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Our experience in treating meningiomas with radiosurgery

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Abstract
Introduction: Radiosurgery is ionizing radiation treatment. Concentration of a large amount of radiation in an area of the brain results in ablation of the lesion. The technique was designed and perfected by Dr. Lars Lexell, Swedish neurosurgeon, in 1951. Meningiomas are usually benign and slow-growing tumors, derived from the leptomeninges. First line treatment for meningiomas is surgery. They occasionally are difficult to treat surgically because of their location, the associated vascular and nerve structures and patient comorbidities. Stereotactic Radiosurgery (SRS) is an option to manage these cases.
Objective: This studi is retrospective, from Novembner 2013 to January 2018 (4 years), SRS for meningioma in X-Knife Unit, Neurosurgery Service prof. Kurti UC, Mother Theresa,, Tirana. During this period we evaluated the long term effect of SRS on tumor control.
Material and Methods: We analyzed data from 17 Meningiomas in 14 patinets (4 meningiomatosis) to these variables: age, presenting symptoms, intracranial location of meningiomas, surgery prior to SRS, extension of tumor resection, the radiation dose, tumor volume coverage, pre-SRS tumor volume, tumor volume on latest follow up MR biopsy results, Assessment of tumor control was based on VOLUMETRIC criteria and RECIST criteria.
Results: 14 patients in a total (17 meningiomas, 4 of them was meningiomatosis), (Male 4 (23%), Female 13 (77%), Age 45-75 years (average 59.5 Median 62.0). Follow up from (23 months), (Range 59.9-99 99.5), intracranial localization of meningiomas: Medial sphenoid crystal – 8, Convection – 7, Falx/Parasagittal – 2. Residual 4 - (24%), Recurence 5 - (29%), New 8 – (47%), WHO I – 8 (47%), WHO II – 4 (23%), WHO III – 1 (7%). With out biopsy – 4. Prescripted dose – 14-16 Gy, tumor coverage – 59 – 100%, (91.70), median 95.40, tumor volume – 0.27 – 10.36 cc (3.84), 1-isocenter – 9 cases, 2-isocenter – 8 cases. Number for arcs for isocenter – 1-5. Tumor volume, controlled - 12 (70%), reduced – 22 (48%) – 5 (PR), unchanged – 7 (SD), adult (WHO 2 and 3) – 5 (PD), side effects - 0. Follow up from 2-51 months (23 months) Mean tumor volume on follow up MRI was 0.31 cm3 and maximum Diameter over 4.83 cm. According to Volumetric criteria and RECIST criteria (adapted version), remained stable disease and excellent control - 70% total, 100% grade 1 WHO).
Conclusions: SRS is one of the safest and most effective strategies to keep meningiomas under control and management in different patients, both those with primary tumors and those with relapses or those left over from previous interventions. Doing the comparative analysis shows an improved analysis and long-term effects with SRS. The criteria used during the evaluation and standardization of these criteria make possible the effect on the duration of treatment of meningiomas with SRS.

Keywords: SRS stereotactic radiosurgery, tumor volume, volumetric criteria, tumor control meningioma, criteria

Introduction
SRS is ionizing radiation treatment. Concentration of a large amount of radiation in an area of the brain results in ablation of the lesion. The technique was designed and perfected by Dr. Lars Lexell, Swedish neurosurgeon, in 1951. Meningiomas are usually benign and slow growing tumors, derived from the leptomeninges. They are the most frequent non-glial primary tumors and the most common extra axial neoplasm of intracranial location [1]. Since these are benign lesions, surgery is the standard treatment-complete resection being curative in 90% of cases, with reduction of the neurological symptoms and mass effect [1]. Surgery remains the mainstay of treatment with excellent lo-cal control, but may be limited by the size and site of tumor. Therisk of cranial nerve palsies and other morbidities remains sig-nificant despite recent advances in microsurgical techniques [2]. Stereotactic radiosurgery (SRS) is increasingly used for both primary and adjuvant treatment of meningiomas. While this procedure has become widely applied in the treatment of skull base lesions, there have been few large studies describing its use for PFMs and even fewer with long-term follow-up [3]. Advances in radiation oncology include intensity-modulated radiotherapy (IMRT),

