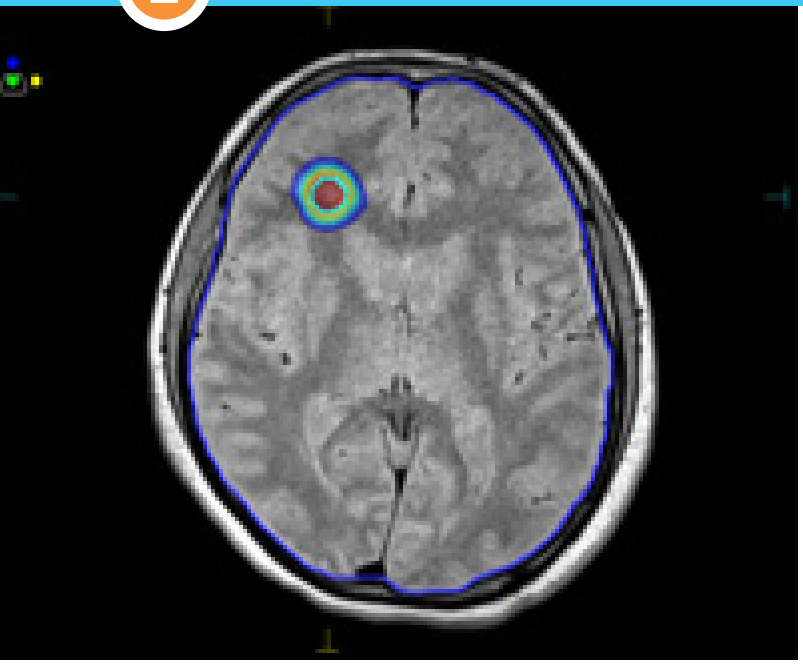
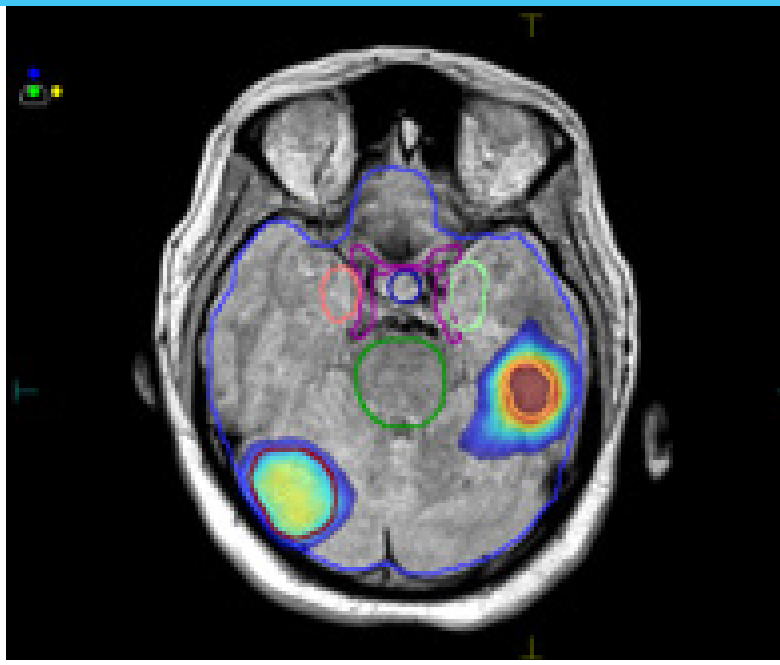
ELEKTA

Linac-based stereotactic radiosurgery for the treatment of multiple brain metastases

CASE STUDY





Institution:

Geetanjali Cancer Center

Location:

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Radiation Oncologist:

Dr Shankar Vangipuram, Director, Division of Radiosurgery

Medical Physicist:

Mr Vinoth Kumar, Chief Medical Physicist

GEETANJALI CANCER CENTRE

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Summary

Patient demographics

55 year old woman treated in 2013 for breast cancer and presenting with symptoms of increased intracranial pressure (ICP).

Treatment

Stereotactic radiosurgery (SRS). Marginal dose prescribed per lesion: GTV1 – 18 Gy; GTV2 – 20 Gy; GTV3 – 14 Gy, delivered in a single fraction using a common isocenter and a double VMAT arc.

