

# Utility of Sodium Fluorescein for Achieving Resection Targets in Glioblastoma Multiforme: The WVU Experience

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## Introduction

Glioblastoma multiforme (GBM), the most common primary malignant tumor, continues to have a dismal prognosis despite advances in medicine. Studies have demonstrated that aggressive extent of resection (EOR) aimed at gross total resection leads to improved survival regardless of age, both with newly diagnosed and recurrent glioblastomas. Efforts to achieve improved yet safe resection have included the use of imaging techniques, neuro-navigation, neurophysiological monitoring, and fluorescence aids such as 5aminolevulinic acid (5-ALA) and fluorescein sodium. This study assessed sodium fluorescein, which penetrates the tumor and regions with impaired blood-brain-barrier. As such, it is used intra-operatively to assist with tumor visualization and improved extent of resection. The goals of this study were to 1. Investigate the role of sodium fluorescein in improving the rates of gross total resection of GBM and 2. Assess whether patients undergoing resection with sodium fluorescein have improved survival as compared to patients undergoing surgery without fluorescein.

## **Methods**

Thirty consecutive patients with suspected or previously proven GBM underwent fluorescein-guided resection from 05/2014 to 06/2016. Standard contrast-enhanced magnetic resonance imaging (MRI) sequences with neuronavigation were utilized for operative planning. Intra-operatively fluorescein was administered at 3-4 mg/kg at the incision of dura. Fluorescent tissue was visualized both in white light and under a fluorescent YELLOW 560nm filter. Post-operative imaging was reviewed. Three categories were distinguished: no residual tumor = gross total resection (GTR); greater than 98% of tumor resected = near total resection (NTR); and <98% of tumor resected = subtotal resection (STR). Univariate analysis using the log-rank test was used to ascertain an association between fluorescein use and survival. A Kaplan-Meier survival curve was constructed. Probability values < .05 were considered statistically significant.

## Results

Table 1 summarizes the patient demographics and results. 30 patients undergoing 33 surgeries were included in the study. Patients' ages ranged from 44 to 89 (mean age of 60). 43% (13/30) of the patients were female. 33% (11/33) surgeries were re-do operations for recurrent GBM. A majority, 70% (23/33), of the tumors were on the left hemisphere. 15% of all cases (5/33) and 22% (5/23) of left sided tumors were resected via awake craniotomies. The average volume of tumor was 19cc. Upon assessment of the pre-operative imaging, 70% (23/33) of the cases were not thought to be amendable to complete resection. Of those 23 cases, 7 (30%) resulted in gross total resection. Of 10 cases that were thought to be amendable to complete resection, gross total resection was achieved in 9 (90%). Overall, complete or near total (>98%) resection was achieved in 82% (27/33) of cases. Overall, the primary surgeon felt that the use of sodium fluorescein facilitated resection and was considered helpful in 97% of cases in which it was utilized, including dominant-side resections particularly within speech and motor regions.

Survival data was compared between patients in this study cohort (n=30) who underwent surgical resection with sodium fluorescein versus control patients (n= 196) who underwent resection without intra-operative fluorescein.

Figure 1 depicts the significant difference in survival (p = 0.0017). The median survival of the control group was 206 days versus 629 days in the sodium fluorescein group (95% CI -0.22-0.87).

No patients were found to develop any local or systemic side effects after fluorescein injection.

## References

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Patient characteristics, resection data, and outcomes



Kaplan-Meier survival curve demonstrating improved survival for patients with GBM who underwent surgery with sodium fluorescein versus those who underwent surgery without it.

## Conclusions

This work demonstrates the promise of an affordable and easy-to-implement strategy for improving rates of total resection of contrast enhancing areas in patients with glioblastoma multiforme, especially in patients in whom complete resection initially seems unlikely. This may potentially improve progression free and overall survival in this cohort.