fractionated stereotactic radiotherapy (FSRT) and stereotactic radiosurgery (SRS) that allow for more localised and precise irradiation. Recent studies using these new techniques report apparently high local control rates and low morbidity for skull base benign tumors as pituitary adenomas, craniopharyngiomas and meningiomas [4]. Occasionally, the proximity of critical neurovascular elements and patient co-morbidities makes their surgical treatment difficult, associated with important morbidity and mortality. Since the 1970s, with the development of microsurgical techniques and advances in neuroimaging studies, the course of these lesions has improved considerably, through in many cases complete tumor removal (Simpson I) remains difficult [5].

The indications for meningioma radiosurgery are [6].

1. Symptomatic primary tumors, acting as surgical challenges, due to their proximity to critical neurovascular elements.
2. Small residual or recurrent tumors (Diameter 3cm and 2-3mm distance from critical neurovascular structures).
3. Patients having co-morbidities making surgery acontraindication.
4. Patient has chosen SRS among other treatment options.
5. Asymptomatic/ patients with minimal symptoms who have chosen SRS over observation alternative.

This study is a retrospective analysis of the results obtained in patients with intracranial meningiomas who have undergone SRS at X-KNIFE: Radiosurgery- Radiotherapy QSUT Tirana, over a period of 4 years from 2013 to 2018.

Material and Methods

In our retrospective study we analyzed data from 17 Meningiomas in 14 patinets (4 meningiomatosis) with intracranial meningiomas, criteria selected thru this inlusions are: Intracranial meningiomas treated with SRS at X-KNIFE Radiosurgery Radiotherapy QSUT Tirana, during 2013-2018 and followed by MRI after treatment at intervals of 6 months, 12 months and thereafter every year. According to the following exclusion criteria, 7 patients were ruled out of the study, 4 patients passed away during studyperiod. 2 patients lacked follow up MRI imaging, 4 patients continue with follo-up according to protocols.

All data extracted from electronic health records and medical records of the X-KNIFE Radiosurgery Radiotherapy QSUT Tirana. The information below is referring to 14 patients with 17 intracranial meningiomas including 3 patient with meningomatozis who treated with SRS. We analyzed patient's data according to these variables: Age, Gender, location on brain of meningioma, symptoms, surgery prior, type of resection, radiating dose, tumor volume coverage, tumor volume prior to SRS, biopsy results the latest follow up MRI, tumor volume on. By presenting symptoms: Headache, Generalized, Cerebellar, Eye Movement, Facial veknes. We included in our study the analysis of tumor diameter, an extrapolated value from volume of the tumor. MRI with contrast to localize the lesion Prior to radiation delivery (Linear accelerator ONCOR siemens), patients had. Stereotactic frame was positioned under local anesthesia and patient underwent a CT scan. With the software (X-Knife RADIONICS software) was used to fusion MRI and CT scan images and then to delimit the target volumes, gross tumor volume,, (GTV), clinical target volume (CTV), planning target volume (PTV)]. (HOROS software) was the technic for tumor volumes on follow up MRI through a process of manual tumor selection and calculation for the tumor volume electronically.

Results

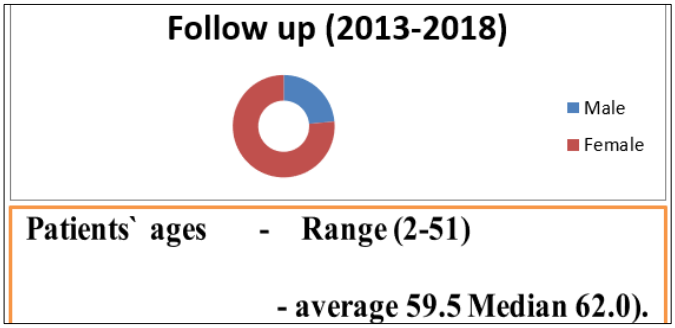


Fig 1: According to gender distribution of the patients.

