Frameless Stereotactic Radiosurgery

A non-invasive, outpatient treatment for brain tumours

by Dr Daniel Tan

Stereotactic radiosurgery (SRS) is a specialised form of radiation therapy which delivers extremely high doses of radiation to target tissue with the aim of ablating the cells within. It is most often used in the setting of tumour ablation in cancer patients, but has also been used for functional disorders where high doses of pin-point radiation are used to 'surgerise' the pathological area. Multiple intersecting beams of radiation converge on the target, resulting in a highly conformal dose distribution which dissipates sharply once away from the target **[Figure 1]**.

In 1968, neurosurgeon Lars Leksell installed and treated his first patients on the gamma-knife prototype system in Sweden. Stereotaxis was achieved using a stereotactic frame fixed onto the patient using screws into the skull under local anaesthesia and radiation was delivered through a helmet with apertures opening and closing to expose the cobalt source within. Radiation beams pass through the apertures and converge onto the target by taking reference from the pre-calibrated frame in which the patient had his MRI imaging in, where the target was visualised and delineated. The first patients treated with stereotactic radiosurgery were those with functional disorders – that is patients with pain or movement disorders, where radiosurgery was used instead of surgery to ablate the causative areas, such as nerve roots for pain or thalamotomy for Parkinson's disease.

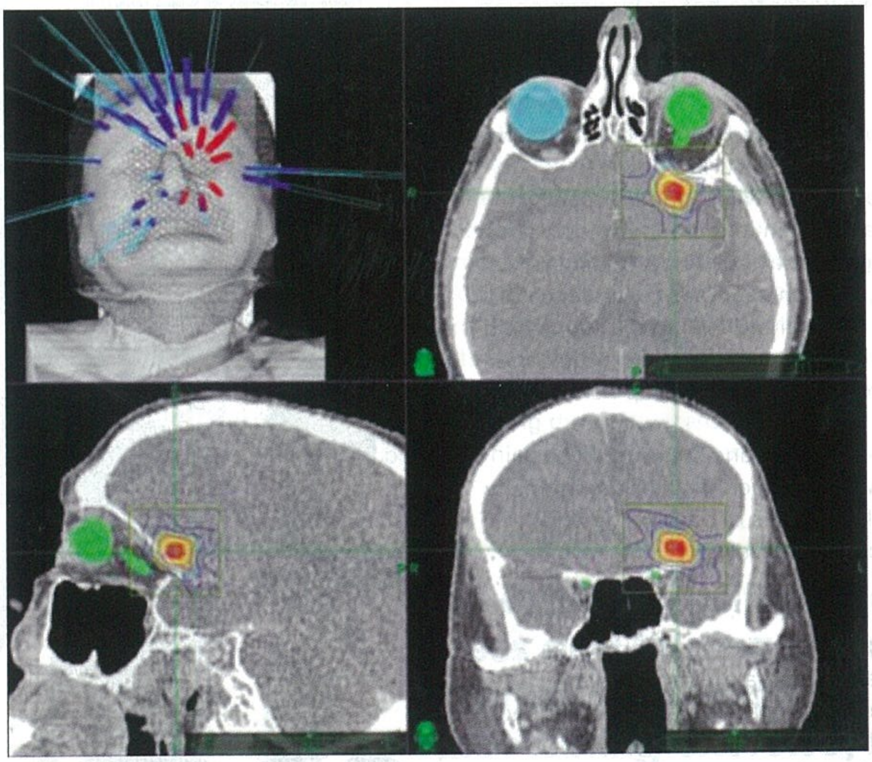

***Figure 1.** Multiple intersecting beams of radiation converge on the target, resulting in a highly conformal dose distribution which dissipates sharply once away from the target.*

Fast forward almost 50 years after radiosurgery was invented, a new level of technology has emerged, together with a wide range of evidence which demonstrates its usefulness in different conditions. What originated as a neurosurgical tool to reach deep seated lesions has evolved to offer patients the possibility of cure and tumour control without having to undergo major brain surgery. Today, SRS is the treatment of choice for oligo-brain metastases, retreatment of brain tumours and a variety of other benign brain tumours. Unlike then, patients can receive SRS as definitive treatment for their tumours entirely as a non-invasive, outpatient treatment, with minimal toxicity and disruption to their daily routine, to the point that they even wonder if they had received any treatment!

