Stereotactic Radiosurgery for Brain Metastases

We’ve previously discussed whole brain radiation therapy (WBRT) has been the historical cornerstone of treatment for brain metastases, and how surgery is sometimes employed in certain cases, but stereotactic radiosurgery (SRS) has dramatically changed the treatment of brain metastases. SRS involves using a high dose of extremely focused radiation to a small area, most commonly in the brain tissue. Several machines can be used for this approach, most commonly Gamma Knife, potentially Cyber Knife, but sometimes other machines.

SRS has been best studied in the setting of just 1-3 brain metastases, but it’s being used increasingly in patients with many brain metastases, a setting in which we have no real data, and there’s a good deal of controversy around whether patients are better served by whole brain radiation in that setting.

The Radiation Therapy Oncology Group began doing large studies of SRS about a decade ago, starting with the RTOG 9508 trial (abstract here), which randomized 333 patients with three or fewer brain metastases to receive WBRT with or without a SRS “boost”. This was building on the base of WBRT, so the question was whether adding to it with SRS provided added benefit. Although the trial wasn’t restricted to patients with lung cancer, nearly two thirds of the patients on this trial had lung cancer as their primary tumor. The study showed that people with a single brain lesion who received the SRS boost had an improvement in median survival, and that improvements in survival were also seen in the overall healthier patients with the best performance status and in patients with lesions of 2 cm or greater diameter. In addition, the patients who received SRS were more likely to show or stable or improved performance status when assessed 6 months after treatment. Local control, in other words no progression of disease in the brain, was significantly better for patients who received WBRT+SRS (82%) compared with WBRT alone (71%).

But in the past few years the question has been turned around, and many patients and physicians are questioning whether SRS is an effective enough treatment that WBRT may not be needed, similar to the question of whether patients who undergo surgery should receive WBRT afterward. Many patients are reluctant to undergo WBRT due to concern for potential cognitive problems later. One trial (abstract here) randomized 132 patients with 1-4 brain metastases, again with two-thirds having lung as their underlying primary cancer, to either SRS alone or in combination with WBRT. There was no improvement in overall survival for the recipients of WBRT, but local tumor recurrence rate (immediately around the treated lesions) was far better in the patients who underwent WBRT after SRS: 76% vs. 47% (p < 0.001). A striking difference was also shown in distant brain recurrence, 52% vs. 18% (p < 0.001).
retrospective review from 10 institutions that looked at over 569 patients with brain metastases, (abstract here), there was no significant difference in survival for patients who received WBRT in addition to SRS, but the need for subsequent treatment for brain metastases was reduced from 36% to 7% in the patients who received WBRT. Taken together, it appears quite clear that while there is no overall survival benefit with WBRT, it convincingly improves control in the brain and markedly reduces the risk of future brain lesions.

With regard to the treatment of SCLC vs. NSCLC, the majority of the patients on these trials have had NSCLC. Because patients with SCLC are more likely to have multifocal brain lesions, they have been less likely to be treated with neurosurgery or SRS for brain lesions, with a much greater tendency to treat SCLC with WBRT. However, a few studies that have included a minority of patients with brain metastases have suggested that they can also have good local control in the brain following SRS (abstracts here and here), so this is certainly a reasonable thing to consider for SCLC, at least in selected patients. I must admit that this hadn’t been my general approach in SCLC with brain metastases, but I have also learned from researching some of these topics, and I will likely be more open-minded to the idea of SRS for SCLC in the future. (I also work with a few radiation oncologists who are very knowledgeable about brain metastases, and their recommendations should count significantly).

One issue that has been controversial is the increasing use of SRS for patients with more than a handful of brain metastases, particularly if WBRT isn’t done. Having more than a few brain lesions predicts for a greater likelihood of more brain metastases, so the person with 8 or 10 brain metastases is at a very high risk for actually having more that can’t be detected and will emerge in the future. And since it’s pretty clear that not pursuing WBRT is associated with a much higher risk of recurrence, people with many brain metastases are highly likely to need not only a large number of SRS procedures initially, but plenty of additional SRS procedures later. This is bad for patients, and the only people it’s good for are the ones who own the machines and make money from doing these expensive techniques. There’s a lot of controversy, it’s fair to say, because there’s really no good evidence to support doing SRS for more than 4-5 lesions. But for people with a small number of lesions, at least, SRS is a very appealing option that is becoming increasingly available.