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VALIDATION OF A NEW METHOD FOR DOSE DETERMINATION IN RADIOSURGERY: "THE SOSA MODEL"

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Abstract: Objectives: to compare and validate the doses determined according to the novel method for calculating doses in radiosurgery called the Sosa Model (MS) with the dose protocols of national and international institutions. **Material and Method:** retrospective study on 403 tumor lesions of different histology found in 172 patients treated by radiosurgery at the Gamma Knife Dominican Center (CGKD), using MRI images of 1.5 and 3.0 Tesla with protocol for neuronavigation. In MS, the Sosa Score (SS) is obtained by adding 3 scores to a constant of 10Gy: Volume Score (VS), Radioresistance Score (RS), Eloquence Score (ES) of the lesion, complying with the formula that supports it. : SS= VS+RS+ES+10. Using the Wilcoxon Signed-Rank Test, it was compared with the conventional doses used in the CGKD, which are similar to those used internationally. **Results:** most lesions received between 12 and 24 Gy, calculated by both methods. Of the meningiomas treated in the CGKD, 65% received a dose of 12 to 14 Gy. Most of the doses suggested by the MS were between 15 and 18 Gy. On average, metastases treated in CGKD received between 16 and 24 Gy (220 of 247, 89%). The doses recommended by the MS were very close, ranging between 15 and 21 Gy (232 of 247, 93.9%). In Non-Functional Pituitary Adenomas, the MS (17-18 Gy) yields doses above those of the CGKD (12-16 Gy) since it does not include adaptations to protect the visual pathway. In Functional Pituitary Adenomas, MS falls below the particularly high doses (25 to 35 Gy) internationally recommended. The Acoustic Neuromas all received between 12 and 13 Gy in the CGKD and most of the doses recommended by the MS were between 14 and 15 Gy. **Conclusions:** Comparing the doses used by CGKD and those recommended by MS, there is a close proximity when it comes to Acoustic Neuromas and Metastases, but an important

difference when it comes to Adenomas and Meningiomas. When applying the Wilcoxon Signed Rank Test to the 403 lesions studied, the mean difference between the two dose calculation systems was 0.23 Gy (95% CI: -0.127-0.60).
Keywords: Radiosurgery, Gamma Knife, Dose Calculation, Sosa Model, Brain Tumors.

INTRODUCTION

In contemporary radiosurgery, the most relevant variants are the Gamma Knife (GK) and Linear Accelerator-Based Radiosurgery (RBAL). Both constitute an essential tool in the management of many intracranial tumors that, for different reasons, are difficult to manage by applying traditional neurosurgery. For more than 50 years, to determine the doses to be applied during the procedures, radiosurgery has used a methodology that does not systematically take into account the volume, histology and intracranial location of the tumors. Probably due to therapeutic inertia, radiosurgical practice has adhered to the uncritical repetition of the doses determined heuristically by first generation radiosurgeons. This has led to a paradoxical situation in which radiosurgery teams have experienced tremendous advances in complexity while the clinical bases for determining doses to administer to intracranial tumors have stagnated. If the immobility that currently prevails in this area continues, it is foreseeable that the toxic effects of radiosurgical procedures may increase and the benefits of this discipline may be limited in a future that must aim at reducing toxicities and increasing the radiosurgical efficiency. This worldwide need for radiosurgery has been highlighted by the recent publication of THE SOSA MODEL, a book in which the Dominican radio-oncologist Fabio Valenzuela Sosa critiques the currently prevailing dose determination model and proposes solution to its limitations [2].

