

# Hypofractionated Radiosurgery for Intracranial Meningioma – A Systematic Review And Meta-Analysis of Literature

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## INTRODUCTION

The location of skull base meningiomas makes surgery a high risk and less preferred intervention. Fortunately, stereotactic radiosurgery has emerged as a less invasive, more effective method of treatment. Single dose stereotactic radiosurgery (SD-SRS) for meningioma obliteration have proven to be beneficial, however, can result in high intracranial toxicity rates (Pinzi, Marchetti et al. 2023). Technological advancements have enabled multisession, or hypofractionated radiosurgery (HFS-SRS), proposing a more effective and safe treatment for skull base meningiomas, while simultaneously improving patient compliance.

## METHODS

PubMed and Embase were searched for literature on ‘hypofractionated,’ ‘radiosurgery,’ and ‘meningiomas’. Patient and meningioma characteristics, procedural details, and outcomes were extracted from eligible studies. Meta-analyses were performed on variables reported by ≥3 studies. Subgroup analyses were conducted for photon- and proton-based HF-SRS, and utilization of either CyberKnife, LINAC, or GammaKnife for HF-SRS.

## RESULTS

We included 33 studies comprising 1943 patients. For HF-SRS, digital subtraction angiography (DSA) confirmed a 22.2% partial (1-99%) obliteration rate (95%CI= 16.3-29.5, I²=83.34%) at 41.1 months (95%CI= 31.9-52.9, I²=98.7%) of follow-up, with an associated 16.9% (95%CI= 9.2-28.8, I²=87.4%) adjuvant surgery rate, 8.7% (95%CI= 6.6-11.3, I²=52.6%) recurrence/tumor progression rate, and 6% (95%CI=4-8.9, I²=13.7%) meningioma-related mortality. Retreatment of meningiomas after HF-SRS was completed by varying interventions, with an additional surgery rate of 3.4% (95% CI = 2.2-5.1, I²=27.2%) additional chemotherapy rate of 1.5% (95% CI = 0.9-2.5, I²=0%), and additional radiosurgery rate of 2.4% (95% CI = 1.4-4, I²=47.2%). Studies comparing total HF-SRS doses of the three modalities (CyberKnife, LINAC, GammaKnife) demonstrate comparable rates of DSA-confirmed obliteration (23.2% vs. 18.6% vs. 33.5%, p=0.14) despite statistically significant differences in total HF-SRS dose (25% vs. 28.8% vs. 20.5%, p=0.02). Total doses of photon-based and proton-based HF-SRS (25% vs 22.3% p = <0.01) resulted in comparable rates of recurrence/tumor progression (8.1% vs. 11.6%, p = 0.16) and meningioma-related mortality (2.0%vs. 2.2%, p=0.88).

## CONCLUSIONS

HF-SRS is promising among radiosurgical strategies for meningioma. Significant heterogeneity regarding HF-SRS dosing strategies warrants additional investigation.

