FALL 2014, VOL. 3, NO. 1

Pathways in Cancer

Clinical insight and analysis in advanced cancer care

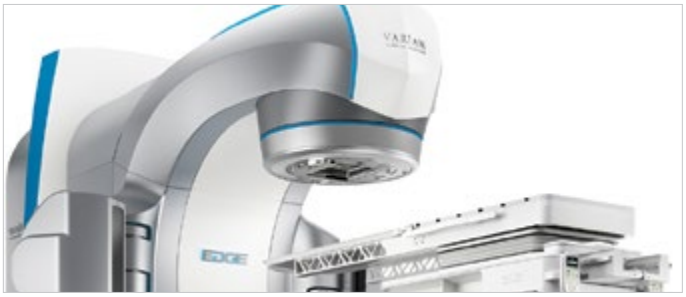
Metastatic Brain Tumors: A Shifting Treatment Paradigm?

Dominique Rash, MD

In patients with brain metastases, stereotactic radiosurgery (SRS) has emerged as a viable treatment alternative to whole brain radiation therapy. First developed in 1949 by Swedish neurosurgeon, Lars Leksell, MD, SRS was initially defined as a "single high dose fraction of radiation stereotactically directed to an intracranial region of interest," with the intent of treating benign functional disorders and arteriovenous malformations. The role of SRS quickly expanded to include the treatment of other spherical lesions including brain tumors and metastases. Over time the machines used to deliver SRS have evolved and include both the Gamma Knife, which employs a Cobalt 60 radioactive source, and Linac-based radiosurgery, which involves a modified linear accelerator adapted for both conventionally fractionated and stereotactic radiotherapy.

With the evolution of technology, our expectations for the management of cancer patients with intracranial disease have also changed. Advances in radiographic imaging have led to the early detection of brain lesions which are often asymptomatic. Additionally, the development of genetic/molecular markers across cancer subtypes has enabled us to identify patients with a more favorable prognosis, despite harboring brain metastases. Among such patients, the goal of therapy is to prevent intracranial progression and potential neurologic deterioration, while extracranial disease is controlled with systemic therapy. Treatment progress is therefore defined by our ability to effectively treat brain metastases in a timely fashion, while minimizing side effects and toxicity.

Whole brain radiation therapy (WBRT) for brain metastases is well established as a means to reduce the rate of, and delay the time to, intracranial relapse, which may minimize the risk of neurological deterioration secondary to new brain lesions. Indeed, the primary advantage of WBRT over SRS is the ability to address micrometastatic disease. However, the recently published EORTC 22952-26001 randomized clinical trial comparing the use of SRS or surgery alone versus SRS or surgery and WBRT failed to demonstrate an improvement in functional independence or overall survival with the eradication of micrometastatic disease by WBRT. Complementary data from Chang et al. in 2009 highlighted an increased risk for memory decline at four months among patients treated with SRS and WBRT compared to SRS alone. Therefore, in carefully selected patients the use of SRS with serial MRI imaging every three months allows early detection of new asymptomatic lesions amenable to repeat SRS. It also reduces the risk of neurologic decline associated with WBRT, which remains a valid concern especially for the cohort of patients with a good Karnofsky Performance Status (KPS), extracranial disease control, and favorable cancer histology.



The new Varian Edge treatment machine, now in operation at the Mercy Cancer Center's C Street location, represents the latest in cutting edge technology designed for SRS. As a linear accelerator, it may be used to treat both intracranial and extracranial sites. Greater degrees of articulation and freedom of positioning enable us to deliver high doses of radiation to sites previously inaccessible or abutting critical normal structures with sub-millimeter accuracy. By using a frameless positioning system and incorporating technological innovations that dramatically reduce treatment times, the Edge is unique in its ability to improve the SRS experience for the patient, which remains our ultimate goal.

Dignity Health
Cancer Institute
of Greater Sacramento

Metastatic Brain Tumors: A Brief Review

Hamid Aliabadi, MD

Metastases to the brain are the most common intracranial tumors in adults. They occur in 20-40% of all patients with cancer with 30-40% presenting as a single metastasis. It is estimated that 170,000 new cases of metastatic brain tumor are diagnosed in the United States each year, and the incidence continues to rise as a result of advances in cancer diagnosis and management. In particular, the use of MRI has led to the detection of small metastases which would not have been visualized in the past. However, the prognosis for patients with metastases to the brain remains poor.

Proper clinical and radiological evaluation is important in determining the optimum treatment strategy for patients with brain metastases. This includes assessing the extent and control of systemic disease and assigning the appropriate cancer stage. This evaluation, be it with CT/PET scans of the body or radionuclide bone scans, is critical since patient prognosis is most accurately based on the extent of systemic disease. The extent of intracranial disease is assessed by contrast-enhanced MRI.