MATERIAL AND METHOD

This is a retrospective, institutional study, using the Gamma Plan X Workstation image processing platform from Elekta (Sweden), coupled to the Gamma Knife Model C of the Centro Gamma Knife Dominicano (CGKD) located at CEDIMAT, Plaza de la Salud, in the Santo Domingo city, Dominican Republic. 403 tumor lesions of different histological nature found in 172 patients consecutively treated by Stereotactic Radiosurgery using Gamma Knife (GK) were collected. Magnetic Resonance Images (MRI) of 1.5 and 3.0 Tesla loaded to the platform were used, selecting the contrast-enhanced T1 sequence as essential to delimit and volume the lesion. In the cases of patients with renal insufficiency in which it was not possible to use DTPA Gadolinium as a contrast medium, the limits of the lesion were clearly determined by the dynamic comparison between the different MRI sequences: T1 without contrast, FLAIR, T2 and TOF. To locate the lesion and determine its diameters and volume, the voxel volumetric method was applied, drawing each image slice millimeter by millimeter on the screen. This is considered as the real volume (VR). The nature of the lesion was determined based on biopsy, surgery, or based on indisputable neuroimaging data. The general objective was to compare and validate the doses calculated according to the Sosa Model (Sosa Score) with the dose protocols of other national and international institutions. The Sosa Score (SS) was determined strictly following what was proposed in the Sosa Model (MS): adding 3 parameters or score: ***Eloquence Score (ES)*** : 1 (high), 2 (moderate), 3 (low), 4 (very low) (see Image 1). ***Radioresistance Score (RS)*** : 1 (low), 2 (moderate), 3 (high), 4 (very high). **Volume Score (VS)** : 1 (>10.51 cc), 2 (7.01-10.51 cc), 3 (3.51-7.00 cc), 4 (0.01-3.50 cc). (*See Tables No. 1, 2 and 3)*. 10 points are added to the total sum, with a minimum final score of 13 and a maximum of 22 points that are converted directly to Gy. Measures of central tendency provided by the SPSS software, version 15.0, Chicago, Illinois, USA, were used. The SS for each lesion was compared using the Wilcoxon Signed-Rank Test with the conventional doses used in the CGKD, which are similar to those in centers of excellence around the world.

VOLUME (VS)		FREQUENCY	%
1	> 10.51cc	59	14.6
2	7.01cc - 10.51cc	3. 4	8.4
3	3.51 - 7.00cc	51	12.7
4	0.01 - 3.50cc	259	64.3
	Total	403	100.0

Table No. 1. Distribution of the 403 lesions studied according to their VS (Volume Score)

HISTOLOGY	FRE-QUENCY	PERCENTA-GE
MENINGIOMA	**83**	**20.6**
MYELOMA	1	.2
MEDULOBLASTOMA	1	.2
LOW GRADE GLIOMA	1	.2
PITUITARY ADENOMA	**37**	**9.2**
NEURINOMA	**21**	**5.2**
METASTASIS	**247**	**61.3**
MALIGNANT GLIOMA	4	1.0
CRANIOPHARYNGIOMA	4	1.0
GERMINOME	1	.2
CHORDOMA	1	.2
GLOMUS JUGULARIS TUMOR	2	.5
TOTAL	403	100.0

Table No. 2. Histology of the 403 lesions studied (the 5 most frequent in red).

ELOQUENCE (EN)		FREQUENCY	PERCENTAGE
1	HIGH	182	45.2
2	MODERATE	188	46.7
3	LOW	2	.5
4	VERY LOW	31	7.7
	TOTAL	403	100.0

Table Number 3. Eloquence Score (ES) of the 403 lesions studied.

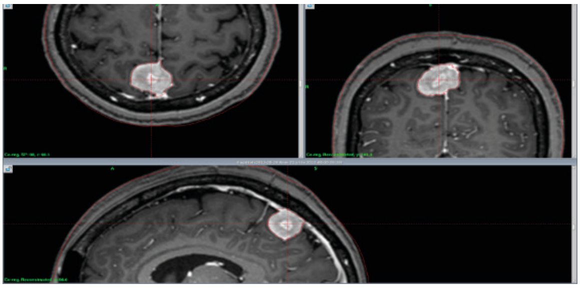


Image 1: Example of ES1. Meningioma of the posterior third of the falx cerebrum and of the right paracentral lobule, a highly functional area (ES1) since it controls motor skills and sensitivity of the contralateral lower limb.

