IGKRF Project Proposal: Multi-institutional analysis of the risk of radiation-associated neoplasia after Gamma Knife radiosurgery

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Overview

A major concern of patients undergoing Gamma Knife radiosurgery (GKRS) for benign tumors is the risk of a separate secondary malignancy and/or malignant transformation. Very few studies have attempted to quantify this risk after radiosurgery and compare it to estimates of population risk based on national cancer registries. The purpose of this study is to address this common patient concern by pooling multi-institutional data with long term follow ups in order to better estimate the incidence of malignant transformation and separate radiation-associated intracranial neoplasia at different follow up time periods (2-5 years, 5-10 years, 10-15 years, >15 years), in patients who underwent GKRS for 1) vestibular or other schwannomas, 2) meningiomas (WHO grade 1), 3) hemangioblastoma, 4) pituitary adenomas 5) trigeminal neuralgia 6) arteriovenous malformation. Furthermore, we will attempt to control for factors that may predispose to radiation-associated neoplasia including genetic predisposition (NF1, NF2, vHL, MEN1, other) 2) other prior radiation treatments.

Keywords: gamma knife stereotactic radiosurgery, secondary malignancy, radiation-associated neoplasia
**Background**

Patients contemplating GKRS for benign entities frequently raise concerns regarding the risk of malignant transformation or the risk of radiosurgery inducing a new separate tumor. The literature to date includes several single-patient case reports of such events, which frequently do not adhere to Cahan’s criteria. Cahan’s criteria of radiation-induced tumor includes: 1) tumor must be localized within the field of radiation, 2) the tumor cannot be present prior to radiation, 3) a latency period is required between delivery of radiation and development of a tumor, 4) the histology of the tumor must be distinct from the original irradiated lesion (Cahan et al., 1998).

Two studies, one from Sheffield, UK and the other from the University of Florida have attempted to report the risk of malignancy after GKRS or LINAC SRS (Rowe et al., 2007; Rahman et al. 2014). Both studies focused on estimating the risk of intracranial malignancy, rather than all intracranial neoplasms including benign tumors. Neither study looked at genetic predisposition. As well, in the Sheffield study, the average follow up period was only 6 years and included patients with malignant disease with shorter overall survival. This study will attempt to estimate the risk of malignant transformation and the development of benign and malignant tumors after GKRS, with longer follow up periods. Tumors that meet Cahan’s criteria will be recorded as such.
Purpose

The purpose of this study is to pool multi-institutional data to determine the incidence of malignant transformation and radiation-associated neoplasia (benign, malignant) in patients who underwent GKRS for 1) vestibular or other schwannomas, 2) WHO grade 1 meningiomas, 3) hemangioblastoma, 4) pituitary adenomas 5) trigeminal neuralgia 6) arteriovenous malformation. Furthermore, we will attempt to control for factors that may predispose to radiation-associated neoplasia including 1) genetic predisposition (NF1, NF2, vHL, MEN1, other) 2) prior/multiple radiation treatments. These results will serve to help council patients of the risk of secondary neoplasia.

Specific Aims

1. Determine the incidence rate of radiation-associated neoplasia and secondary malignancy in a cohort of patients undergoing GKRS for various benign entities at different follow-up time periods (2-5 years, 5-10 years, 10-15 years, > 15 years)
2. Compare the rates benign and malignant intracranial tumor formation to SEERS incidence estimates.
3. Determine the impact of genetic predisposition on incidence of radiation-induced neoplasia

Data Collection

A template excel sheet has been included with this proposal with variables to be documented. Variables of interest include: age, gender, date of birth, Diagnosis, date of primary diagnosis, tumor location, Histologically verified (y/n), Histology, Treatment date, KPS at treatment, tumor volume, prescription isodose volume, margin dose, isodose, maximum dose, total tumor volume,
prior radiation (no, SRS, RT), additional GK procedures, malignant transformation (y/n), date of malignant transformation, histological confirmation (y/n), pathology, new benign tumor (y/n), date of new benign tumor, location of new tumor, genetic predisposition (none, NF1, NF2, vHL, other), date of last follow up, date of death, cause of death.

**Statistical Analysis**

Statistical analysis will be performed using SPSS, version 20.0 (SPSS Inc., Chicago, IL). Patients’ number of years at risk will be calculated from first SRS treatment. Patients with less than 2 year follow up or no follow up will be excluded. For each diagnosis cohort, the number of neoplastic cases (benign, malignant) will be compared to the number of expected cases in age- and gender-matched groups based on SEER database, in order to determine whether prior exposure to radiation treatment results in increased observed incidence rates of newly formed intracranial neoplasms.
References