Diagnosis

3 brain metastases detected by MRI, located in the right cerebellum, the left temporal lobe and the right frontal lobe with dimensions: GTV1 - 0.82 x 1.01 x 1.15 cm; GTV2 - 1.07 x 1.62 x 1.42 cm; GTV3 - 2.58 x 2.48 x 3.8 cm.

Treatment planning and delivery system

- Monaco® treatment planning system version 5.0.1.
- Versa HD™ with Agility™ MLC
- Fraxion™ cranial immobilization
- HexaPOD™ evo RT robotic couch
- XVI image guidance

Patient History and Diagnosis

A 55 year old female presented in May 2015 with symptoms of increased intracranial pressure (ICP), including headache, nausea and vomiting. The patient was previously diagnosed with breast cancer in 2013. In February 2014 she had a radical mastectomy. Subsequently she received chemotherapy (four cycles of AC and four cycles of Taxol) followed by radiotherapy to the chest wall.

Since this patient had triple negative breast cancer (negative for estrogen receptors, progesterone receptors and HER2/neu), the presence of brain metastases was suspected. An MRI scan of the patient's brain revealed 3 brain metastases located in the right cerebellum, the left temporal lobe and the high frontal lobe.

The patient had no other comorbidities, making her a good candidate for stereotactic radiosurgery (SRS) according to the standard protocol for brain metastases at this institution (Figure 1), which is based on ASTRO recommendations[1,2], IRSA guidelines[3] and recent published evidence[4-6].

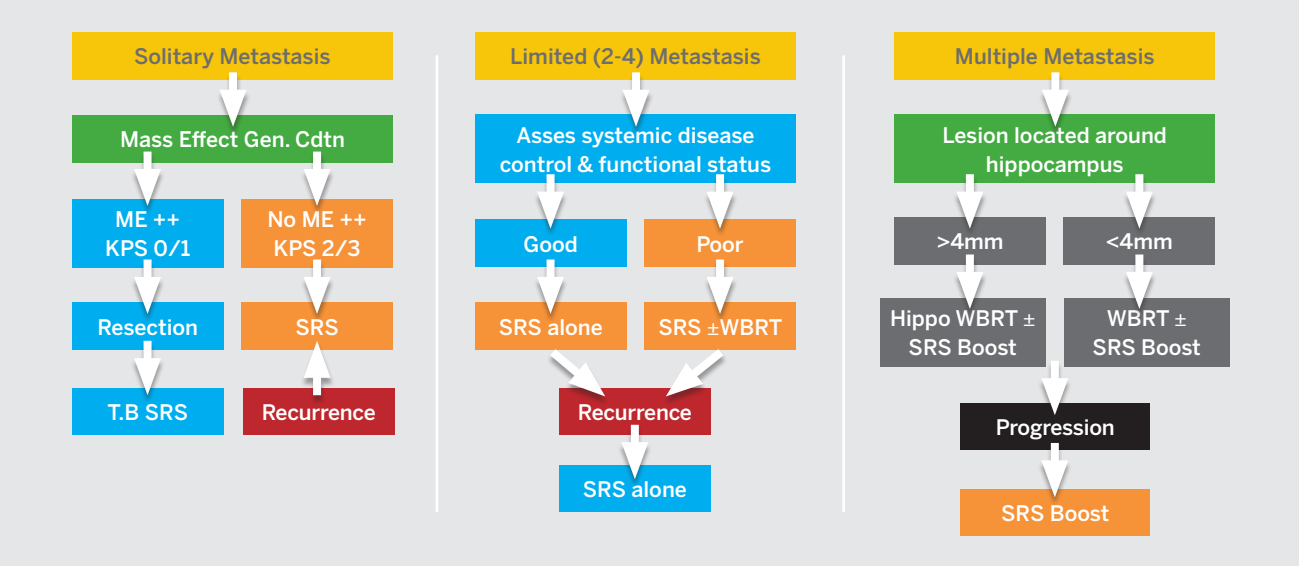


Figure 1 . Standard protocols for brain metastases at Geetanjali Cancer Center

There is a strong case for performing SRS as a primary treatment for patients with 2-4 metastases and good functional status in order to reduce the risk of neurocognitive decline associated with whole brain radiotherapy (WBRT). The treatment modality used for SRS should be fast, to reduce the time that the patient must remain still on the couch, and its target-hitting precision must be very robust, to spare healthy tissue and critical structures in the brain. Such speed and precision can now be achieved with the Versa HD linear accelerator with Agility multileaf collimator (MLC), using the Monaco treatment planning system (TPS).