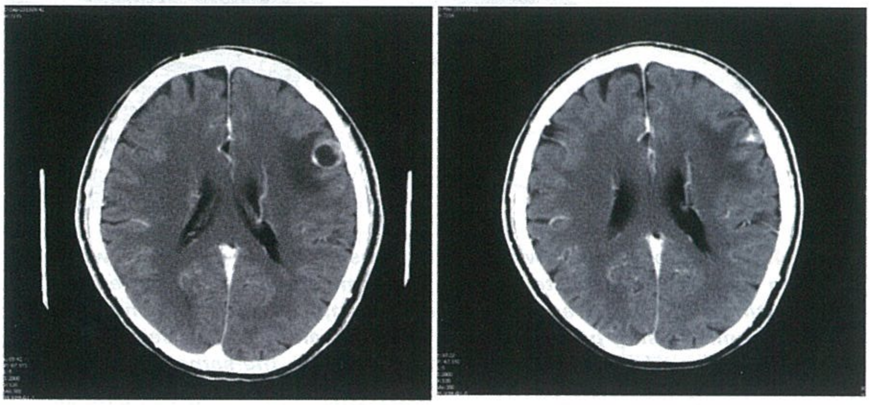

***Figure 2.* Before and after: At eight months, what was left at the area was a small nubbin of treated tumour that remained stable in size and no new tumours were noted.**

Case Illustration

Mr Tan is a 40-year-old gentleman who was diagnosed with renal cell carcinoma and had undergone radical nephrectomy two years ago. He was completely well for 23 months until he complained of heaviness in the head for a period of two weeks during a routine follow-up. An MRI was done at his request and unfortunately showed a 2cm enhancing lesion in the left fronto-pareital region with surrounding oedema but no mass effect, suspicious for brain metastasis. He was started on steroids with immediate relief of his heaviness and proceeded with a PET scan which showed no other sites of disease. His treatment options were discussed and this included neurosurgical excision, stereotactic radiosurgery followed by whole brain radiation or stereotactic radiosurgery or whole brain radiation alone. He opted for SRS alone as he did not want to undergo another major operation within two years. He was not keen on whole brain radiation therapy because of concerns regarding the late side effects on neurocognition and agreed to undergo surveillance MRIs every three months. His first MRI showed shrinkage of the tumour to 1cm with the characteristic central necrosis. At eight months, what was left at the area was a small nubbin of treated tumour that remained stable in size and no new tumours were noted **[Figure 2].** Life carried on as usual for Mr Tan without a single day of downtime because of the radiosurgery, except that he had a small patch of hair loss measuring the diameter of a 50 cent coin. There were no screw marks on his skull as he was treated using a frameless stereotactic system. All he needed was a customised, firmly fitted thermoplastic mask which he wore for his planning scans, and returned a week later for SRS, by being repositioned in the same mask, with the treatment delivered within one hour. His steroids were tailored down after one week and life indeed has carried on as normal since then.

Stereotaxis

Historically, stereotaxis, which refers to the identification of a target within a three dimensional space, was achieved using a fixed frame with pre-calibrated references along the X-Y-Z axis. With the frame attached to the patient's skull and imaging done with the frame on, the position of the brain tumour could be accurately localised to these references and targeted using openings within a helmet which contained a radioactive cobalt source to deliver the radiation dose. Up to 10 years ago, the main option for patients in Singapore who needed radiosurgery was the gamma-knife system which required the screwing of the fixed frame onto the patient's skull under local anaesthesia on the day of treatment. This frame had to be kept on throughout the day while the radiation plan was being prepared and could only be removed after the treatment was delivered **[Figure 3].** During the late 1990s, advances in image processing and on-board imaging led to the advent of radiosurgery capable linear accelerators. Traditional radiotherapy machines were now integrated with

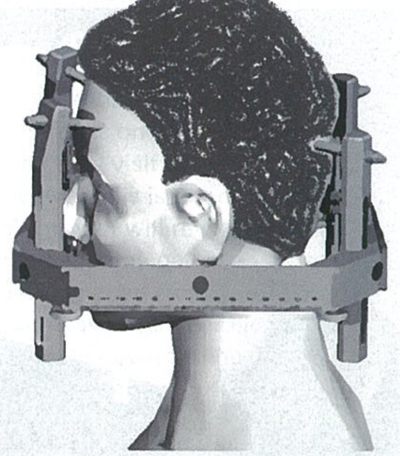

***Figure 3.* The gamma-knife system required the screwing of the fixed frame onto the patient's skull under local anaesthesia on the day of treatment. The frame had to be kept on throughout the day while the radiation plan was being prepared and could only be removed after the treatment was delivered.**

Surgical excision of tumours which are situated near cranial nerves risks damage to these nerves and it is not uncommon for acoustic neuroma patients to suffer from permanent hearing loss and facial nerve damage after surgery. SRS is suitable for tumours less than 3cm that are sufficiently away from critical structures.