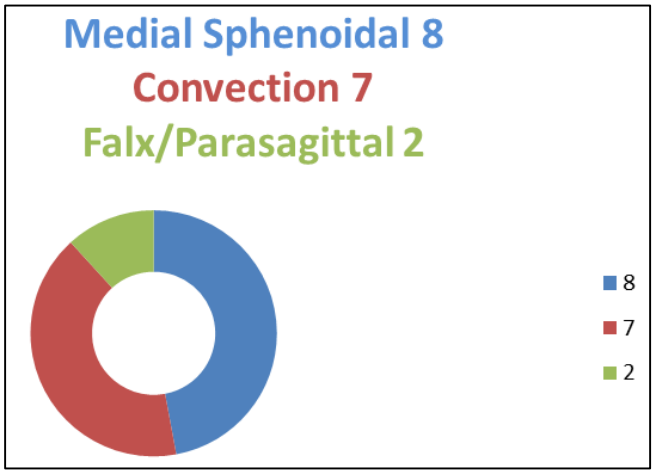
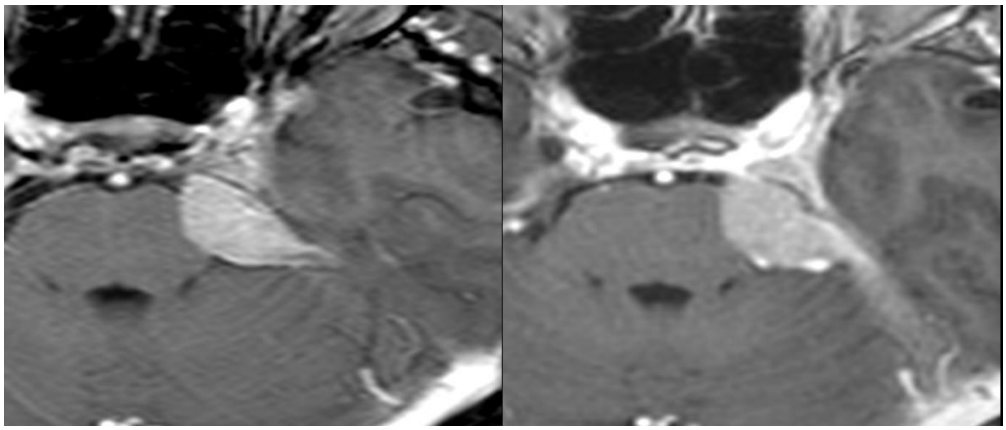


Fig 2: The distribution of meningiomas according to their intracranial location.



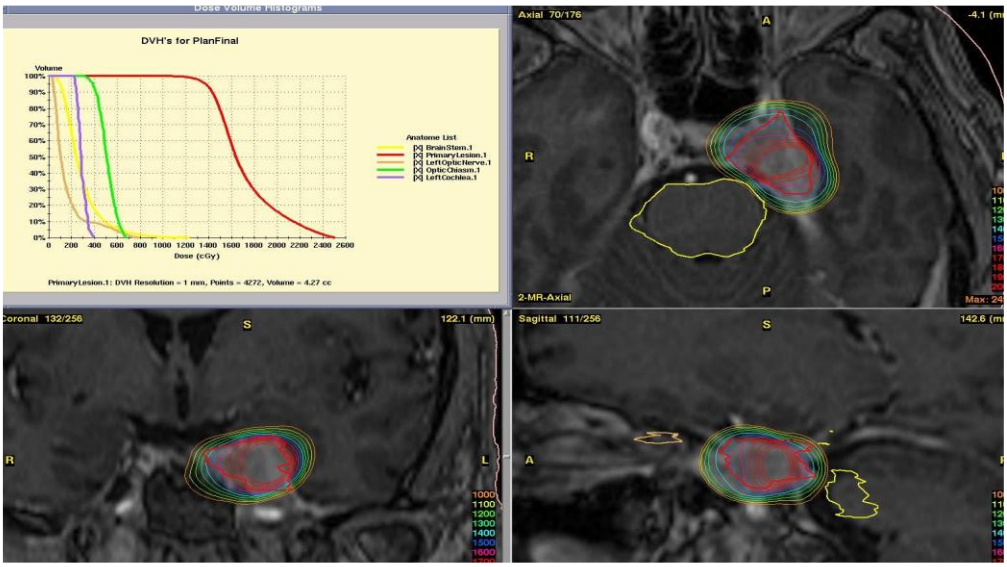


Fig 3: T1W MRI images showing: cavernous sinus meningioma; petroclival meningioma; meningioma of cerebello-pontine angle; meningiomatosis

