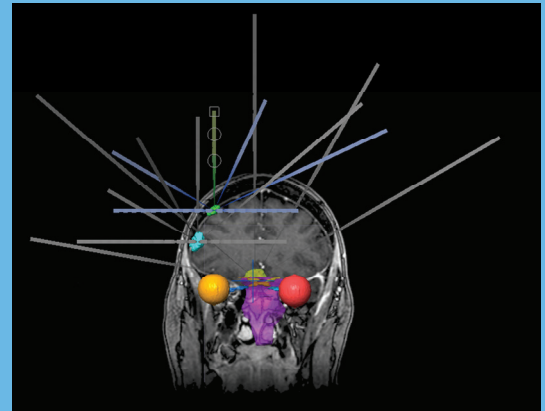


STEREOTACTIC RADIOSURGERY FOR BRAIN METASTASES

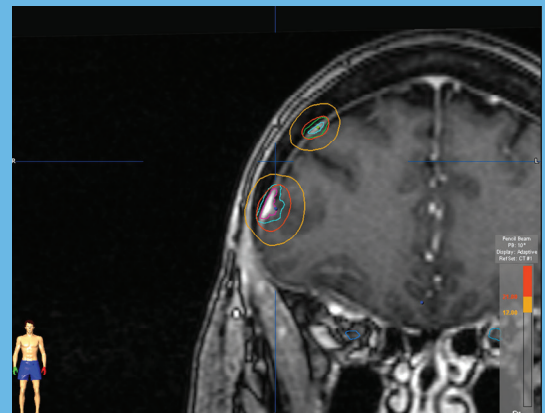
Cancer metastasis remains a leading cause of death in the United States. Brain metastases, in particular, represent one of the most feared complications of disseminated cancer, resulting in a very grave prognosis. Systemic chemotherapy has a very limited role in the direct management of brain metastases largely due to delivery constraints across the blood-brain barrier. Patients with uncontrolled brain metastases could have a survival of less than 3 months. Whole brain radiotherapy (WBRT) has been delivered over the past thirty years with evidence of successful palliation of symptoms but concern about the potential for long term neurologic sequelae from treatment. While radiotherapy still remains the main management modality for patients with brain metastases at present, there has been much interest in exploring alternate treatment strategies, such as optimizing patient selection for the integration of surgery and advanced stereotactic radiation modalities.

In select cases, surgery followed by radiotherapy is desired. When indicated, surgery is often reserved and effective for large symptomatic lesions, ideally solitary. Post surgical radiotherapy options include WBRT or fractionated stereotactic radiotherapy to the surgical resection bed (FSRT), either of which is favorable to local disease control. In patients with small asymptomatic lesions (<3cm), stereotactic radiosurgery (SRS) is ideal in lieu of surgery. **SRS REFERS TO THE DELIVERY OF A HIGH DOSE OF RADIOTHERAPY TO A VERY PRECISE TARGETED VOLUME. WHEN GIVEN AS A SINGLE FRACTION, IT COULD REPRESENT A DOSE APPROXIMATELY 10 TIMES GREATER THAN THE TYPICAL RADIATION DOSE.** Unlike WBRT, SRS is very focally applied. SRS has the advantage of targeting lesions in areas that are not easily surgically accessible, as well as for patients who might not be optimal surgical candidates given their debilitated status. SRS thus provides a relatively lower morbidity alternative compared to conventional surgery.

At the Moffitt Cancer Center and Research Institute, we have made tremendous advances in the treatment of brain metastases with a paradigm shift towards SRS as a primary treatment modality for most of our brain metastases. As a consequence, we have realized several long-term survivors within our radiosurgery cohort. Being a comprehensive cancer center with nationally renowned breast, thoracic and melanoma oncology programs, we encounter a substantial volume of patients with brain metastases. The radiosurgery program comprises an interdisciplinary team of radiation oncologists, neurosurgeons, and radiation physicists. **PATIENTS ARE EVALUATED SIMULTANEOUSLY BY A NEUROSURGEON AND A RADIATION ONCOLOGIST TO DETERMINE RADIOSURGERY ELIGIBILITY.** We employ a frameless system which has the added benefit of enhanced patient comfort compared to frame-based systems. Our experience with this approach mirrors those of other institutions whereby we have found excellent local control of metastatic lesions, even for tumors that were usually radio-resistant to conventional radiation. Interdisciplinary collaboration is essential to the effectiveness of this treatment approach.



