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## Refresher course: Oligometastasis

# Radiosurgery in multiple metastases ( $\geq 4$ ): Treatment criteria



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The efficacy of Radiosurgery (RS), whether or not combined with Whole Brain Radiotherapy, is well known in the treatment of patients with a reduced number of brain metastases (1–3). However, there is still no consensus on the efficacy of RS as a treatment in patients who have 4 or more brain metastases, and their treatment, on many occasions, is reduced to the administration of Whole Brain Radiotherapy only.

In an extensive review of the literature published in the Journals of Neurosurgery and Radiation Oncology, including the RTOG 9508 and ASTRO reports published in 2004 and 2005, it is considered that patients who have 4 or more brain metastases have a poor disease prognosis, and are treated with whole brain radiotherapy. In none of these studies or reports is it explained why this “magic” number 4, and not 3 or 5.

What does this number demonstrate?

- More brain dissemination?
- More extra-cerebral disseminated disease?
- More difficult techniques?
- Or perhaps, it is a random number?

Aims of radiosurgery in brain metastases:

- To control the neurological deficit.
- To prolong survival.
- To reduce neurological morbidity.

There is no doubt that the higher the number of brain metastases the lower is the patient survival. However, this relationship is not so obvious if we look at the morbidity and cerebral toxicity.

Overall survival is considerably significant, with a median of almost 12 months and an acceptable quality of life. This, although less if we compare it to single metastasis group, leads us to believe that combined treatment with whole brain radiotherapy and radiosurgery may be the treatment of choice in patients with multiple metastases.

Those of us who work in the brain radiosurgery field must bear in mind that there are two unavoidable concepts: the volume and the dose.

The mean volume in the case of the multiple metastases group is less than in the patient group with one, two or three brain metastases, since the lesions are smaller in the first group, and the majority of the patients had received combined treatment with whole brain radiotherapy.

In the multiple metastases group, the number of lesions has not limited us to administering the effective therapeutic dose. It is possible that the maximum dose could be high, but it has not been assessed.

We do not know at what brain volume a neurological deficit is produced on administering a dose of 1000–800 cGy, (there are some indications not related with Radiosurgery) or what is the brain volume limit that would prevent us from performing radiosurgery treatment in this group of patients with  $\geq 4$  metastases. However, if we take less than 3 cm diameter as the criterion to treat lesions, we estimate that lesions around 14 cm<sup>3</sup> could be treated.

In our study, the mean was  $\approx 2$  cm<sup>3</sup> and without knowing the effects of the maximum dose, the toxicity obtained was acceptable.

Noël and Mazon (Bull Cancer 2004;91(1):81–93) in their review of brain metastases put forward as an obstacle

the long time that the patient has to be strictly speaking on treatment (on the machine) which according Suzuki et al, is between 2 and 11 h (mean 5 h). However, technical or administrative difficulties or barriers must not be a greater obstacle than the medical benefits that are obtained.

Take, as an example, the unquestionable success assumed from the improvement in the overall survival of patients with glioblastoma multiforme, with a median of 12 months, and why not with multiple brain metastases?

Based on these results and in other publications, we may summarise that:

- The number “4” must not prevent the radical treatment of brain metastases with radiosurgery.
  - This is not associated with extra-cerebral tumour dissemination.
  - It is not associated with greater morbidity.
  - It is not associated with a more difficult technique.
  - There is directly proportional relationship between the prognosis and the metastasis number, the higher the

brain metastasis number the worse is the prognosis (similar to the performed literature review).

- The therapeutic decision should be associated with the prognostic factor, the RPA and the individual assessment of each case.
- The total PTV could affect the therapeutic decision.
- The administration of multiple RS treatments improves patient survival and their quality of life.

Assuming as treatment criteria:

- Patients with RPA 1.
- Life expectancy greater than 6 months.
- Primary diseases controlled or controllable.
- Total PTV less than 14 cm<sup>3</sup>.
- Assess organs at risk, trunk and basal ganglia.

We strongly believe that we have to personalize the treatment of the patients with brain oligometastases.

A new era is coming; multiple brain metastases can be treated with Radiosurgery.