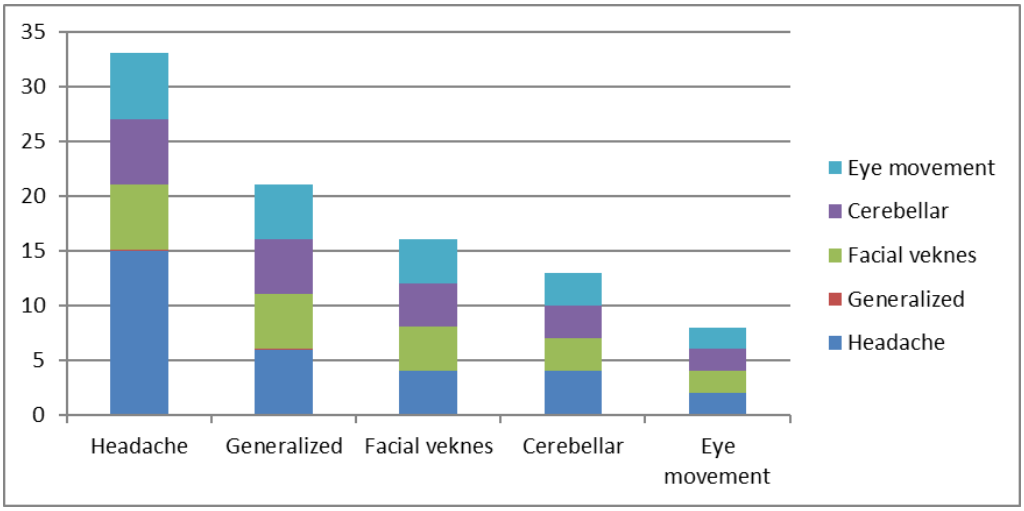


Fig 4: Patients' presenting symptoms

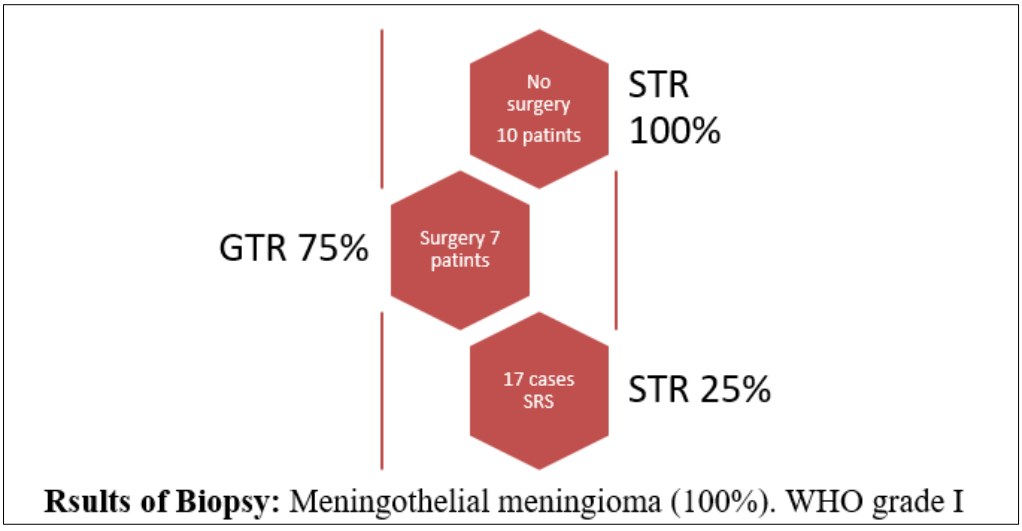


Fig 5: Representetion of patints with or without Surgery pre-SRS

Table 1: Volume of the Tumor (X-knife radioniks Software), dose of radiation and coverage of the Tumor.