RESULTS

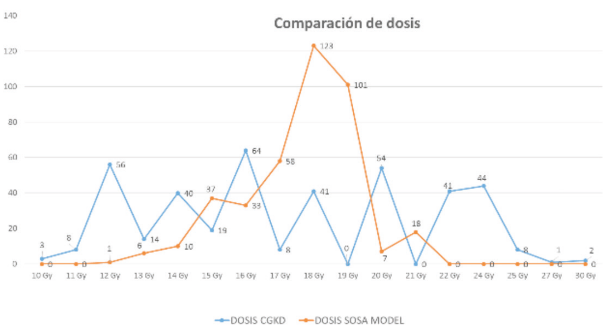
Most of the lesions received between 12 and 24 Gy (dose calculated by the CGKD. Table *no. 5* : 381 of 403 (94.5%)). This confirms the estimation in which the Sosa Model was structured: a minimum dose of 13Gy and maximum of 22. Counting with 3 parts of the Scale with a unit value of 4 that are added (VS+RS+ES), they give a minimum of 3 and a maximum of 12Gy.When adding a constant of 10 they make a minimum of 13Gy and a maximum of 22Gy as a result of the application of the Equation SS= VS+RS+ES+10 (*Table no. 4*).

Dose		Frequency	Percentage
valid	12Gy	1	.2
	13Gy	5	1.2
	14Gy	10	2.5
	15Gy	37	9.2
	16Gy	33	8.2
	17 Gy	58	14.4
	18Gy	123	30.5
	19 Gy	101	25.1
	20Gy	7	1.7
	21 Gy	18	4.5
	Total	393	97.5
lost		10	2.5
Total		403	100.0

table no. 4. Dose applying Sosa Model in 403 lesions.

Dose		Frequency	Percentage
	10Gy	3	.7
	11 Gy	7	1.7
	11 Gy	1	.2
	12Gy	56	13.9
	13Gy	14	3.5
	14Gy	40	9.9
	16Gy	19	4.7
	16Gy	64	15.9
	17 Gy	8	2.0
	18Gy	41	10.2
	20Gy	54	13.4
	22Gy	41	10.2
	24Gy	44	10.9
	25Gy	8	2.0
	27 Gy	1	.2
	30gy	2	.5
	Total	403	100.0

table no. 5. Conventional dose of the Dominican Gamma Knife Center (CGKD) in 403 lesions.



graph no. 1: comparison of CGKD Dose and Sosa Model on 403 lesions.

Of the Meningiomas treated in the CGKD (conventional dose), 65% received a dose of 12 to 14 Gy (54/83). Most of the doses suggested by the MS ranged between 15 and 18 Gy (62/83, for 74.6%). MS does not correct the dose for base lesions, especially perisellar lesions, where no more than 10Gy must reach the optic pathways, and ideally around 8.5Gy. The meningiomas of the base of the skull predominated with respect to those of the convexity. There were 52 in this series of 83 (62.6%). Only 31 were in the convexity, in these higher doses can be used, such as those proposed by the MS. This reality is at the base of the difference between the doses proposed by both methods. It is interesting to note that the calculated SS, even though the lesion is around the visual pathway, can serve as a basis for knowing the ideal total dose when trying to treat with Fractionated Radiosurgery.

Most of the Pituitary Adenomas treated in the CGKD with conventional doses received between 12 and 16 Gy. Another peak was at 25 Gy when it came to Functional Adenomas. Most of the doses recommended by MS were between 17 and 18 Gy, which reveals the lack of adjustment for the tolerance of the visual pathway and the fact that Functional Adenomas are not considered in the SS calculation. These adenomas usually receive doses ranging from 25 to 30 Gy. In some cases of very aggressive Pituitary Adenomas such as the ACTH-secreting ones that cause Cushing's Syndrome, even 35 Gy is recommended. It is worth noting the interesting opportunity offered by MS by yielding absolute doses, not adapted to the presence of the visual pathway, which is important when it is desired to know the ideal total dose of a perisellar lesion when planning fractionated radiosurgery.

