

Talking about Radiosurgery

Luis Moreno Sanchez

External Advisory Chief of Radiosurgery at Cancer Center Santiago Metropolitan Hospital (HOMS), Radiation Oncology Coordinator at Radioncology Center - National Cancer Institute Rosa Sanchez de Tavares (INCART), External Advisory at Abreu Clinic - CDD Radiotherapy, Dominican Republic

***Corresponding Author:** Luis Moreno Sanchez, External Advisory Chief of Radiosurgery at Cancer Center Santiago Metropolitan Hospital (HOMS), Radiation Oncology Coordinator at Radioncology Center - National Cancer Institute Rosa Sanchez de Tavares (INCART), External Advisory at Abreu Clinic - CDD Radiotherapy, Dominican Republic.

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Dear patient, intracranial stereotactic radiosurgery or SRS for its English acronym (stereotactic radiosurgery) is a treatment technique that allows to concentrate high doses of radiation in a small and precise area of the brain, respecting as much as possible nearby organs, all achieved through stereotaxy, which means three-dimensional representation of an object in space, in this case within the brain.

It was created by Swedish neurosurgeon, Dr. Lars Leksell of the Karolinska Institute in Stockholm, Sweden, together the biophysicist Professor Börje Larsson.

Although the term includes the word “surgery”, radiosurgery is a treatment, not a surgical procedure, so the patient is not operated. It is minimally invasive, painless, does not need recovery income or intensive care unit, does not need general anesthesia, it is 100% outpatient and the patient can return to their daily activities almost immediately.

Importantly, the correct term is: radiosurgery, and can be performed with different equipment such as Gamma Knife, Cyber Knife and Linear Accelerator, therefore, say Cyber Knife, LINAC or Gamma Knife refers only to a machine type - not the procedure itself (Figure 3).

Every patient must be evaluated by a multidisciplinary medical team. “Depending on the location, size of the lesion, nearby organs and tumor type, the radiosurgery team will decide the dosage and number of sessions required”

Radiosurgery can be performed in a single session using a special frame (Figure 1), or in multiple sessions using a bite block mask (Figure 2), also called “frameless”, in any cases not reduces its effectiveness, allowing at all times protect organs or nearby structures at risk.

In the original description of SRS (1951) [1], Dr. Lars Leksell did not specifically state that the procedure needed to be performed in a single session. Once again in 1983, Leksell described as “a technique for the non-invasive destruction of intracranial tissues or lesions, in which the open stereotactic method provides the basis....” without specifying that it must be done in one session [2].



Figure 1: Bite Block Radiosurgery.



Figure 2: Stereotactic Frame Radiosurgery.

According to statistics from the Central Brain Tumor Registry of the United States (CBTRUS) published in 2015 [3], for the period 2008-2012 a total of 356.858 cases, 67.2% (239.835) were represented by benign brain tumors and this percentage 35.9% and 15.5% were meningiomas and pituitary tumors respectively.

The word benign is of Latin origin “benignus” and consists of the words “bene” meaning “good” and “genus” indicating “born”, i.e., well conceived or created. But in medicine, the term indicates a benign disease, tumor, or growth that is not serious, that is, it is not cancerous. Therefore, it is characterized by not spread to other parts of the body or destroy nearby tissue, but, and generally



Figure 3: Radiosurgery Equipments.

there is always one, considering the above, you should know that despite the absence of spread, the tumor may grow and cause serious problems to your health.

We know that the procedure is usually expensive and in some countries coverage of it, is only approved for malignant lesions, without considering that some benign tumors can cause side effects that significantly compromise the quality of life of the patient and sometimes life itself.

A classic example represent pituitary tumors or adenomas (Figure 4), which despite being benign, could cause endocrine disorders, i.e., hormonal, depended on their secretory character and whether they are functioning or not; additionally according to their size are often classified as microadenomas if they are less than 1 cm and macroadenomas when they exceed this measure. Non functioning macroadenomas are the most common, accounting for 25-30% of all pituitary tumors. Additionally depending on the tumor compression exerted on the optic chiasm, the patient gradually cease to see, which may or may not be reversible, thereby affecting the quality of life of patients, and we are still talking about a benign tumor. The diagnostic approach includes complete eye examination and hormonal evaluation.

Initial treatment of these tumors or “gold standard” is surgery, there is no doubt, and preferably transsphenoidal whenever feasible; the neurosurgeon will remove as much tumor as surgically possible, so observe the presence of residual tumor in imaging studies after surgery is not indicative of a failed process, we must remember the maxim in medicine: First Do No Harm, which translated means that have left residual tumor is probably due to the need to prevent damage or surgical complications of a wider resection performed.

Importantly, regardless of their functional condition or not, irradiation is used to treat and prevent recurrences and tumor persistence after surgery.

Returning to the central theme, related to the term benign it is worth mentioning that despite this condition, these tumors tend to grow and because of its location can compromise the visual pathways, causing progressive decreased vision through one or both eyes, and compressing the optic chiasm.

Other symptoms, although they are benign tumors, can occur in cases of meningiomas, vestibular schwannomas, etc, because that could arise for example in the skull base with a significant impact on quality of life, and despite surgical advances, microsurgery, etc, the total removal of the lesion is surgically often impossible, is at this point where adjuvants procedures after radical treatments, must be considered.

Is radiosurgery an option in benign tumors?

The answer is yes, and with very good results, either in their mode of a single session or multisession (fractions 2-5) [4], all depend on the size of the lesion, organs at risk, tumor characteristics, previous irradiation, etc.