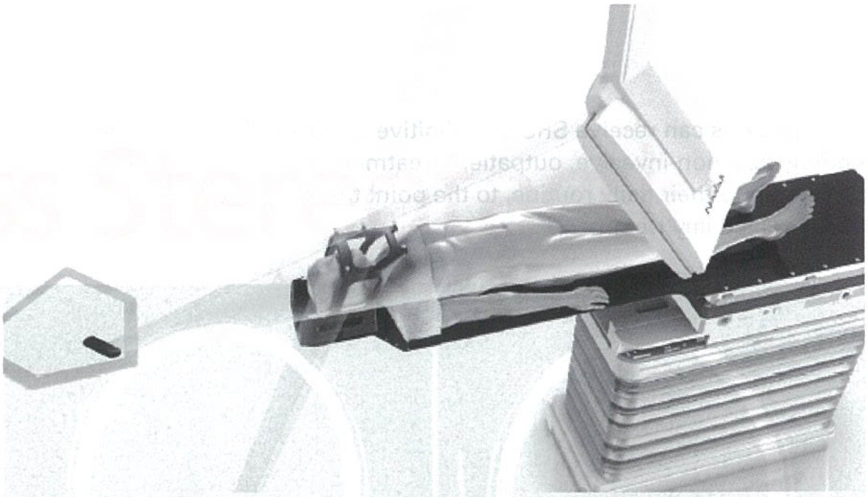

Figure 4. Stereotaxis can now be achieved using image guidance, whereby planning scans are co-registered with real time scans on the patient, with the resulting shifts required calculated by computer software. These shifts are then applied using proprietary systems, usually with six degrees of freedom (pitch, roll, yaw), to bring the patient into the same position with reference to the isocentre of the beams as the treatment was planned in.

advanced imaging and patient positioning capabilities and were able to produce sharper beams due to the use of mini-multileaf collimators. These advancements brought in the era of frameless stereotactic radiosurgery which allowed patients to undergo cutting edge therapy without downtime and sometimes, even without side effects.

Today, stereotaxis can be achieved using image guidance, whereby planning scans are co-registered with real time scans on the patient, with the resulting shifts required calculated by computer software. These shifts are then applied using proprietary systems, usually with six degrees of freedom (pitch, roll, yaw), to bring the patient into the same position with reference to the isocentre of the beams as the treatment was planned in **[Figure 4]**. A repeated image verification is obtained after these adjustments are made and the radiosurgery beams are turned on only after confirming that the target is now spot on. Using image-based stereotaxis, all the patient needs is a customised thermoplastic mask **[Figure 5]** which, while tight to prevent motion during treatment, does away with the need for physical screws in the skull, and allows the patient to return home after the planning scans while the treatment plan is being prepared. The patient only returns on the day of his convenience and undergoes the radiosurgery which is usually at most, a one hour procedure, the bulk of the time being spent on preparation and set-up. Numerous studies have shown that the accuracy rates of frameless systems are comparable

