

First-in-Human Intraoperative Near-Infrared Fluorescence Imaging of Glioblastoma Using Cetuximab-IRDye800: Results From a Pilot Study

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INTRODUCTION: Extent of resection, a key determinant of length of survival in patients with glioblastoma (GBM), may be improved by better methods of intraoperative tumor detection.

METHODS: We evaluated intraoperative imaging of GBM with a near-infrared (NIR) fluorescent dye conjugated with an EGFR-targeted antibody. With IRB approval and informed consent, escalating doses of Cetuximab-IRDye800 were injected systemically into three patients 2 to 5 days prior to surgery. NIR fluorescence imaging of tumor and histologically negative peritumoral tissue was performed intraoperatively, ex vivo on the back table, and in a closed-field device. Fluorescence was measured as Mean Fluorescence Intensity (MFI), and tumor-to-background ratios (TBRs) were calculated by comparing MFIs of tumor to those of non-fluorescent and histologically negative peritumoral tissue.

RESULTS: The mean TBR was higher in tumor tissue (4.0 ± 0.5) than in normal brain (1.18 ± 0.3 , $p=0.02$). The TBR was higher in the high dose cohort (100mg) than in the low dose cohort (50mg) (4.3 versus 3.6). Sensitivity and specificity of tumor fluorescence for viable tumor were assessed using tumor serial sections and punch biopsies. The smallest detectable volume of tumor in a closed-field setting was 30cc for low doses of dye and 10cc for high doses. Fluorescence correlated highly with neuropathologists interpretation of formalin-fixed paraffin-embedded tissue sections. Fluorescence was highly specific for viable tumor tissue in disease patients with enhancing tumor, normal peritumoral tissue showed minimal fluorescence. No adverse events were reported.

CONCLUSIONS: This first-in-human pilot study demonstrates the feasibility and safety of Cetuximab-IRDye800 imaging in GBM. A larger prospective study is under review.