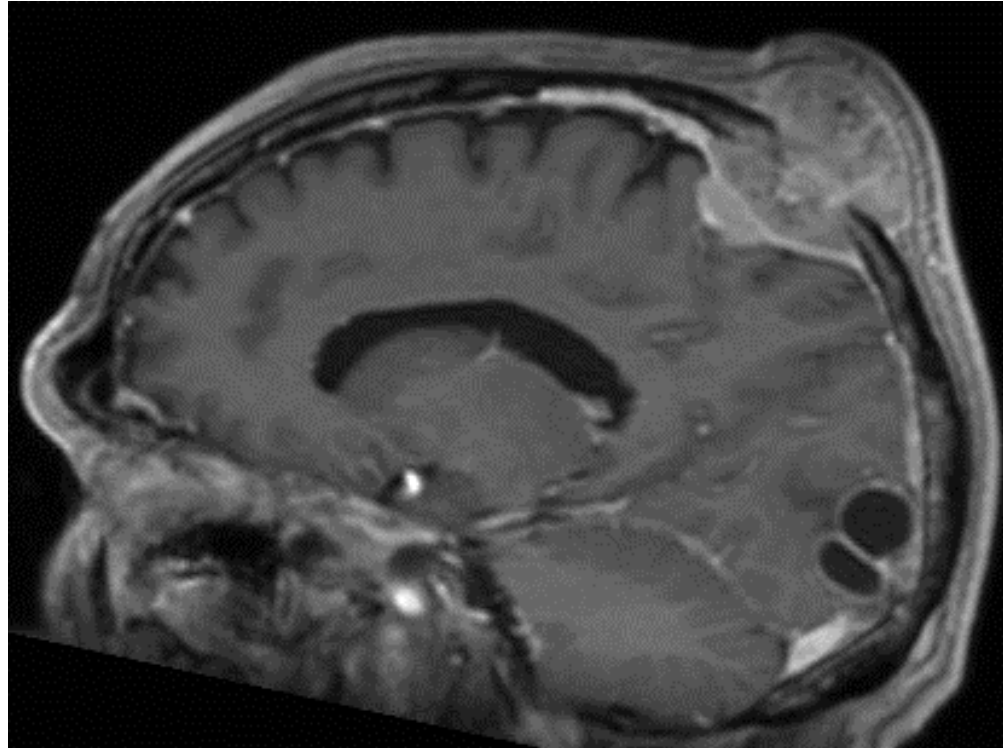
5° Does the location influence surgical decision making?



6° Impact of the primary tumor's histology on surgery?

- *Some met's can be highly vascular (renalCa)*
- *Some met's tend to be cystic*
- *Some met's have no capsule/friable*
- *Surgical technique must be adapted*

6° Impact of the primary tumor's histology on surgery?



7° Can surgery act as a single therapy ?

- *Solitary lesion*
- *Complete resection with safety zone*
- *Redo surgery after failure of adjuvant therapies*
- *Not first choice if adjuvants are possible*

8° what about stereotactic radiosurgery (SRS)?

- *Non invasive local control*
- *For primary and recurrent lesions and adjuvant control*
- *Multiple lesions, deep seated, advanced disease*
- *Only for smaller lesions= <3cm?*
- *Does SRS fully replace surgery?*

9° What about combined therapies?

- SRS+WBRT vs WBRT alone

Based on the two randomized controlled trials above, there is class I evidence that SRS plus WBRT yields significantly improved local tumor control rates compared to WBRT alone in patients with 1–3 brain metastases. Moreover, the study by Andrews et al. [30] suggests that there are particular populations such as RPA class I patients and those with single brain metastases that have an overall survival benefit with SRS boost. It is likely that the patients who benefit from an SRS boost are the ones that have an improved life expectancy, as these patients will live long enough to potentially experience the sequelae of local brain failure.

- SRS+WBRT vs SRS alone

There are multiple retrospective cohort studies (class II evidence) that reveal similar survival results in patients receiving SRS alone versus those receiving SRS plus WBRT [37–44]. These studies contain conflicting evidence, however, regarding the risk of local recurrence in the patients receiving SRS alone. As a result, while SRS alone is a reasonable treatment option in patients with up to 4 brain metastases, it should be followed by frequent MRI surveillance for local and distant failure.

- SRS alone vs WBRT

One class III study revealed similar outcomes for either treatment modality, while a second showed a significant survival advantage for SRS alone. On the basis of this data, SRS alone is a reasonable treatment option for patients with limited brain disease although concern about distant failure necessitates frequent radiographic followup.

9° What about combined therapies?

Surgery+WBRT vs WBRT alone

Two of these three randomized controlled trials demonstrate that the addition of resection to WBRT rather than WBRT alone leads to improved survival and functional status in patients with a single, surgically accessible brain metastasis. A fourth study found no survival benefit to adding adjuvant WBRT to surgical resection. While much of these data were acquired twenty years ago, it continues to be quite relevant in the management brain metastases. It should be recognized, however, that the majority of patients enrolled in these trials were probably symptomatic or had larger metastases, as these were the common presentation of brain metastases in that era.

Surgery+WBRT vs Surgery+SRS

Increasing number of studies comparing these two treatment strategies, demonstrate that survival is at least equal with some studies showing better quality of life in the surgery+SRS group.

Surgery+WBRT vs SRS+WBRT

Both strategies are reasonable in patients with solid tumors <3 cm in diameter. However, surgery may be more suitable for patients with symptomatic, accessible lesions in order to palliate symptoms.

9° What about combined therapies?

Surgery+WBRT vs SRS alone

Given the inconclusive results of most studies, no definitive recommendations can be made regarding the superiority of one of these treatment strategies over the other.

Surgery+SRS vs SRS alone

An increasing number of studies comparing these two treatment strategies, demonstrate that survival is better in the surgery+SRS group.

10° what is the role of neurosurgery in brain metastases?

State of the art surgery as well as WBRT, SRS and chemotherapy should be incorporated in the treatment portfolio of approach of metastatic disease of the central nervous system