



## A RETROSPECTIVE STUDY TO ANALYZE THE ROLE OF STEREOTACTIC RADIO SURGERY IN MANAGEMENT OF PITUITARY ADENOMA.

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### ABSTRACT

**Introduction:** About two-thirds of pituitary adenomas may secrete excess hormones. While radiation therapy provides excellent radiographic local control for functioning adenomas, the actuarial rate of biochemical normalization is far less predictable and heavily depends on histology. The goal of pituitary adenoma radiosurgery is to permanently control tumor growth, maintain pituitary function, normalize hormonal secretion in the case of functional adenomas, and preserve neurological function, especially vision. The major role of pituitary adenoma stereotactic radiosurgery (SRS) is as an adjuvant to surgical resection, although it has a primary role for selected cases that are higher medical risk for general anesthesia or microsurgery, for patients with cavernous sinus tumor involvement, and for patients who consciously choose not to undergo microsurgery. Treatment of pituitary hormonal hyper- and hypo function is necessary to optimize overall quality of life and reduce comorbidities and mortality. These patients require life-long observation to ensure optimal hormonal management and monitor for tumor recurrence. While surgical excision offers rapid biochemical remission, SRS has a long latency period. It may extend up to 2 years. Amongst all functional adenomas, Prolactinomas have the longest time for remission. As on date there are no clear guidelines for SRS with respect to functional pituitary tumors. There are very few outcome predictors post SRS. In the backdrop of no clear cut guidelines this retrospective study was undertaken and attempt has been made to come up with management guidelines for functional pituitary tumors.

**Materials & Methods:** This retrospective study was conducted in a tertiary care institute with facility of Gamma Knife Radiosurgery. All pituitary tumors treated with SRS were included in this study from 2007 to 2016. All cases were followed up for a period of 2 years. Almost all cases were subjected to SRS following surgery based on radiological evidence of mass effect. Functional Pituitary tumors (FPA) were given a dose of 20 Gy while the Non Functional Pituitary Tumors (NFPA) were offered dose of 15 Gy. They were monitored for endocrinological improvement and visual field defects.

**Observation:** Our study has shown that combined treatment is the ideal treatment of choice as it provides control of tumor growth and also endocrinological control in 84% of tumors. Main complications include hypopituitarism and visual deterioration. Large tumor is a potential risk factor for recurrence.

**Conclusion:** This study prove that SRS has a definite role in management of Functional pituitary tumors.

**KEYWORDS :** Stereotactic Radio Surgery (SRS), Functional pituitary Adenoma (FPA)

### Introduction

Pituitary adenomas comprise 10–20 % of all intracranial tumors. Out of these 50% microadenomas are functional and 80% of Macroadenomas are nonfunctional [1,2]. Microadenomas are more likely to be diagnosed as incidental lesions or due to hormone hypersecretion, while Macroadenomas are more likely to be diagnosed secondary to mass effect resulting in pituitary insufficiency, hyperprolactinemia, or focal neurological deficit.[3]

Harvey Cushing performed over 2000 operations on patients with brain tumors, including 832 for gliomas. He implanted radioactive radium needles, known as a “radium bomb,” in a small number of these patients. Trans nasal trans sphenoidal endoscopic excision is accepted as a conventional surgical approach to excise these tumors. Endoscopy offers a panoramic view, which leads to higher rates of complete tumor removal than the traditional microscopic view. It remains to be proven whether the endoscopic approach results in higher remission rates for functional adenomas.[4,5]

The Gamma Knife was employed by Leksell to treat the first pituitary adenoma patient in 1968. There are several types of radiosurgery systems including cobalt-based systems, such as the Gamma Knife (Elekta AB) and Infini system (MASEP), linear accelerator (LINAC) based systems, such as the Cyber Knife, and proton beam units.

With improvement in technological research stereotactic radiosurgery (SRS) for functional pituitary tumors is acquiring more and more indications. SRS aims at permanently controlling tumor growth, normalizing hormonal secretions in functioning tumors and preserving neurological functions. Stereotactic radiosurgery offers certain advantages over fractionated stereotactic radiotherapy (FSRT). SRS has lower incidence of hypopituitarism and is more convenient to patient. It offers greater radiobiologic effect on late responding tissues and provides rapid endocrine remission. FSRT leads to lesser incidence of visual deterioration and also is suited for tumors larger than 3.5 cms which are irregular in shape and close to vital structures.[6]

So far no study has shown a difference in the treatment efficacy of

either of these radiation treatment modalities.

While radiosurgery can be used as first line of management Cushing's disease, Acromegaly cases respond better to surgical intervention as the first line of management. Medical management is considered as first line for prolactinomas

SRS following surgical excision is generally done by 3 month. MRI imaging also is done to reconfirm the post-operative tumor volume. Imaging findings depend on tumor type, biochemical parameters, and overall disease activity. 6 weeks post-surgical excision, re-evaluation of the hormonal status is done to determine hormonal integrity. In addition to the specific hormone, thyroid, adrenal, gonadal, and GH axes are assessed. During the interval between radiation and biochemical normalization (i.e., “latency period”), medical suppression is required as this period can last for several years or decades. Additional neurological, neuroimaging, and endocrinological follow up of patients must be performed to assess for delayed complications or tumor recurrence. Finally, physicians caring for pituitary patients should establish uniform endocrinological criteria and diagnostic testing for pre radio surgical and post radio surgical evaluations. The rate of biochemical remission of hypersecreting adenomas is comparable with the results of transsphenoidal surgery, but requires a latency of several years. Biochemical remission rates on long term follow up are similar for patients with ACTH, GH or prolactin secreting adenomas, however the length of time of remission varies, with prolactinomas, having the longest time to remission.

