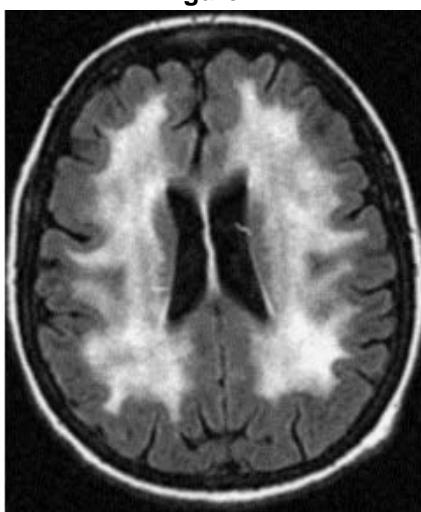


## Introduction

Adverse radiation effect (ARE) after stereotactic radiosurgery (SRS) for brain metastasis (BM) often compromises quality of life (Figure 1). Here, we determined risk factors for ARE following SRS.

**Figure 1.**



Axial T2-FLAIR MRI demonstrating diffuse cerebral edema

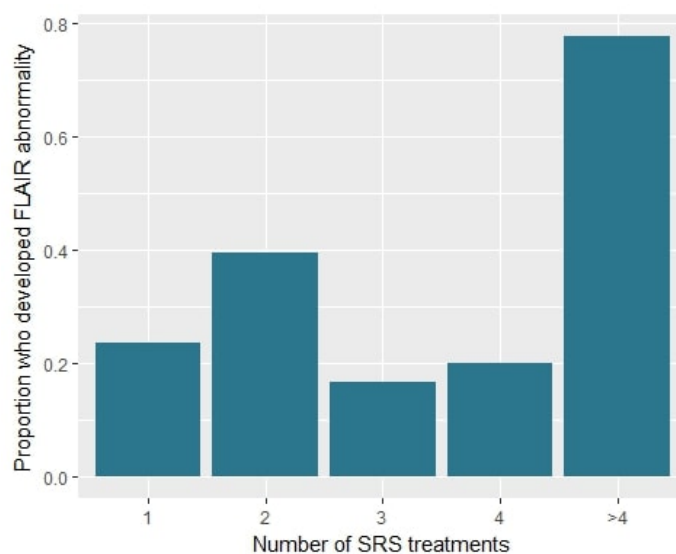
## Methods

We identified 214 BM patients (1,106 BM) treated between 2007 and 2017 at our institution with MRI follow up. We collected demographic, clinical, and dosimetric information ARE was defined as the presence of FLAIR hyperintensity in >25% of the area of any of four axial MRI images defined by 1) the centrum semiovale, 2) third ventricle, 3) temporal horns, and 4) the fourth ventricle. Statistical analysis was carried out using Student's t-test, Pearson's chi-squared test, and univariate and multivariate logistic regression.

## Results

Of the 214 patients, 62 patients (28.97%) suffered ARE following SRS. On univariate logistic regression, the odds of ARE were increased with higher cumulative intracranial tumor volume (CITV) (odds ratio (OR) 1.026 per 1 cm<sup>3</sup> increase, 95% CI 1.009 - 1.043, p=0.003), >4 rounds of SRS sessions (OR 9.545, 95% CI 1.924 - 47.352, p=0.006), and prior history of whole-brain radiation therapy (WBRT) (OR 4.459, 95% CI 2.233 - 8.907, p<0.001). On multivariate logistic regression adjusted for length of follow-up, these associations remain robust: CITV (p=0.036), >4 rounds of SRS (p=0.033), and prior history of WBRT (p<0.001) (Table 1). Variance analysis indicated that the relative importance of these risk factors in contributing to ARE, in descending order, is: prior history of WBRT, CITV, and >4 rounds of SRS.

**Figure 2.**



Percentage of patients who developed new FLAIR signal after SRS as a function of the number of treatments

**Table 1.**

Variable	Odds ratio	p value
Length of follow up in days	1.000	0.301
Cumulative treated tumor volume (cm <sup>3</sup> )	1.020	<b>0.036</b>
>4 SRS sessions	7.364	<b>0.033</b>
Receipt of whole-brain radiation therapy	4.281	<b>&lt;0.001</b>

Multivariable logistic regression demonstrating significantly increased odds of new FLAIR with >4 SRS treatments

## Conclusions

In this analysis of our decade-long experience, we discovered three risk factors for ARE, including prior history of WBRT, increasing CITV, and >4 rounds of SRS. Consideration of these factors should facilitate patient counseling and clinical decision making.

## Learning Objectives

1. Identify risk factor for adverse radiation effect in patients with brain metastases treated with stereotactic radiosurgery
2. Describe the relative importance of each of these factors in contributing to this complication