Nr	Volume of Tumor (cm3) x-knife	Dose of Radiation (Gy)	Meningiomas coverage (%)
1	1.70	14-16 Gy	96.1
2	4.01	14-16 Gy	78.2
3	4.83	14-16 Gy	?
4	3.32	14-16 Gy	89.90
5	3.19	14-16 Gy	90.2
6	1.20	14-16 Gy	99.0
7	2.50	14-16 Gy	91.33
8	3.47	14-16 Gy	80.8
9	0.31	14-16 Gy	99.5
	Mean: 2.5 cm3 Range (031-4.83)	Median 14-16 Gy	Mean 84.9% (Range 59.9-99 99.5)

Table 2: Assessment of tumor control according to Volumetric criteria

Nr	SRS (cm3) (software HOROS) Tumor volume prior	MRI follow up (cm3) (software HOROS) Tumor volume	Follow up duration (in months)	Tumor volume change
1	4.83	3.00	22	-11%
2	1.72	1.88	21	-19%
3	3.32	2.55	23	-24%
4	4.00	2.83	17	-36%
5	3.20	2.79	27	-29%
6	2.50	1.95	48	-25%
7	1.50	0.90	15	-61%
8	1.23	0.93	15	-77%
9	0.31	0.04	12	-80%
	Mean: 2.2 cm3 Range: [031-4.83]	Mean: 2.50 cm3 Range: [0.27-3. 84]	Mean: 22 months Range: [12-48 months]	

Table 3: SLD-longest sume diameters

Nr	Prior SRS diameter (cm) of tumor	Follow up Tumor on (cm)	Follow up (month	Chanfges of Tumor diameter
1	1.50	1.48	28	-2.6%
2	1.67	1.57	19	-6%
3	3.12	2.80	18	-10%
4	1.78	1.73	22	-2.6%
5	1.97	1.77	26	-11%
6	4.00	3.30	48	-30%
7	2.30	2.05	12	-9%
8	1.24	1.04	15	/
9	1.57	1.50	15	/
	SLD= 2.80	SLD= 2.0		-29%
	Mean: 2.0 cm Range 1.0cm- 2.50cm	Mean: 1.60 cm Range: 0.70cm-2.50cm	Mean: 22 momths Range: 12-48 months	