### Materials & Methods

This single institutional retrospective study was conducted taking into consideration all pituitary tumors which were treated with SRS from 2007 to 2016. All cases were initially subjected to endoscopic trans sphenoidal surgery or trans cranial surgery. SRS was done three months following surgery where there was MRI evidence of mass effect or biochemical parameter showing disease activity. In addition to the specific hormone, thyroid, adrenal, gonadal, and GH axes were assessed. Pituitary suppressive medication was stopped 8 weeks prior to SRS to maximize the chances of biochemical remission. Biochemical parameters were tested up to 2 years. All

tumors which showed normalization within 2 years were considered to be successfully treated while those which failed to normalize were considered as failure to treat. These case swere further managed by Endocrinologist and radiation Oncologist.

**Observation**

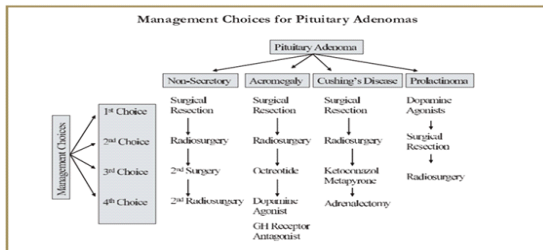
Observations of the study were divided into two groups .FPA and NFPA respectively. The data of the observation is given in Table1.

**Table 1**

Factor evaluated	Functional Pituitary Adenoma(FPA)	Non Functional Pituitary Adenoma(NFPA)
Total cases	27	76
Radiation Dose in Gy	20	15
Endocrinological Improvement	21	76
Hypopituitarism	03	33
Visual deterioration	02	10
Tumor growth control	24	63

Management choices for Pituitary Adenomas depend on many factors. The various choices can be given with an algorithm as shown in table 2

**Table 2**



Complications like Cranial Neuropathies, Radiation necrosis, ICA stenosis/ occlusion and Radiation induced secondary malignancy were not encountered in our study.

**Result**

Combined treatment controlled tumor growth in 84% of the pituitary tumors. Main complication included ,Hypopituitarism and visual deterioration.Large tumor were a risk factor for recurrence. Combining surgical excision and SRS gave satisfactory tumor control and endocrinological control .

**Discussion**

SRS following surgical excision is done after 6 weeks .Hormonal status and MRI are the two reliable parameters which determine wether SRS needs to be given post excision.

Pituitary suppressive medication is stopped 8 weeks prior to SRS to maximize the chances of biochemical remission. Patients with hyper functioning tumors such as acromegaly and Cushing disease also require long-term monitoring of clinical status including biochemical parameters and imaging. Many require an individualized multimodality treatment program for management and maintenance of biochemical remission. Generally, if endocrinological normalization is going to occur following radiosurgery, it usually does so within the first 2 years. The effects of treatment volume and dose selection on the rate and extent of hormonal normalization remains the subject of debate.Our study has shown that 20Gy for FPA and 15 Gy for NFPA are optimal in controlling tumor growth. Patient selection,Tumor volume,Radiation Dose,use of suppressive medication,type of secretory adenoma and duration of follow up., are some factors which bring about discrepancy in sensitivity.

Hypopituitarism determinants include, Pre SRS status of pituitary function,type and timing of prior treatment,radio surgical dose per volume delivered to normal pituitary Gland,dose delivered to pituitary stalk .Never theless optimal dose to target tissue should not be compromised.

Radiation injury to the optic system is a major challenge. Improved

conformity, steeper dose gradients, and adequate shielding may help minimize this risk.Amongst FPA Cushings disease achive endocrine remission the earliest while Nelsons disease have the longest remission rates.

Combined Micro neurosurgery and Gamma Knife Surgery are safe and effective for functional Pituitary Adenomas.Time taken for Post SRS Hormonal control not very predictable.No absolute predictors of recurrence.Post surgery, SRS ,Tumor Control and Endocrinological improvement are satisfactory with minimal complications.

**Conflict of Interest**

Nil

**References:-**

- [1] Dekkers OM, Pereira AM, Romijn JA (2008) Treatment and follow-up of clinically nonfunctioning pituitary macroadenomas. J Clin Endocrinol Metab 93(10):3717–3726. doi:10.1210/jc.20080643
- [2] Vance ML (2004) Treatment of patients with a pituitary adenoma: one clinician's experience. Neurosurg Focus 16(4):E1.
- [3] Dekkers OM, Pereira AM, Romijn JA (2008) Treatment and follow-up of clinically nonfunctioning pituitary macroadenomas. J Clin Endocrinol Metab 93(10):3717–3726. doi:10.1210/jc.20080643.
- [4] Starke RM, Raper DM, Payne SC, Vance ML, Oldfield EH, Jane JA Jr. Endoscopic vs microsurgical transsphenoidal surgery for acromegaly: outcomes in a concurrent series of patients using modern criteria for remission. J Clin Endocrinol Metab. 2013; 98:3190–3198. [CrossRef][CrossRef]
- [5] Wagenmakers MA, Boogaarts HD, Roerink SH, et al. Endoscopic transsphenoidal pituitary surgery: a good and safe primary treatment option for Cushing's disease, even in case of macroadenomas or invasive adenomas. Eur J Endocrinol. 2013;169:329–337.
- [6] J PSheehan,J Jagannathan,N.Pouratian,L.Steiner.Stereotactic radiosurgery for pituitary adenomas: A review of literature and our experience.Front.Horm.Res.34(2006)185-205.