

Topic: Glioma management using Rapid Perioperative *IDH1* Mutation Detection in High-Grade Gliomas using Novel LAMP assay and IDH1 Peptide Nucleic Acid

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Background/Purpose

Gliomas, a type of brain tumor, are classified based on molecular subtyping, particularly the presence of IDH1 mutation, which significantly impacts prognosis and treatment decisions. However, current molecular studies are time-consuming, delaying crucial surgical and therapeutic interventions. This study aims to develop a rapid perioperative IDH1 detection assay (Perioperative IDH1-LAMP) to guide real-time decision-making during surgery and to assess the effectiveness of IDH1-PNA as a potential treatment option.

Methods

Loop-mediated isothermal amplification (LAMP) was used to produce Perioperative IDH1-LAMP utilizing fluorescent and colorimetric measurements, a novel IDH1 detection technique. Grade 3 oligodendroglioma (BT-142, IDH1 mutant/-) and glioblastoma (U87, IDH1 WT/WT) cell lines were used in duplicate to calibrate this new assay. Assay was evaluated with five human glioma tumor samples blinded-prospectively per a fixed protocol and results were compared to accepted CLIA standards methods, immunohistochemistry and Sanger-sequencing. Furthermore, in a case study in-vitro attempt, a validated glioblastoma fresh tissue was cultured in human tissue media at 37^{0C} and treated with IDH1-PNA or non-treatment (H2O) in day1-2 and weighted at day 0-3.

Results

The Perioperative IDH1-LAMP assay successfully detected the IDH1 mutation within 35 minutes, with high accuracy. Furthermore, the assay was tested on patient-derived glioma samples during surgery, demonstrating 100% concordance with CLIA approved molecular testing methods. Additionally, the study investigated the efficacy of IDH1-PNA via the LAMP model and in-vitro glioblastoma tissue model in suppressing the growth of glioblastoma with WT-IDH1. Results showed a significant suppressing amplification and reduction in tumor weight when treated with IDH1-PNA compared to controls, suggesting its potential as a therapeutic intervention.

Conclusion

Perioperative IDH1-LAMP assay offers a rapid and accurate method for detecting the IDH1 mutation during surgery, facilitating timely decision-making. Moreover, IDH1-PNA shows promise as a therapeutic agent for WT-IDH1 gliomas. Further research is warranted to added validate findings for clinical application.