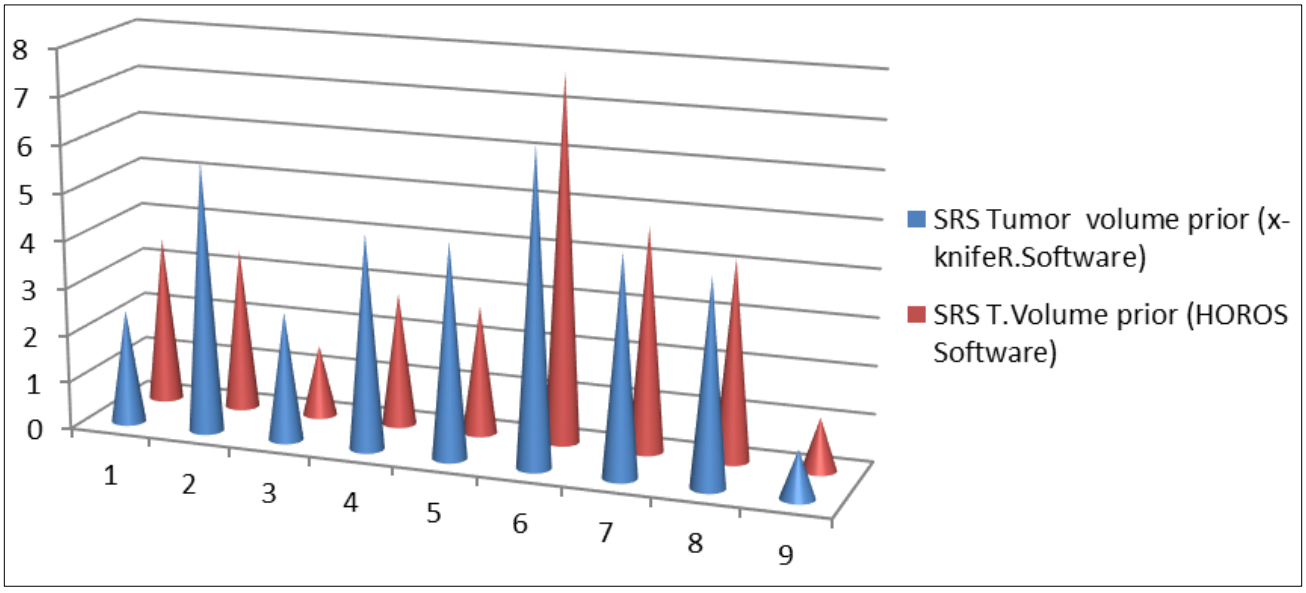


Fig 6: Show the SRS tumor and T volume prior

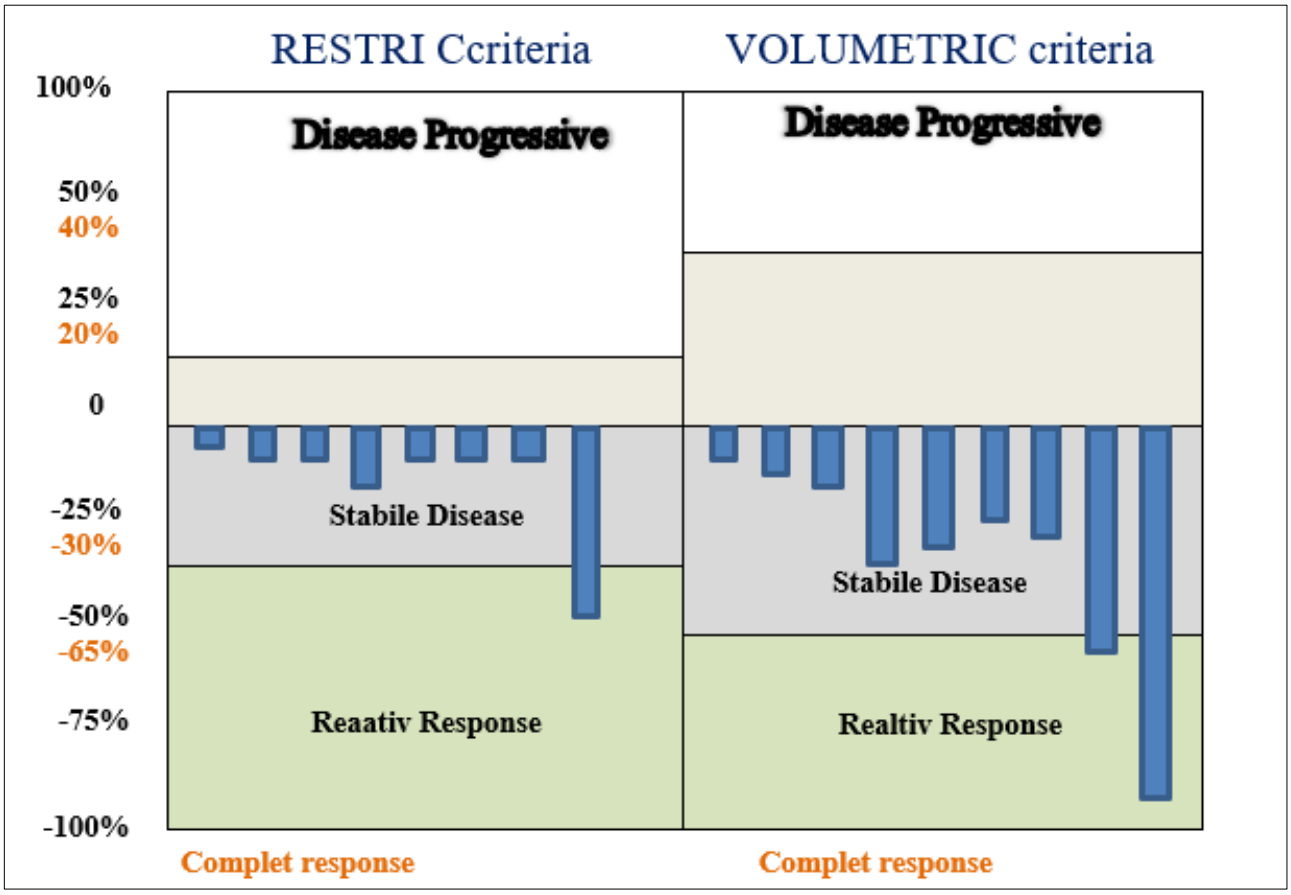


Fig 7: Tumor volume and tumor diameter changes - graphical representation of RECIST criteria