The average of metastases treated in CGKD received between 16 and 24 Gy (220 of 247, 89%). The doses recommended by MS ranged from 15 to 21 Gy (232 of 247, 93.9%). This reveals that in most cases no dose adjustment was required to respect some ultra-sensitive structure such as the visual or auditory pathway.

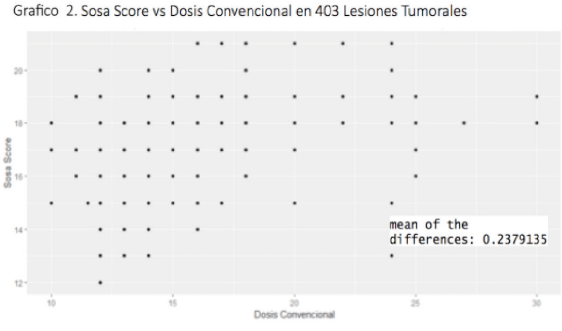
Acoustic Neuromas treated in CGKD received 12 Gy, which is the most frequently used dose in recent years in most stereotactic radiosurgery centers. The doses recommended by MS were around 15Gy. This means that the size of the lesions was not very large, corresponding to a SV of 3 and 4, as verified by the fact that the average volume of the treated neurinomas was 5.10cc.

DISCUSSION

The doses used by the CGKD are based on the conventions accepted by the world radiosurgical community [7,31,32,33.] Therefore, there is much similarity between the doses proposed by this institution and those published in the international literature. When comparing these doses with those resulting from the application of the MS, it was found that in general terms, the doses applied in the 403 lesions studied in the CGKD were between 12 and 24 Gy (94.5%). This confirms the correctness of the general principle of MS that intracranial radiosurgery doses must range between 13 and 22 Gy [2.]

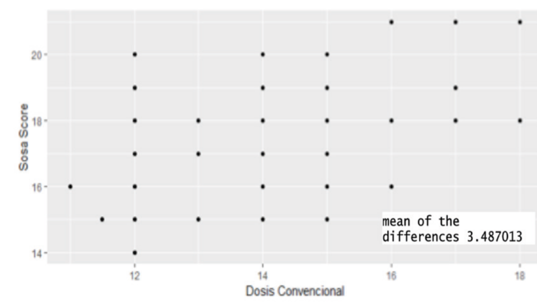
When comparing the doses used by CGKD and recommended by MS, a great similarity is noted when it comes to Metastases and Acoustic Neuromas, but an important difference when it comes to Adenomas and Meningiomas. This yields a *Wilcoxon with a difference of 0.23Gy between the two compared dose calculation systems (95% CI: -0.127-0.60).* (See Graph no. 2).

Grafico 2. Sosa Score vs Dosis Convencional en 403 Lesiones Tumorales



If we analyze Meningiomas, most of the doses used by the CGKD were between 12 and 14Gy (54 of 83 lesions), while those recommended by MS were between 16 and 18 (51 of 83 lesions). This was due to the fact that in this series there was a predominance of skull base meningiomas (51/83 = 61.4%) with respect to those of the convexity (31/83 = 38.5%). In the former, dose adjustments must be made to avoid affecting the visual pathway because, as established by Hiniker and Modlin 37, the optic nerve can receive up to 8Gy and the optic chiasm up to 12. Regarding the auditory pathway : Lo, Ayre et al.. recommend cochlear doses of less than 5 Gy 38. This is not contemplated by the MS as it is precisely expressed in its foundations 2. For this reason, the doses of CGKD (the dose was reduced so as not to affect the visual or auditory pathway) were lower than those of MS (absolute doses were left, without refinement, as established by the new method) 2. This yielded a Wilcoxon with an average difference of 3.48 Gy between the two dose protocols compared (see graph 3). Convexity meningiomas do not require this dose adjustment to protect extremely radiosensitive structures and in them conventional doses would be close to those provided by MS, as occurred with the metastases studied, most of which were far from visual and auditory pathways.