	All Studies						Photon-based HF-SRS			Proton-based HF-SRS			p-value
Variables	N	N'	n	Simple estimate (100 x n/N')	Meta-analyzed estimate [95% CI]	I²	N	Meta-analyzed estimate [95% CI]	I²	N	Meta-analyzed estimate [95% CI]	I²	
Patient demographics and tumor characteristics													
Age (in years)	25	1462			57.8 [55.9-59.9]	86.2	21	58.8 [56.7-61]	85.7	4	53.7 [52.3-55.1]	0	<0.01
Total Cranial Floor	31	1828	1585	86.7	91.8 [84.3-95.9]	88.2	27	91.7 [82.9-96.2]	88.1	4	91.1 [86.5-94.3]	0	0.88
Recurrent Meningioma	25	1748	476	27.2	22.8 [16.1-31.3]	81.1	23	22.2 [14.8-32]	81.5	2	-	-	-
Total Adjuvant Surgery	25	1733	373	21.5	16.9 [9.2-28.8]	87.4	23	14.3 [7.5-25.7]	87.2	2	-	-	-
Primary HF-SRS	27	1774	931	52.5	52.1 [43.6-60.4]	86.6	24	55.8 [47.8-63.5]	82.4	3	25 [19.5-31.3]	0	<0.01
HF-SRS Dosing Schedule and Regimen													
Total Mean Dose (in Gy)	29	1706			25.1 [23.2-27.2]	100	26	25 [25-25]	100	3	22.3 [21.9-22.8]	64.5	<0.01
Total Maximal Dose (in Gy)	10	559			33.7 [29.9-38]	99	10	32.4 [32.1-32.6]	99	0	-	-	-
Total Fractions	29	1493			4.2 [3.7-4.7]	100	26	7.4 [7.4-7.4]	100	3	3 [3-3]	99.8	0.13
Total Dose Fraction (in Gy)	26	1405			6.2 [5.6-6.8]	100	24	6.8 [6.8-6.8]	100	2	-	-	-
Follow up and tumor response													
Tumor reduction or stable disease	30	1644	1506	91.6	90.3 [86.9-92.9]	60.5	27	91.2 [87.9-93.7]	56.9	3	82.3 [61.1-93.2]	77.3	0.17
Reduction in size (1-99% Obliteration)	24	1365	308	22.6	22.2 [16.3-29.5]	83.4	22	22.6 [16.4-30.4]	84	2	-	-	-
Stable disease (0% obliteration)	24	1365	951	69.7	70.1 [62.6-76.7]	85.8	22	69.8 [62-76.7]	86.6	2	-	-	-
Recurrence/Tumor progression	31	1736	127	7.3	8.7 [6.6-11.3]	52.6	28	8.1 [5.9-11]	56.3	3	11.6 [7.9-16.7]	0	0.16
Radionecrosis	32	1900	11	0.6	2.2 [1.5-3.3]	0	29	2 [1.3-3.1]	0	3	3.1 [1.5-6.6]	0	0.30
Survival and Retreatment													
Meningioma-related mortality	33	1919	15	0.8	2.1 [1.4-3.3]	0	29	2 [1.3-3.3]	1.5	4	2.2 [0.9-5.2]	0	0.88
All-cause mortality	32	1879	131	7	4.5 [2.5-8]	70.1	28	4 [2-7.6]	72.2	4	13.3 [9.3-18.6]	8.1	<0.01
Overall Survival (OS)													
OS 1 year	28	1568	1568	100	98.7 [97.8-99.2]	0	25	98.8 [97.9-99.3]	0	3	97.4 [88.1-99.5]	0	0.38
OS 2 year	27	1363	1360	99.8	98 [96.8-98.8]	0	23	98 [96.8-98.8]	0	4	97.4 [88.1-99.5]	0	0.74
OS 3 year	25	1058	1053	99.5	97.3 [95.7-98.3]	0	22	97.4 [95.7-98.5]	0	3	97.4 [88.1-99.5]	0	1.00
OS 5 year	25	1058	1050	99.2	97.2 [95.5-98.3]	0	22	97.2 [95.4-98.4]	0	3	97.4 [88.1-99.5]	0	0.94
Progression-Free Survival (PFS)													
PFS 1 year	30	1825	1810	99.2	97.8 [96.5-98.6]	21.2	27	97.9 [96.5-98.7]	23.3	3	97 [89.9-99.2]	31.1	0.61
PFS 2 year	28	1567	1539	98.2	96.4 [94.4-97.7]	35	25	96.6 [94.6-97.9]	34.6	3	95 [83.5-98.6]	58.3	0.58
PFS 3 year	29	1813	1747	96.4	94.8 [92.5-96.5]	56.6	26	95 [92.4-96.7]	58.9	3	94.3 [84.8-98]	42.2	0.81
PFS 5 year	29	1813	1676	92.4	92.3 [89.3-94.6]	68.5	26	92.7 [89.3-95.1]	71.2	3	92.1 [87.5-95.1]	0	0.81
Retreatment													
Additional surgery	30	1836	29	1.6	3.4 [2.2-5.1]	27.2	27	3.2 [2.1-4.9]	20	3	4.2 [0.6-25.3]	66.8	0.79
Additional chemo	30	1836	3	0.2	1.5 [0.9-2.5]	0	27	1.5 [0.9-2.6]	0	3	1.2 [0.2-5.8]	0	0.79
Additional radiosurgery	30	1836	23	1.3	2.4 [1.4-4]	47.2	27	2.2 [1.3-3.9]	48.2	3	3.5 [0.6-18.1]	57.2	0.63