The combination of Monaco, with its advanced dose modulation capabilities and its ability to achieve excellent dose distributions, and Agility, with its rapid leaf speed, low transmission and high-resolution beam shaping, allows very accurate dose placement. This is particularly important for the high doses per fraction required for stereotactic approaches and can be achieved, even for small targets and complex plans, using these tools. In addition, the large field size and interdigitation capabilities of Agility allow plans to be generated for multiple targets using a single isocenter, which has the desirable effect of reducing treatment time and Monitor Units to the patient.

Treatment planning

For treatment planning and treatment delivery the patient was immobilised using the Elekta Fraxion cranial immobilisation system with a thermoplastic mask. CT and MRI scans (T1 post contrast, T2 and proton density sequences) were obtained, each with 1.25 mm slice thickness, and fused prior to image registration and delineation of target volumes and critical structures (figure 2).

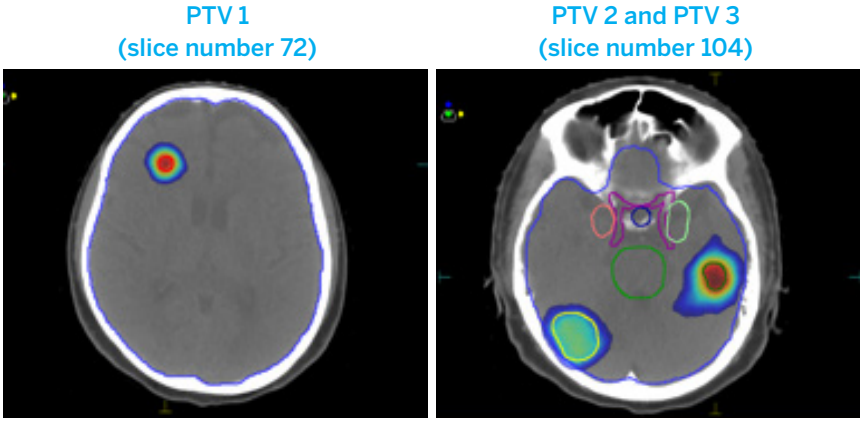


Figure 2. T1 Planning images showing delineated targets and critical structures

A margin of 2 mm was applied to the gross tumour volumes GTV1, GTV2 and GTV3 in all directions, except for the superior and inferior sides, to form planning target volumes PTV1, PTV2 and PTV3 respectively. The volume, dimensions and dose prescription for each volume is shown in Table 1. Dose constraints for critical structures are shown in table 2 and the dose volume histogram (DVH) for target volumes and critical structures are shown in Figure 3.

Volume name	Volume (cc)	Dimension (cm)	Dose Prescription
GTV1	0.446	0.82 x 1.01 x 1.15	18 Gy
PTV1	0.799	1.05 x 1.01 x 1.15	
GTV2	0.953	1.07 x 1.62 x 1.42	20 Gy
PTV2	1.461	1.37 x 1.62 x 1.42	
GTV3	15.144	2.58 x 2.48 x 3.8	14 Gy
PTV3	18.252	2.8 x 2.48 x 4.8	

Table 1. Dimensions and prescribed dose for each of the 3 brain metastases.

Critical structure	Volume (cm3)	Min dose (cGy)	Max dose (cGy)	Mean dose (cGy)
Brain stem	26.645	34.7	827.6	341.2
Left eye	10.444	15.3	323.6	146.2
Right eye	9.550	9.4	318.0	174.4
Left hippocampus	2.255	127.5	593.1	348.1
Right hippocampus	2.328	225.5	523.5	357.8
Left optical nerve	0.563	118.8	369.9	244.4
Right optical nerve	0.573	188.6	395.6	255.0
Optic chiasma	2.469	212.9	619.1	403.4
Pituitary	0.972	287.5	629.3	483.8
Patient (unspecified tissue)	133.820	0.2	845.8	50.4

Table 1. Dimensions and prescribed dose for each of the 3 brain metastases.