Gráfico 3. Sosa Score vs Dosis Convencional en Meningiomas



In the case of Pituitary Adenomas, the CGKD doses were distributed in two predominant areas: between 14-16 Gy (14 patients, Non-Functional Adenomas) and between 24-30 Gy for 12 patients with functional adenomas. Gupta and Kano specify that this type of lesions must have a dose greater than 25 Gy [36.] While the doses emanating from the application of the MS were between 15 and 19 Gy for the 37 patients, without discriminating between functional adenomas or not and without adapting the

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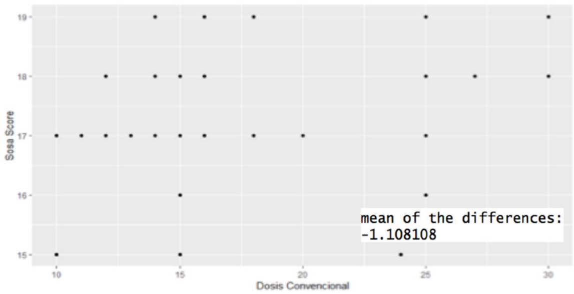
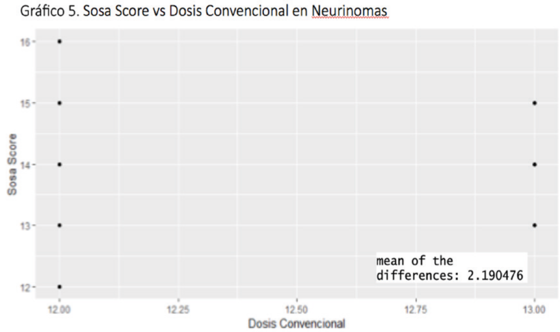
dose to the tolerance of the optical pathways. This gave a *Wilcoxon of -1.10Gy (see graph 4).*

Gráfico 4. Sosa Score vs Dosis Convencional en Adenomas Hipofisarios



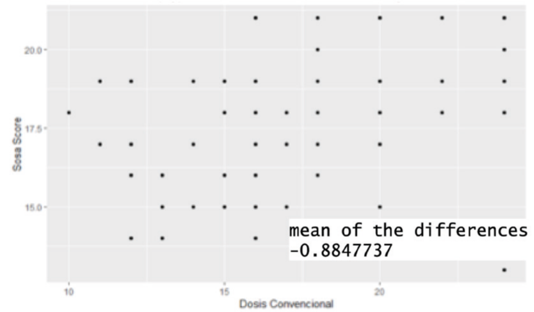
The Acoustic Neuromas all received between 12 to 13 Gy in the CGKD. The MS recommended between 12 and 16 Gy, with most cases calculated with 15 Gy, since the volume of the lesions was moderate (average 5.10 cc), which corresponds to a high SV of 4 or 3 in most cases. cases, which produces an SS of 15 and 14 Gy respectively, which was what was calculated for 16 of the 21 lesions analyzed. This produces a Wilcoxon result of 2.19 Gy [2,7,8,12,15,19,27,28.] (See graph 5).

Gráfico 5. Sosa Score vs Dosis Convencional en Neurinomas



Brain metastases were mostly treated in CGKD in the 16-24 Gy range (220 of 247 lesions, 89%). The doses recommended by MS were between 15 to 21 Gy (232 of 237 lesions, 93.9%). A great proximity is noted between the doses emanating from the two dose protocols despite the fact that this is not significant: Wilcoxon -0.88 (graph no. 6). Most of these lesions were not at the base of the skull, nor were they close to the visual or auditory pathways. This shows that when it comes to absolute doses, that is, not refined or adjusted to respect some extremely delicate surrounding structure, the irradiated doses of MS are very close to the conventional ones [2,10,11,12,16,20,23,25,26,29,32,33].