While we treat patients and not just disease and that each case should be considered individually, we know that a patient can be surgically intervened many times as deemed necessary, but even more when it is considered possible and beneficial; there are tumors that despite being classified as benign, have a fast or aggressive growth, similar to that observed in malignant tumors, in other cases its difficult approach because of its location represents a challenge for the neurosurgeon, who is seeking his patient leave surgery in better condition than he entered.

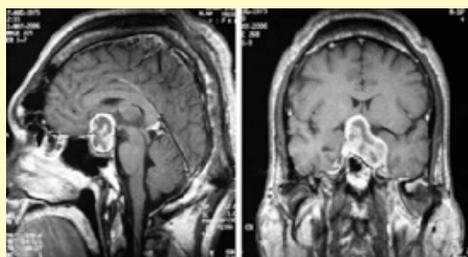


Figure 4: Pituitary Macroadenoma.

The diseases most commonly treated with radiosurgery in addition to those already mentioned are: brain metastases, arteriovenous malformations, trigeminal neuralgia, schwannomas, oligodendrogliomas, etc.

Who should participate in the procedure?

Despite being a multidisciplinary procedure, in some centers involved only neurosurgeons or radiation oncologists, when the team should be composed of the aforementioned specialists [5], in addition to medical physicists, dosimetrists, neuroradiologists, radiotherapy technicians, nurses, etc.

Like the rest of the procedures or treatments, this is multidisciplinary and we should not take the protagonists or individuals.

Actually there are “conservatives” who prefer the original term of radiosurgery offered by neurosurgeon Lars Leksell, more than 60 years ago, while other subscribe to the concept of a procedure that has evolved with the advances of the technology¹, and knowledge of radiobiology.

“On 03/20/2006, AANS, CNS and ASTRO refined the definition of stereotactic radiosurgery in a discipline that utilizes externally generated ionizing radiation in certain cases to inactivate or eradicate defined targets in the head and spine without the need to make

and incision. The target is defined by high resolution stereotactic imaging. To assure quality of patient care the procedure involves a multidisciplinary team consisting of a neurosurgeon, radiation oncologist and medical physicist. Typically is performed in a single session, using a rigid attached stereotactic guiding device, other immobilization technology and/or a stereotactic image-guidance system, but can be performed in a limited number of sessions, up to a maximum of five" [1].

Radiosurgery should not be done without the full presence of the multidisciplinary team. In some countries some radiosurgery units considered less necessary the presence of the radiation oncologist and the selection of the dose to be administered can be found in tables, programs and textbooks, however, this does not preclude the presence of the radiation oncologist, likewise the presence of the neurosurgeon is essential, and cannot be supplemented by the fact that the radiation oncologist know placing a stereotactic frame. Currently both the neurosurgeon and radiation oncologist should know delineate and define treatment targets, despite the presence of a neuroradiologist would be ideal. All participants should know how to perform all or part the work of other members, which does not rule out the presence of anyone.



Figure 5: IAEA Human Health Reports N^o 1.

The medical physicist performs or supervises the measurements and calculations necessary to determine absorbed dose or dose distributions in patients. These can be manual or computerized calculations and/or direct measurement of radiation. Medical Physics provides the radiation oncologist the assessment and proposals for optimization of treatment planning [6] (Figure 5).

And what about the doses?

It is important to consider the dose administered, knowing that 1 session of 20 Gy represents a certain biologically effective dose (BED) [7,11], for example, using an $\alpha\beta_3$, generally assigned to healthy tissues, that session of 20 Gy represent the equivalent of 153.3 Gy, however, if $\alpha\beta$ used is 10, usually assigned to malignant tumors, the BED would drop to 60 Gy, all depend on the $\alpha\beta$ used according on the type of tumor, organs at risk, etc. For example: 1 session of 20 Gy considering only the physical dose could be considered as 5 sessions of 4 Gy, however, the expected result will not be the same, because to achieve an equivalent of 20 Gy BED these 5 sessions should be 8.2 Gy with $\alpha\beta_3$ or 7 Gy with $\alpha\beta_{10}$.

Something similar happens to the organs at risk (OAR) [8], the dose limiting for the visual pathways in 1 single session is 8 Gy [9], but again depending on the distance between the tumor and OAR could perfectly perform the procedure on 3-5 sessions, rising dose tolerance to 15.3 Gy and 23 Gy respectively [8], aware that we are faced extrapolation of linear quadratic model [9].

It is also important to know that the 5 "R" of radiobiology [4,8] not behave in the same way during radiotherapy and radiosurgery. Re-oxygenation: Tumors treated in one single session or extremely high dose fraction \rightarrow intratumoral hypoxic microenvironment \rightarrow vascular damage by cell death. Repair: Tumors treated with SRS or SBRT may have significant repair sublethal damage due to prolonged exposure during radiation, with 10% loss of biological effect with sessions of 30 minutes or more. Redistribution: High doses of radiation $>$ 15-20 Gy in one session causes arrest of cells in the cell cycle phase where they were, going interphase death. Repopulation: Radiosurgery and

SBRT short time (< 2 weeks) repopulation of tumor cells will not be substantial and Radiosensitivity/Radioresistance: Some diseases such as metastatic from primary melanoma (Figure 6) or renal, are less sensitive to radiation fractionation therefore could benefit from high single doses.



Figure 6: Right Hallux Melanoma.

Finally, whenever we head towards hypofractionation, more personalized treatments will be based not only on histology and immunohistochemistry, but also in immunotherapy or biological therapy, molecular biology, radiobiology, etc. But even with all the progress we should make treatment decisions by multidisciplinary teams, and stop the selfishness and unnecessary competition.

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