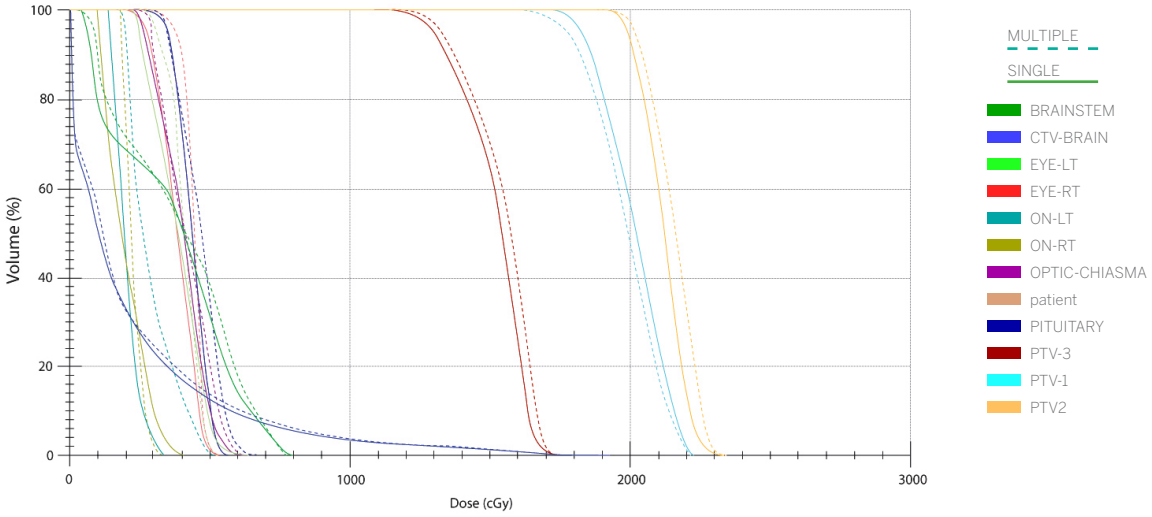
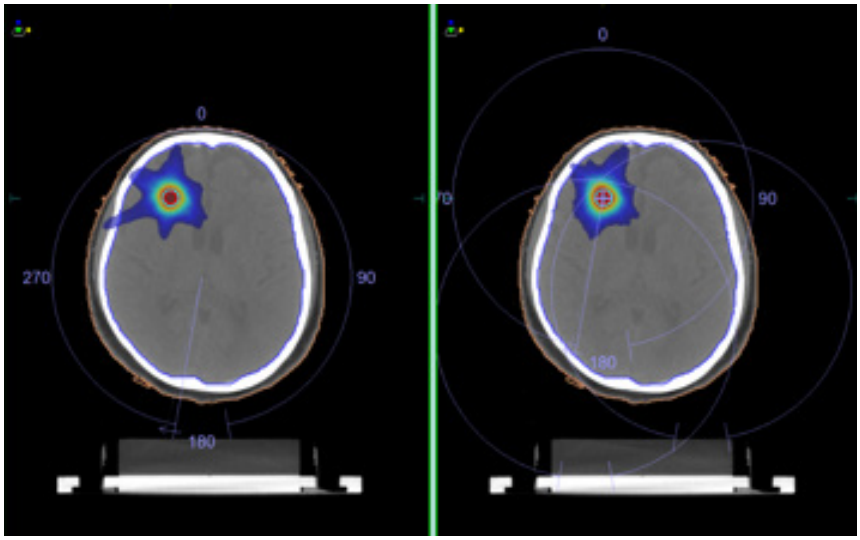


Figure 3: Dose Volume Histogram (DVH) for target volumes and critical structures using a single isocenter and multiple isocenters.