Grafico 6. Sosa Score vs Dosis Convencional en Metástasis



Luther and Kondziolka [26] demonstrated that the majority of patients with Brain Metastases located near or just over the motor stria maintain neurological function without deficits after radiosurgery and that those with some focality improve or remain stable. These authors analyzed 47 patients without motor deficits, of whom 10 (22%) presented mild motor weakness (3/5 or 4/5) after GK, these deficits being temporary. Of the patients who had a motor deficit prior to radiosurgery (44 cases), 18% worsened and the remainder improved or remained stable.

efficacy of GK radiosurgery in lesions treated with conventional doses in CGKD is clearly evidenced. With a reduction in the volume of meningiomas from a significant 18.05% to an impressive 66.03% in the case of metastases, 57.17% in Pituitary Adenomas and 25.29% in Acoustic Neuromas.

		REAL PRE-GK VOLUME (cc)	POST-GK REAL VOLUME (DC)
	VALID	403	253
	LOST	0	150
HALF		4.737568	3.32527
MEDIAN		1.380000	.52000
FASHION		.0100	.000

Table No. 5. Volume pre and post-Gamma knife, 403 lesions.

All this achieved with a minimum percentage of Adverse Radiation Reaction (Adverse Radiation Effect=ARE) of 1.5%. It must be noted that the international literature shows an ARE figure between 8 and 9% [30,31,32,33,34].

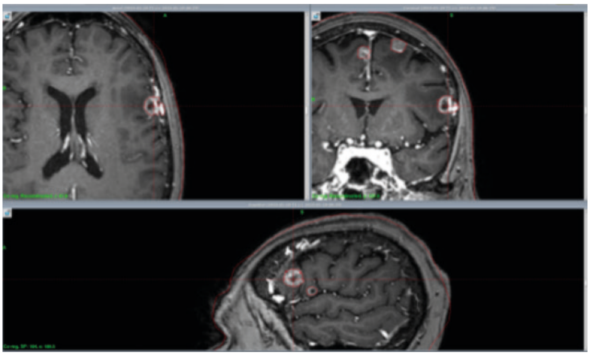


Image 2. Highly Functional Areas (ES1): 2 metastases in Broca's Area. Treated with high doses in the CGKD and minimal toxicity.

The volumetric measurements that attest to the post-radiosurgery evolution of these lesions were guaranteed by a well-regulated follow-up protocol that ensured regular and constant short- and medium-term surveillance in most lesions [2,23,24,25,26].

CONCLUSION

When comparing the doses used by CGKD and recommended by the MS, a great similarity is noted when it comes to Metastases and Acoustic Neuromas, but an important difference when it comes to Pituitary Adenomas (it does not discriminate between functional or non-functional, nor does it refine according to tolerance of the visual pathway in MS) and Meningiomas (the calculation of tolerance of the visual pathway, cochlea and skin is not contemplated in MS). With these well-defined realities, the fact that MS yields absolute doses is established, which must be refined according to possible neurotoxicity of surrounding areas.

The determination of dose applying the MS obliges the user to develop an integrating dynamic of the basic concepts of radiosurgery: Volume, Radioresistance and Cerebral Eloquence. This way, the therapist is compelled, rather than consulting a dose manual, to contextualize his calculation on the circumstances of a particular patient, with a pathology of a well-determined nature, an exact known volume, located in a finely located brain region. This customization and systematization in the search for the optimal dose is a great contribution of the MS application.

The doses provided by the MS are absolute, they do not go between one range and another as is customary in the dose manuals that are published internationally. They are conceived to be individual and specific for each lesion studied. They were designed to be tuned according to visual, cochlear or skin protection criteria. In the case of perisellar lesions, close to the optic pathway, if it is decided to perform Fractionated Radiosurgery to avoid Optic Neurotoxicity, the absolute doses of MS can serve as a basis for calculating the total dose and determining the number of fractions and doses of each fraction.

From this analysis it can be deduced that the doses emanating from the MS are reasonably close to those conventionally used by the international radiosurgical community, and that they must always be polished and adapted according to the tolerance of the neighboring special functional structures (visual pathway, cochlea, etc.).

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