SRS tumor volume was 2.5cm3 Range (031-4.83), Prescripted dose 14-15 Gy Range (59.9-99 99.5), Coverage of the tumor was 90% Range (59.5 Median 62.0). Patints follow up from period of 12 to 24 months (Range 12-48) months the mean. MRI follov up was Mean: 2.50 cm3 Range: [0.27-3.84]. Volume criteria 2 lesions (12%), While 10 lesions (80%) remined stabile desase 1 one patient relative response or (8%).

Discussion

Evolution of tumor response in oncology is based on standard criteria. Some of these response criteria are as follows:

1. (WHO criteria) World Health Organization criteria
2. Criteria by Mc Donald
3. (RANOcriteria) Response Assessment in Neuro-Oncology.
4. Solid Tumors Criteria Response Evaluation in (RECIST) (1.0 (2000); 1.1(2009); 1. 1 update (2016))

Table 4: SPD=sum of products of diameters, SLD=sum of longest diameters, the single longest diameter of the lesion or the sum of longest diameters for multiple lesions; the product of orthogonal diameters on postcontrast image section with largest tumor area or the sum of products if multiple lesions present in our cases.

	RECIST	Mc Donald WHO	RANO	Volume criteria
CR (Complet response)	Tumor Elimination of all enhancing	Tumor Elimination of all enhancing	Tumor Elimination of all enhancing	Tumor Elimination of all enhancing
Partial response	29% SLD sume descrease	51% SPD tumor enhancing descrease	51% SPD tumor enhancing descrease	66% Volume enhancing descrease
SD (Stabile disease)	All other findings	All other findings	SPD enhancing tumor incrase in 51% descrease or 25%	All other findings
DP (Disease progress)	SLD sume 22% increase	SPD 23% tumor increase enhancing	SPD 23% tumor increase enhancing	41% volume

Analysis of criteria variabilis as below found these answers

1. RECIST criteria [1. 0 (2000); 1. 1 (2009); 1. 1 update] (the largest diameter of tumor)
2. WHO criteria (4 largest diameters of tumor perpendicular to eachother)
3. Mc Donald criteria (3 largest diameters of tumor perpendicular to each other)
4. RANO criteria (2 largest diameters of tumor perpendicular to eachother)

The RANO group has standardized criteria to assess tumor control rate following a type of treatment for most of intracranial tumors, but still not for meningiomas [7-9].

According to RECIST criteria, meningiomas fall into category non- measurable, which means its criteria are only a recommendation, not a standard to assess meningioma response to treatment [8]. Recently, the delimiting of tumor volume and volumetric comparisons has gained importance [10].

Many studies, in a time lacking of standard criteria, have made a lot of recommendations on how to assess meningioma response to treatment. Table 4 contains an overview of these recommendations [9, 10].

MRI before SRS was evaluated in our study as tumor percentage and volume change as well as recent follow-ups according to volumes and criteria presented in table (table 4), hoping that the spherical shape of the tumor is present with radius r exploring the diameter of tumor by its volume even with the use of mathematics as follows.

$$R a \sqrt[3]{3V nd D 2 R}$$

constant
Spher radius - R
Volume – V
Diameter – D

The RESTRICT and VOLUME criteria are approximately similar (figure 7)

Conclusions

Alternatives for meningioma tumors as primary as well as for secondary deposits in the brain and their management by treating tumors with a size of 2-4 cm and a safety distance of 2-4 mm from blood vessels close to the lesion performed by SRS. 14-16 Gy radiation covering the tumor almost 92% enough to keep the lesion under control. The long-term effects of SRS have been significantly improved.

Recommendations

SRS is recommended in slow-growing tumors, but the number of case in our study was relatively low and the study period to follow the volume is relatively short and continuously diagnosing with MRI we have used different literature (PubMed and HINARI as well as experience of studies conducted within our School of Neuroscience in the same period as our study suggests that the SRS is recommended in slow-growing meningiomas.

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