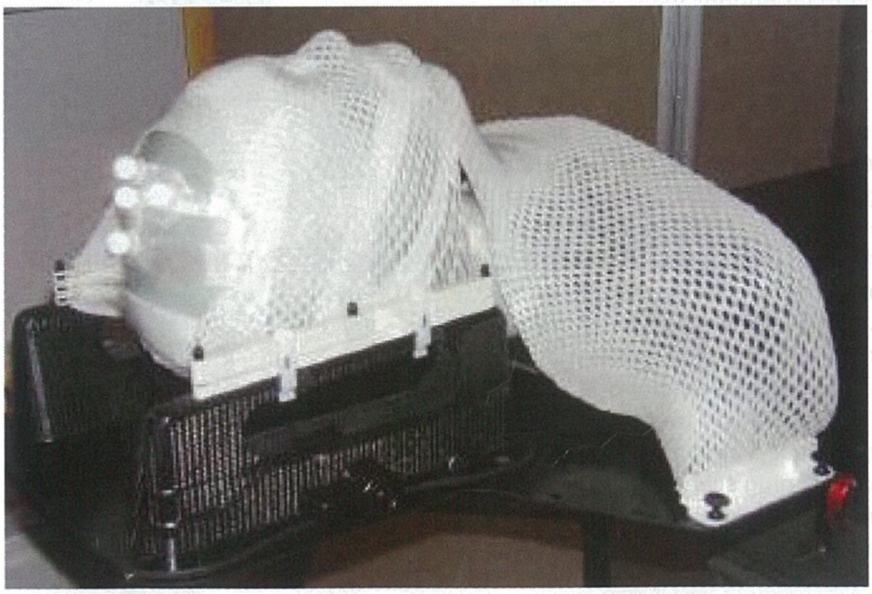

Figure 5. Using image-based stereotaxis, all the patient needs is a customised thermoplastic mask which, while tight to prevent motion during treatment, does away with the need for physical screws in the skull, and allows the patient to return home while the treatment plan is being prepared.

to frame-based systems, and clinical results have been similar. A recent survey presented at a radiosurgical meeting showed patients'preference was clearly towards frameless delivery.

Radiosurgery for Oligo-brain Metastases

Traditionally, patients with brain metastases were thought to have a grim prognosis, and were often told that they only had six months to live. In this setting, many were given best supportive care or if treated, received whole brain radiation therapy (WBRT). This was achieved by positioning two rectangular radiation fields from each side of the head using an imaginary line between the lateral cantus and the lower tragus as the lower border **[Figure 6]**.

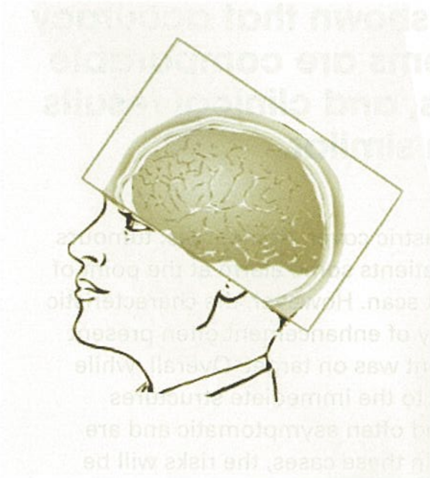

Figure 6. ***Whole brain radiation therapy (WBRT) was achieved by positioning two rectangular radiation fields from each side of the head using an imaginary line between the lateral cantus and the lower tragus as the lower border.***

The whole skull and its contents, minus the eyes and the lenses, were treated to a palliative dose (30Gy) over two weeks. This was thought to be sufficiently effective for controlling the patient's symptoms for their remaining duration. At that time, complete hair loss was taken for granted as a common side effect and wasn't questioned. In longer term survivors, it was noticed that neurocognitive dysfunction was present and this was confirmed in randomised studies. With better systemic treatments, patients are surviving longer and modern era data shows that in some patients, median survival after the diagnosis of brain metastasis can be more than two years. In such patients, neurocognition is important to preserve, and the SRS has been shown to provide more durable local control than WBRT alone. WBRT can be added after SRS, and this has shown to provide better local and distant control (than SRS alone), but with more side effects, including neurocognitive decline. SRS alone with regular MRI surveillance and appropriate treatment instituted upon distant recurrence, has shown no survival difference than upfront WBRT. Therefore, this approach is increasingly favoured among neuro-radiation-oncologists. Patients receive 'targeted' treatment for their tumour instead of to the entire brain, and are spared the side effects of WBRT. At the point when it is required, they will receive further appropriate treatment without the loss of any benefit. This makes their treatment duration shorter (one day versus two weeks) and the patient has minimal side effects (no complete hair loss) and lesser risk of neurocognitive dysfunction. The ability to ablate brain tumours easily and effectively has revolutionised the management of brain metastasis and given many patients hope and dignity.