In a study by Patchell et al. in 1990, it was found that treatment outcomes for cerebral metastases were better when surgical resection was combined with whole-brain radiation therapy (WBRT). Recurrence at the original site was reduced in these patients when compared with those receiving only WBRT. Furthermore, the patients who underwent resection plus radiation survived longer with a better quality of life. However, WBRT has also been associated with an acute detriment in quality-of-life measures, potentially delayed neurocognitive deficits, and in some studies, a lack of overall survival benefit.

An alternative approach, post-operative stereotactic radiosurgery (SRS), is used at many institutions in lieu of WBRT for treatment of brain metastases. This focal radiation technique offers several potential advantages and may avoid the acute and delayed effects of WBRT, including neurocognitive decline. In addition, SRS requires a much shorter elapsed time for treatment and reduces the volume of normal brain parenchyma irradiated. SRS is often offered to patients with a good Karnofsky Performance Status (KPS) score and **three or fewer** metastases of < 4 cm in maximum dimension. When it is selected as the treatment modality, the neurosurgeon, radiation oncologist, and radiation physicist work together to perform target delineation, dose selection, and radiosurgical planning.

> "It is estimated that 170,000 new cases of metastatic brain tumor are diagnosed in the United States each year."

In a retrospective study by Soltys et al. published in 2008, post-resection, adjuvant SRS yielded a local control rate that was comparable to that of post-operative WBRT. The local failure rate at 12 months was 21% when using SRS to the resection cavity, 46% with surgery alone, and 10 to 20% in patients with surgical resection followed by WBRT. Similarly, Patchell et al. in 1998 demonstrated that when an isolated metastasis is removed and treated with post-operative WBRT versus no additional therapy, the WBRT decreased the rate of local failure at the original tumor site from 46% to 10%. An additional advantage of WBRT is that it reduces the rate of appearance of distant brain metastases. However, given early detection of brain metastases, effective intracranial salvage therapy, and improved systemic control of malignant disease, one could argue that it would be equally appropriate to treat a solitary metastasis with surgery followed by SRS.

Although the long-term prognosis for patients with metastatic brain tumors is poor, advances in early detection, accurate cancer staging, and post-operative radiation therapy are producing benefits to the patient. Both WBRT and SRS are effective tools to reduce local recurrence, prolong survival, and improve quality of life after primary tumor resection. Optimal outcomes are most likely to be achieved through a team-based approach to the selections of appropriate treatment options.

t-RFA Offers Pain Relief, Hope for Spinal Tumor Patients

George Luh, MD

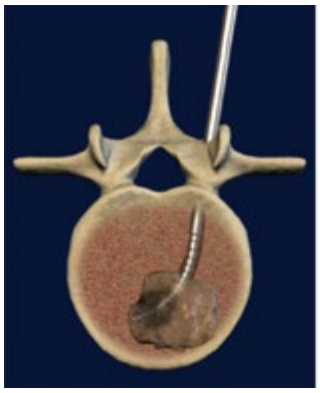
It is estimated that more than 1.6 million people received a new cancer diagnosis last year and up to 10% of them developed symptomatic spinal metastasis. In addition, spinal metastasis may be the first presenting sign of cancer in up to 20% of patients. Autopsy studies show that skeletal metastases are present in up to 85% of patients who die from breast, lung, and prostate cancer, with the spine being the most common site. Metastatic spinal tumors are a significant cause of pain and disability. In addition to the side effects of treatment, decreased quality of life results from intractable pain, decreased mobility, increased dependence on others, increased anxiety, and depression. The treatment of painful spinal metastasis is primarily palliative and may involve local therapy (radiation and surgery), systemic therapy (chemotherapy, hormonal therapy, radiopharmaceuticals, and bisphosphonates), and analgesics (mainly opioids and NSAIDs).

The standard of treatment for painful localized spine metastases is external beam radiation therapy (XRT). However, up to 40% of patients do not experience pain relief following XRT and, unfortunately, for a variety of reasons many of those patients are not candidates for repeat XRT.

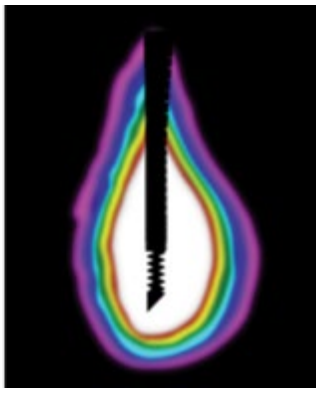
Targeted radio-frequency ablation (t-RFA) of spinal tumors offers patients another option for pain control. It is important to note that t-RFA does not replace XRT. In fact, a recent study of 45 patients comparing the combination of t-RFA and XRT to XRT alone found the combination of t-RFA and XRT to provide quicker (three weeks vs. nine weeks) and more complete pain relief than XRT alone. In addition, combining t-RFA with vertebral augmentation (injection of bone cement) has been reported to provide 90-100% of patients with significant pain relief.