A VMAT plan was generated using a single, common isocenter for all three targets. The isocenter was placed at the centre of the volume containing all three target volumes. The distances between the isocenter and the plane containing the central slice of each PTV are 2.62 cm for PTV1, 0.7 cm for PTV2 and 1.70 cm for PTV3. An optimal plan was generated using a 6 MV flattened beam using Monaco version 5.0.1 and Agility, which was reviewed by the Head of Radiation Oncology prior to treatment delivery. Dose coverage for each target volume was comparable to an equivalent plan generated using three separate isocenters (figure 3/figure 4).

PTV 1 single isocenter

PTV 1 multiple isocenter



PTV 2 and PTV 3 single isocenter

PTV 2 and PTV 3 multiple isocenter

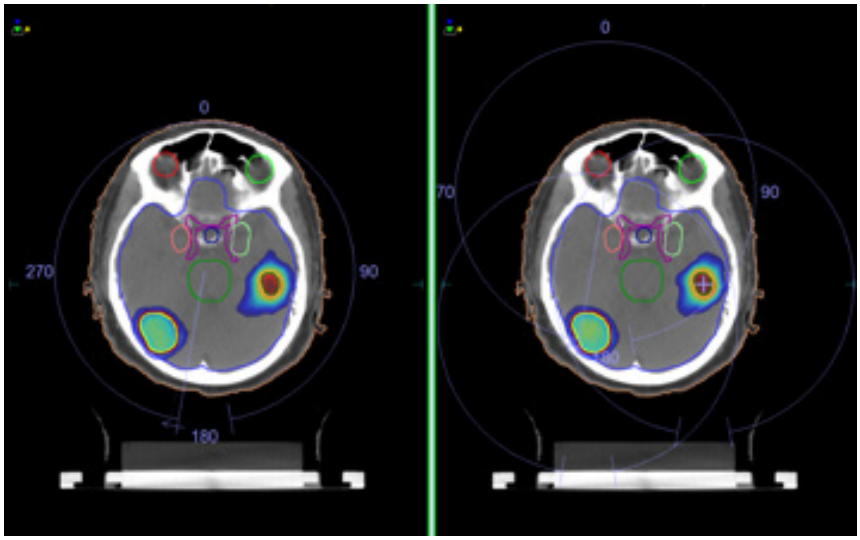


Figure 4. Comparison of single and multiple isocenter plans

In addition, excellent dose fall-off was achieved as demonstrated by measuring the distance between the 100% and 80% isolines and between the 100% and 50% isolines (table 4). This is particularly important for normal brain tissue and critical structure sparing in SRS.

Target volume	Max distance between 100% and 80% isoline (mm)			Max distance between 100% and 50% isoline (mm)		
	Lateral	Anterio-Posterior	Superior-Inferior	Lateral	Anterio-Posterior	Superior-Inferior
PTV1	2.8	2.7	2.0	7.4	7.1	3.8
PTV2	4.0	3.9	1.6	10.5	14.5	3.6
PTV3	4.2	2.6	1.1	14.7	13.5	4.0

Table 4. Dose fall-off for planning target volumes

Treatment delivery

Following patient setup, XVI 3D cone beam CT was used for patient position verification prior to initiation of treatment. Translational and rotational corrections were made using the HexaPOD robotic treatment couch, which allows submillimeter patient alignment in 6° of freedom.

SRS was delivered by an Elekta Versa HD linear accelerator with the Agility MLC (collimator 0°, couch 0°) and a 6MV flattened beam, using a double 340° VMAT arc (gantry 190° - 170°). The treatment consisted of 255 segments and 7309.85 MU. The total beam on time for the treatment of all 3 brain lesions using a double VMAT arc was just 12 minutes. This would have taken more than twice as long (25 minutes) if multiple isocenters had been used.

XVI 3D cone beam CT patient position verification was also performed post treatment to confirm the accuracy of the SRS treatment delivery.