Multiple beams deliver "pin-point" radiation to two tumors in the brain

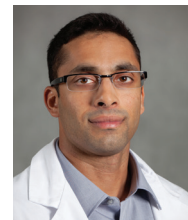


Different colors represent the doses of radiation delivered to each tumor, note how quickly the dose decreases from the high to low dose region



Arnold B. Etame, MD, PhD is a neurological oncology surgeon who works in collaboration with radiation oncology specialist **Dr. Nikhil Rao** at the Moffitt Cancer Center.

Dr. Etame specializes in Image-guided and Awake craniotomies for primary and metastatic brain tumors as well as Stereotactic Radiosurgery. He serves as an Assistant Professor of Oncological Sciences at the University of South Florida College of Medicine. He completed his undergraduate degree at the State University of New York at New Paltz, medical degree at the University of Iowa, neurological surgery specialization at the University of Michigan, graduate degree and fellowship at the University of Toronto.



Dr. Rao specializes in the treatment of central nervous system tumors, melanoma and has a special interest in stereotactic body radiation therapy. He completed his

undergraduate and medical school at the University of Virginia. His radiation oncology training took place at the University of Texas at Galveston. Dr. Rao is the associate program director for the radiation oncology residency program. They both work in collaboration with Dr. Chinnaiyan as part of the Radiosurgery Program at Moffitt for brain and spine metastases. They are both accepting new patients

For Dr. Etame, new patients can be scheduled by calling **813-745-2011** or **813-745-3871**.

For Dr. Rao, new patients can be scheduled by calling **813-745-3980**.

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Once patients are deemed to be ideal SRS candidates, a planning high-resolution MRI of the brain is obtained. The very high-resolution scan enables detection of metastases that are in the millimeter range. In addition, for frameless SRS applications, patients require immobilization with a mask, with a resulting precision to less than 1 mm. The targeted tumor volume is delineated and dose histograms are generated by our physicist. The final plan is evaluated and approved by the neurosurgeon and radiation oncologist. In designing the radiosurgery treatment plan, special emphasis is placed on radiation dose to normal brain, and also to critical areas such as the motor cortex, deep white matter tracts, brain stem, and optic tracts. Several non-overlapping arcs are employed such that there is pin-point convergence at the target.

IN OUR EXPERIENCE, PATIENTS OFTEN TOLERATE TREATMENT EXTREMELY WELL AND GO HOME THE SAME DAY. For those that are expected to develop swelling or who developed post-treatment nausea or headaches, a short taper of dexamethasone is given. While the treatments can be very effective in controlling brain metastases, there is an approximately 10% chance of delayed radiation necrosis. More importantly, unlike WBRT, the incidence of neurocognitive dysfunction is markedly lower with SRS.

Another approach that we have begun to utilize is highly focused radiotherapy to the postsurgical cavity also called FSRT. We deliver a high dose per fraction to the cavity typically in 5 treatments. This treatment utilizes similar technology to SRS. The reason that the treatments are fractionated is to decrease the chances of long-term brain injury such as radiation necrosis. **WITH THIS APPROACH, WE HAVE NOTED APPROXIMATELY 80-90% LOCAL CONTROL OF THE SURGICAL CAVITY IN OUR PATIENTS.** Previously, these patients would have almost uniformly been treated with WBRT.

Future directions are geared towards exploring synergies between radiation and systemic chemotherapy. There is evidence that radiation may enhance blood-brain barrier permeability, suggesting possible translation to improved efficacy for chemotherapy agents. Lastly, as SRS becomes increasingly effective against metastatic tumors, there is always the risk of radio-necrosis to the normal brain. Therefore, strategies that can simultaneously minimize toxicity while demonstrating therapeutic efficacy are warranted.

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