Targeted radiofrequency ablation of spinal tumors involves placing a single coaxial needle system through one pedicle into the vertebral body. The inner needle is curved, which allows the user to steer the needle into the proper position. Then radiofrequency energy is delivered in a controlled fashion to the tumor with constant monitoring of tumor temperatures. Bone cement is then injected following the tumor ablation. An additional benefit of this approach allows the option of a tissue biopsy to be performed prior to the t-RFA and vertebral augmentation.

Any patient with focal pain due to a metastatic spinal tumor may be a candidate for t-RFA. Specific subgroups of patients that may benefit include patients with radioresistant tumors, persistent and/or recurrent pain after XRT, posteriorly positioned tumors, and patients who have reached their maximum radiation dose limit. Also, for those patients who are part of a chemotherapy clinical trial or on a chemo protocol that requires suspension to administer XRT, t-RFA is usually allowed and lets the patient continue their chemotherapy treatment.



Controlled Energy Delivery: RF energy is delivered as the instrument actively monitors tumor temperatures and provides real-time feedback



Controlled thermal distribution produces a consistent and predictable ablation zone

Possible mechanisms for pain relief include the intense heat from t-RFA, which may destroy local sensory nerves, and by destroying tumor cells, the production of cytokines and tumor-derived factors involved in sensitizing sensory nerves to pain and stimulating painful osteoclastic activity is decreased. Tumor growth into the periosteum and surrounding tissues may also be inhibited.

The benefits of t-RFA include rapid pain relief. It's a minimally invasive outpatient procedure (it takes about 90 minutes), that requires no repeat treatment and maintains options for any future treatments (e.g., XRT or chemotherapy). Common reasons not to do t-RFA include starting pain <4/10 on a pain scale (it is difficult to effectively treat mild pain), standard treatments not received (e.g., XRT), proximity to vital structures (e.g., spinal cord), pain not localized to one or two painful lesions, or purely blastic lesions.

Overall t-RFA of spinal tumors offers select cancer patients significant pain relief and hope for a better quality of life.

Dignity Health
Cancer Institute
of Greater Sacramento

6501 Coyle Avenue
Carmichael, CA 95608

TUMOR BOARDS

Dignity Health Cancer Institute of Greater Sacramento's multidisciplinary approach to cancer care includes regularly scheduled Tumor Boards held throughout Greater Sacramento, offering clinical review of patient cases for optimal treatment results. For each of our Tumor Boards, physicians are eligible for 1 CME credit.

To present a case at an upcoming Tumor Board, please email, fax, or call contacts noted below. To present a case, please provide:

- **Patient's name**
- **Date of birth and/or medical record number**
- **Disease site**
- **Diagnosis**
- **Where path and imaging can be found**

Hospital Cancer Conferences

Mercy General Hospital

Wednesdays at 12:15 p.m.
Location: Greenhouse Conference Room

Contact: Renae Huwes
renae.huwes@dignityhealth.org
916.536.3157 (phone)
916.536.3044 (fax)

Mercy Hospital of Folsom

4th Wednesday of every other month at Noon
(January, March, May, July, September, November)
Location: CC1 and 2 or PCU conference room

Contact: Mansoor Javeed, MD
mansoor.javeed@dignityhealth.org
916.984.6230 (phone)

Mercy San Juan Medical Center

Thursdays at 12:30 p.m.
Location: Conference Room 2

Contact: Renae Huwes
renae.huwes@dignityhealth.org
916.536.3157 (phone)
916.536.3044 (fax)

Methodist Hospital of Sacramento

3rd Friday of each month at Noon
Location: Bistro Conference Room

Contact: Starr Fesler
sfesler@uscmc.com
916.683.9616 (phone)

Sierra Nevada Memorial Hospital

Thursdays at 12:30 p.m.
Location: OPC 110-120

Contact: Debby Kirk
debby.kirk@dignityhealth.org
530.274.6872 (phone)

Woodland Healthcare

Tuesdays at 12:15 p.m.
Location: DCR 5

Contact: Michelle Ing, PA
michelle.ing@dignityhealth.org
530.662.3961 (phone)

Tumor-specific Cancer Conferences

Breast Cancer Conference

3rd Friday of each month at 12:30 p.m.
Location: Mercy Cancer Center
3301 C Street, Suite 550
Large Conference Room

Contact: Renae Huwes
renae.huwes@dignityhealth.org
916.536.3157 (phone)
916.536.3044 (fax)

GU Cancer Conference

4th Tuesday of each month at 7:30 a.m.
Location: Mercy San Juan, CC3

Contact: Renae Huwes
renae.huwes@dignityhealth.org
916.536.3157 (phone)
916.536.3044 (fax)

Cases may be brought directly to the conference. Pathology and imaging will not be routinely ordered unless there is a question regarding the results.

Thoracic Cancer Conference

2nd Wednesday of each month at 4 p.m.
Location: Mercy San Juan, CC3

Contact: Renae Huwes
renae.huwes@dignityhealth.org
916.536.3157 (phone)
916.536.3044 (fax)

Cases may also be brought directly to this conference.