Radiosurgery for Benign Brain Tumours

Radiosurgery has also changed the landscape of the management of benign brain tumours. These tumours are non-cancerous and do not have the propensity to infiltrate or metastasise. However, they can be locally recurrent and can cause neurological damage by mass effect. Before the advent of SRS, the only option for common benign tumours such as acoustic neuromas, meningiomas and pituitary adenomas requiring treatment, was neurosurgery. Even with advancement in navigational techniques and endoscopic surgery, these procedures are invasive and not without risks. Surgical excision of tumours which are situated near cranial nerves risks damage to these nerves and it is not uncommon for acoustic neuroma patients to suffer from permanent hearing loss and facial nerve damage after surgery. SRS is suitable for tumours less than 3cm that are sufficiently away from critical structures. With control rates up to 90%, SRS offers an outpatient, non-invasive yet effective treatment option with minimal side effects. In such cases, SRS has overtaken surgery as the treatment of choice and has become standard treatment.

Side Effects of Radiosurgery

Radiosurgery alone causes little or no side effects. Depending on the number and size of radiation fields, some patients can have hair loss the size of a fifty cent coin that is only discovered when they visit the hairdresser. However, this is temporal and hair growth will return in a few months. Many patients do not feel anything apart from the ultra-tight face mask which literally holds their face down for the duration of the treatment, but some report fatigue on the day of treatment which recovers spontaneously. In tumours which have oedema surrounding them, SRS can cause a temporal increase in swelling leading to more prominent neurological symptoms if present beforehand, or cause some heaviness or headaches. These can be managed with a tailing

Numerous studies have shown that accuracy rates of frameless systems are comparable to frame-based systems, and clinical results have been similar.

dose of steroids with appropriate anti-gastric cover. Sometimes, tumours swell before shrinking and may cause patients some alarm at the point of their third or sixth month post-treatment scan. However, the characteristic central necrosis and decrease in intensity of enhancement often present after SRS demonstrates that the treatment was on target. Overall, while there is a small risk of radiation damage to the immediate structures surrounding the tumour, they are low and often asymptomatic and are mainly related to the tumour's location. In these cases, the risks will be properly discussed with the patient.

Frameless Stereotactic Radiosurgery Platforms

Frameless SRS systems consist of two main components. Firstly, these systems must be equipped with collimators which are refined enough to shape the radiation beam around small tumours so as to reduce the spillage of high dose radiation onto normal tissue. Next, each system has image-guidance capabilities which enable on-board imaging and co-registration of planning scan images and on-treatment images. It also has the ability to calculate shifts, whether by moving the couch or the treatment unit so as to achieve perfect alignment, enabling the target to be treated to sub-millimetre accuracy. While the treatment unit design, image acquisition, and image processing capabilities enable frameless SRS, it is paramount that each member of the radiosurgery team (which consists of radiation oncologist, neurosurgeon, medical physicist, and radiation therapists) has undergone specialty training. They should be integrated as a team to ensure that every step of the treatment, from planning to delivery, is well coordinated, so as to avoid systematic error being carried over into the patient's treatment. Appropriate physics quality assurance checks on the machine components as well as the radiosurgery treatment plan are done to ensure patient safety. To use a military analogy, an SRS treatment can be likened to an artillery or air-strike, whereby a successful hit is the result of perfect coordination between all components of the system.

Future Developments and Other Applications

Researchers are now looking to exploit the potential immunogenic properties of SRS by pairing immunotherapeutic agents with SRS to see if a greater response can be achieved. On the technological front, SRS is being studied as a means to boost doses to malignant brain tumours in the hope of achieving better control or shorter treatment duration. SRS is also returning to its neurosurgical roots where it is again being investigated for the management of functional disorders.

The availability of frameless SRS technology has led to the delivery of SRS below and outside the cranium and now SRS is being done for spinal tumours (spine metastasis) and for tumours in the lung and liver. It is also used to target tumours in the abdominal and pelvic cavity such as lymph nodes and the pancreas. It is increasingly being used as a tool to reach deeply located targets without subjecting the patient to invasive surgery. Similar findings in terms of efficacy and efficiency have been found, with equally low rates of toxicity. Again, as with SRS of brain tumours, the margin for error is small with potential serious consequences due to the high radiation dose delivered. Thus, restrained enthusiasm is advised.

Conclusion

The field of radiosurgery is challenging to describe in one article. Enabled by technological advancement, the biological tool of extreme ablative doses of radiation can now be exploited in cancer and tumour care of various sites and different conditions, providing equivalent rates of cure and control without the need for major surgery. Depending on the oncological strategy chosen, SRS can be employed as main or adjunct treatment of choice to control gross disease. With the advent of frameless SRS, patients can now have their tumour destroyed in just a matter of two trouble-free, non-invasive, outpatient visits. MG

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