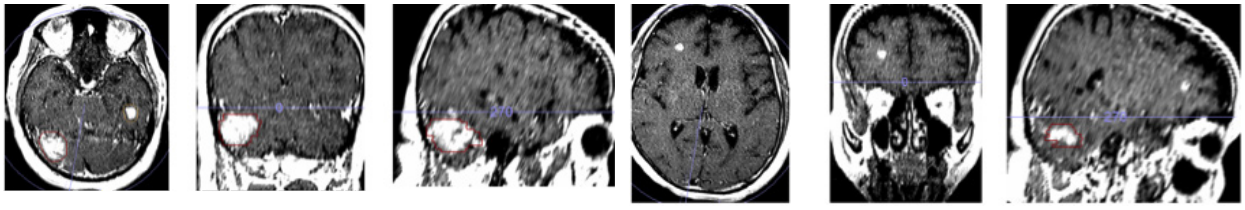
The treatment was well tolerated by the patient and she was able to return home on the same day as treatment.

Outcome and follow up

Following SRS, the clinical symptoms of increased ICP decreased and the patient was comfortable to commence chemotherapy within one week.

Follow up MRI scans three months post treatment demonstrated lesion regression for all three brain metastases (figure 5).

Pre-treatment



Post-treatment

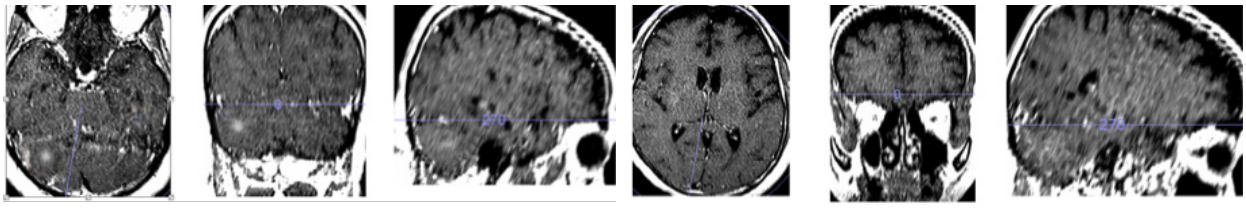


Figure 5. Brain MRI scans

Discussion and conclusions

The standard protocol for brain metastases at Geetanjali Cancer Center

For solitary, limited (2-4) and multiple metastases, this institution follows ASTRO recommendations[1], IRSA guidelines[3] and additional published evidence[4-6] for the use of SRS and WBRT (figure 1). Recent ASTRO recommendations[2] state that adjuvant WBRT should not be added routinely to SRS for limited brain metastases due to the risk of diminished cognitive function, worse patient-reported fatigue and quality of life. Randomized studies have demonstrated no overall survival benefit with the addition of adjuvant WBRT to SRS in the management of selected patients with good performance status and solid tumor brain metastases[2].

Radiosurgery alone, in cases where there are no additional metastases and greater than 6 months median life expectancy (less than 5% of the patient population at this institution), is only used in a trial setting at this center and does not form part of the standard protocol currently.

For multiple brain metastases with disseminated disease and less than 6 months life expectancy (greater than 95% of the patient population), patients are stratified according to the distance of the nearest lesion to the hippocampus. If the distance is greater than 4 mm, then hippocampus sparing WBRT is used, with or without SRS boost, in order to reduce the risk of cognitive decline. If the distance is less than 4 mm, then WBRT is used with or without SRS boost. A narrow margin (4 mm) around the hippocampus, used in hippocampus sparing WBRT, is achievable due to the increased modulation that can be delivered using Agility without compromising plan evaluation criteria. Furthermore, the positional accuracy of the HexaPOD™ patient positioning system (0.3 mm, 0.3°) provides confidence for accurate treatment delivery.

Linac-based SRS to multiple targets

In the delivery of linac-based SRS to multiple targets in the brain there are a number of particular challenges:

- **Accurate delineation**

Accurate delineation is essential for dose targeting precision and the sparing of normal tissue and critical structures in the brain. Any errors in SRS are critical due to the high doses delivered in a single fraction and the proximity of critical structures. For this reason, it is important to use the same slice thickness for the planning MRI and CT scans to minimise errors when the images are fused together during registration. This is essential for high precision procedures and allows accurate delineation of targets and critical structures.

- **Patient immobilisation & image guidance**

The second challenge for minimising errors in linac-based SRS is robust patient immobilisation. The options are to use frame-based or frameless immobilisation for cranial radiotherapy. At the Geetanjali Cancer Center, a frameless immobilisation protocol using the Fraxion cranial immobilisation system with a thermoplastic mask is used. This method improves patient comfort, compared to frame-based immobilisation, and provides sufficient rigid immobilisation for cranial radiotherapy techniques when used in combination with accurate image guidance procedures.

