

This practice is based on reported experience from single institutions.

In the first decade of the 21st century, local control using stereotactic radiotherapy or surgical resection of individual brain metastases has emerged as a clinically beneficial modality for highly selected patients. Whole brain radiotherapy is increasingly seen as a treatment provided in addition to this local control, or is held in reserve for salvage management should new or recurrent brain metastases develop at a later date - without RCT evidence supporting this approach (4,5,6).

The majority of patients with brain metastases, however, are not suitable for stereotactic or surgical approaches and WBRT continues to be seen as the standard of care for this group, particularly if they are perceived to have a durable prognosis (5). Until the MRC QUARTZ trial was undertaken in non-small cell lung cancer (NSCLC) (Mulvenna et al 2016-in press), there were no sufficiently powered randomised controlled trials specifically addressing the utility of WBRT compared to supportive care (7).

Although prophylactic cranial irradiation has enhanced overall survival and reduced incidence of brain metastases for patients with the exquisitely radiosensitive small cell variant of lung cancer, trials addressing this issue in NSCLC and Breast cancer have failed to accrue. This lack of high quality evidence added to the fear of neurocognitive decline remains a potential barrier to applying this technique to other solid tumours with a propensity for metastasising to the brain.

#### Questions to address:

Can we apply prognostic indices reliably to all solid tumour types?

Do we really know which patients will benefit from WBRT, whether used as a sole palliative modality or as an adjunct to local (stereotactic or surgical) modalities?

If so, how can we best use Image Guided radiotherapy to minimise long term neurocognitive impact?

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#### SP-0588

##### Focal radiotherapy for multiple brain metastases

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Brain metastases (BM) develop in up to 30% of patients with cancer. There is marked heterogeneity in outcomes for patients with BM, and these outcomes vary not only by diagnosis, but also by diagnosis-specific prognostic factors; we should not treat all patients with brain metastases the same way, treatment should be individualized.

Phase III randomized trials have shown that upfront whole brain radiotherapy (WBRT) may decrease brain recurrence both in terms of better local and improved distant brain tumour control rate, and that neurological death rate may be reduced in patients treated with WBRT + stereotactic

radiosurgery (SRS), but no survival benefit is reached. The EORTC 22952-26001 study (Kocher M et al) shows that adjuvant WBRT fails to improve the duration of functional independence.

The use of SRS in the treatment of multiple BM has increased dramatically during the past decade to avoid the neurocognitive dysfunction induced by WBRT.

One of the biggest (1194 patients) multi-institutional prospective observational studies (JLKG0901, Yamamoto M et al and Watanabe S et al) including patients with multiple BM (even more than 10) have shown that SRS without WBRT in patients with five to ten BM is non-inferior to that in patients with two to four BM in terms of median OS (10.8 months for both groups), 1-year local recurrence (6.5% and 7%), with a very low incidence of side effects (less than 3%). They also concluded that carefully selected patients with 10 or more BM are not unfavourable candidates for SRS alone, having these patients a median survival time and neurological death-free survival times comparable to the group with 9-10 BM; their results suggest also that even among patients 80 years and older, those with modified-RPA Class I+IIa or IIb disease are considered to be favourable candidates for more aggressive treatment of BM.

SRS has been an option for limited (1-3) metastatic brain lesions, and nowadays the updated guidelines (for example, the NCCN panel) have recently added SRS as a primary treatment option for multiple (>3) metastatic lesions.

The exclusive SRS approach for patients with multiple BM is mostly curative for each treated lesion, it can be repeated several times (the limits in terms of median cumulative dose to the normal brain must be explored), and WBRT remains an option as salvage treatment.

Exclusive SRS with frequent magnetic resonance imaging-based follow-ups (every 2-3 months) in order to salvage recurrent BM before symptomatic manifestations, should be routinely offered to selected patients as a treatment option to consider (Lester SC et al). Initial treatment with a combination of SRS and close clinical monitoring should be recommended as the preferred treatment strategy to better preserve learning and memory in good prognosis patients with newly diagnosed BM (Chang EL et al).

The Lausanne University Hospital (CHUV) has created a brain metastases clinic to provide medical and radiation oncology, neurosurgical, and supportive services to this complex patient population. During the first 18 months, 250 cases were discussed, 55% of patients had more than one brain metastases, and focal treatments were proposed in 69% of treated cases (for 50% of them radiosurgery or fractionated stereotactic radiotherapy, FSRT). WBRT was proposed to only 16% of patients (some of them as salvage therapy after sequential treatments with SRS).

Higher BM burden (in terms of size and volume) and higher integral SRS dose to the brain are the main predictive factors for late toxicity after SRS. The cumulative neurocognitive effect of numerous SRS sessions remains unknown. In order to reduce the cumulative median dose to the brain, the SRS technique must be carefully chosen.

At CHUV, we have performed a dosimetric comparison study in cases with multiple brain metastases (up to 10), comparing a radiosurgical planning (same dose and isodose prescription) with Gamma Knife (GK), CyberKnife (CK), VMAT and Helical Tomotherapy (HT). Gradient index was better with GK and CK (3.4 and 4.1, compared to 17.8 and 19), as well as PTV coverage (100% with GK and CK, compared to 97% with VMAT and 90% with HT); brain Dmean was lower with GK (3 Gy) and CK (2.66 Gy), compared to VMAT (6.4 Gy) and HT (6.72 Gy). SRS alone should be considered a routine treatment option in patients with multiple BM due to favourable neurocognitive outcomes, less risk of late side effects, without adversely affecting the patients performance status.

#### SP-0589

##### Role of systemic therapy in the treatment of brain metastases

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