

BRAIN METASTASES - WHETHER TO ADD RADIOSURGERY

By: Gil Lederman, M.D.

Brain metastases are nodules of cancer that spread through the blood stream to enter the brain. The common primary site of cancer usually is within the lung, breast, kidney, intestines, melanoma or sarcoma.

Historically, the whole brain was treated with radiation. In years past, and to a large degree in many facilities even today more sophisticated radiation is neither available nor offered.

The problem with whole brain radiation is that it can cause adverse intellectual function and does not select out the tumor for a higher dose. It gives the same exact dose to healthy normal brain as to the cancerous nodule. Yet many physicians believe bulky sites of cancer should receive a greater dose of radiation for best outcome.

In a recent report by Kondziolka et al, published in the prestigious International Journal of Radiation Oncology Biology and Physics, patients with two to four brain metastases were randomly allocated to receive either whole brain radiation or whole brain radiation plus radiosurgery.

Radiosurgery is not surgery but pinpoint radiation. It allows higher doses to be administered to the visible cancer nodule. This is an important issue since there are more than 200,000 Americans who develop brain metastases each year and improvement in survival and control rates should lead to longer life and better quality of life for many.

A recently randomized study published allowed patients to be randomly allocated either to whole brain radiation or whole brain radiation plus radiosurgery. Required was pathologic confirmation of cancer and evidence of spread to the brain. Metastases measuring in diameter less than or equal to 25mm (or about an inch) and having one to four areas present in the brain as determined by MRI scanning were entrance criteria. All patients, as well, had to have reasonable physical function. This is indicated as Karnofsky performance status.

Control of the cancer was called cessation of the metastases' growth and no change in symptoms. Systemic staging to determine the extent of cancer in the body included chest x-ray and bone scan when indicated, CT scan of the chest, abdomen and pelvis when indicated within several months of randomization.

The patients underwent MRI's of the brain every three months. Patients had whole brain radiation with individual doses of radiation of 250 rad per treatment. Three thousand rad in 12 treatments was administered. Rad is a measurement of radiation dose. Radiosurgery was offered either before, during or after whole brain treatment.

The dose of radiosurgery was 1600 rad. Patients undergoing radiosurgery were all hospitalized for their single shot treatment while the whole brain was given as outpatient. That contrasts to fractionated radiosurgery where a non-invasive head frame is used and there is no need for hospitalization or medication. Our results show a superiority of treatment and less toxicity with fractionated radiosurgery compared to single shot treatment..

Twenty seven patients were randomized. Fourteen patients received whole brain radiation only and 13 patients received whole brain plus radiosurgery.

The most frequent diagnosis in each group was non-small cell lung cancer and there was said to be similar numbers of patients with melanoma, renal cell cancer and breast cancer.

Seventy one percent of the patients with whole brain radiation alone had active cancer systematically while 62% of the whole brain plus radiosurgery group did. This would favor the whole brain plus radiosurgery group somewhat since less had active systemic disease.

Seventy nine percent of the whole brain group had two metastases while 62% of whole brain plus radiosurgery group had two metastases. This would also somewhat favor the radiosurgery group.

The study was stopped after 27 patients because statistical analysis studies showed the whole brain plus radiosurgery group was doing better. There was said to be no complications in the radiosurgery group. Local failure was 100% in the whole brain group meaning all patients had progressive disease after whole brain radiation only while those having radiosurgery had an 8% local failure rate. This suggests a marked benefit to stereotactic radiosurgery.

Time to progression with whole brain radiation was six months compared to 36 months in the radiosurgery group. This means radiosurgery patients were free of cancer six times longer in the treated areas. Time to new tumor development was five months in the whole brain group and 34 months in the whole brain plus radiosurgery group.

It was noted that some patients who progressed in the brain after whole brain were indeed treated with radiosurgery. Patients who received only whole brain had a median survival of seven months while those having radiosurgery for recurrence lived eleven months. This would suggest that there is salvage benefit to radiosurgery even at the time of recurrence.

In a Kaplan-Meyer plot of patients' survival there was no difference in survival based upon whole brain plus radiosurgery versus whole brain alone. There was indeed a survival benefit for using radiosurgery at the time of recurrence. This paper would point out the benefits of radiosurgery for those with metastases - even multiple metastases from a variety of sources.

Radiosurgery can be used at diagnosis, saved for progression or it can be used in certain patients at the time of diagnosis and as well progression.

There are different forms of radiosurgery including single fraction or fractionated and the appeal of fractionated radiosurgery is that it is outpatient and avoids the pins into the skull associated with single fraction therapy. It is administered over several sessions to minimize potential adverse effects to healthy surrounding tissue. We believe its appeal is multifold - avoidance of the painful intervention and hospitalization as well as the known beneficial effects of fractionation to minimize harm to the healthy surrounding brain. Of course, another beauty of radiosurgery is that it can be repeated if necessary.

Our experience includes a select group of patients with brain metastases who desire to avoid whole brain radiation altogether and proceed with highly focusing radiosurgery to hit the cancer and minimize adverse effects on the healthy brain. This is great appeal to this approach.