For this patient, XVI CBCT imaging was performed to verify patient position before and after treatment delivery, and the HexaPOD robotic couch was used to align the patient with sub-mm accuracy prior to treatment initiation. Since the treatment time was less than 15 minutes, intrafraction imaging was not performed in this instance. Generally, if treatment time is greater than 15 minutes and/or if 2 VMAT arcs are used in treatment delivery, XVI intrafraction imaging is performed to ensure there is no patient movement during delivery.

- **Treatment delivery**

Accuracy and speed are essential for SRS delivery. Dose targeting precision is ensured by accurate delineation and data input during the planning process, as already described. Accuracy in dose delivery is also enhanced by reducing beam-on time and, hence, further minimising the risk of intrafraction motion. Previously, using multiple

The team at Geejentali Cancer Center

isocenters, treatment times were much longer. With the accurate dose placement and speed of delivery that can now be achieved using Monaco TPS and Versa HD (using VMAT and Agility), in addition to the possibility of using a single isocenter for multiple targets with Agility, three brain metastases were treated in 12 minutes. A single isocenter also has the benefit of reducing the number of MUs to the patient and reducing planning time compared to a multi-isocenter plan. The reduction in treatment time increases patient comfort and reduces the risk of errors cause by intrafraction motion.

The alternative treatment option for this patient would have been whole brain radiotherapy (WBRT). Linac-based SRS allowed this patient to benefit from faster treatment with reduced risk of neurocognitive decline and resulted in immediate subjective improvement of symptoms and lesion regression 3 months post treatment. The aim of this treatment was to minimise treatment time and to improve overall comfort for the patient, which was achieved. Where there is not access to Gamma Knife radiosurgery, this method is an option for clinics, allowing SRS to be considered for more patients.

This single isocenter method has been shown to increase treatment planning and delivery efficiency, reduce treatment time and ensure efficient use of MU. The next step is to use flattening filter free (FFF) radiotherapy, which provides the opportunity to further increase efficiency by reducing treatment times for SRS deliveries. For this particular case, subsequent to treatment, the flattened beam plan was compared to an equivalent plan created using FFF 6MV beams. The FFF plan was delivered to a phantom using a double VMAT arc in just 4 minutes compared to 12 minutes for the flattened beam delivery. In addition, the FFF beam produced comparable dose coverage to the flattened beam plan. Planning efficiencies are also being investigated, particularly applying single arc VMAT plans where applicable. These approaches may be of added value for providing further treatment efficiencies and reduced beam on times in the treatment of multiple brain metastases using linac-based SRS.

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Director, Division of Radiosurgery

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ABOUT ELEKTA

Elekta's purpose is to invent and develop effective solutions for the treatment of cancer and brain disorders. Our goal is to help our customers deliver the best care for every patient. Our oncology and neurosurgery tools and treatment planning systems are used in more than 6,000 hospitals worldwide. They help treat over 100,000 patients every day.The company was founded in 1974 by Professor Lars Leksell, a physician. Today, with its headquarters in Stockholm, Sweden, Elekta employs around 4,000 people in more than 30 offices across 24 countries. The company is listed on NASDAQ OMX Stockholm.

Disclaimer

This case study is based on the experience and application of medical experts, and is intended as an illustration of an innovative use of Elekta solutions. It is not intended to promote or exclude any particular treatment approach to the management of a condition. Any such approach should be determined by a qualified medical practitioner.

It is important to note that radiation treatments, while usually beneficial, may also cause side effects that vary depending on the area being treated along with other medical circumstances. The most frequent side effects are typically temporary and may include, but are not limited to, skin redness and irritation, hair loss, respiratory, digestive, urinary or reproductive system irritation, rib, bone, joint or soft tissue (muscle) pain, fatigue, nausea and vomiting. In some patients, these side effects may be severe. Treatment sessions may also vary in frequency, complexity and duration. Finally, radiation treatments are not appropriate for all cancers, and their use along with the potential benefits and risks should be discussed before treatment.

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