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Intraoperative Raman Spectroscopy Identifies Key Mutations in Human Glioma: A New Platform for Precision Medicine

Babar Vaqas MD, PhD, FRCS, BSc; Michael Short; Imran Patel; Hannah McGregor BS, PhD; Umar Fiaz; Clara Limbaeck-Stokin; Haishan Zeng; Sergei Kazarian; Kevin S. O'Neill

Introduction

Human glioma can be a devastating disease with at best a median survival of only 14 months in high grade tumors. Diagnosis of these tumors increasingly relies on genetic testing of tumor tissue for IDH, ATRX and MGMT status which can take many weeks during which treatment can not be started. We describe the application of intraoperative Raman spectroscopy for the instant, label-free and non-destructive detection of key driver mutations in human glioma in an effort to shorten the time to diagnosis and help improve the detection of tumor tissue during surgery.

Methods

This study involved a prospective series of patients undergoing tumor resection through an open surgical technique (standard craniotomy). At various stages during the operation Raman analysis of tissue was performed using the sterile hand held Raman probe attached 5mm from the tip of a navigation probe positioned over the brain tissue being analysed. All biopsies were submitted and processed for genetic analysis for IDH mutation and PCR assay for MGMT promotor methylation. Data was analysed using PCA-LDA and PLS-DA to built predictive models.

Results

Using our invivo Raman system we collected 471 Raman spectra from 17 patients undergoing brain surgery for a range of WHO grade 2-4 gliomas. The predictive models achieved 98% accuracy for identifying MGMT methylation and 94-96% accuracy for identifying ATRX and IDH mutation invivo. Peak analysis revealed characteristic peaks for each mutation type.

Conclusions

Raman spectroscopy is capable of the invivo detection of key mutations in human glioma. This can drastically shorten time to diagnosis and first treatment. It also allows the identification of good and poor prognostic groups of patients immediately at surgery. Through stratifying patients into key molecular groups for targeted therapies intraoperative Raman spectroscopy is a promising new platform for precision medicine in Neurosurgery.

Learning Objectives

Genetic basis of glioma, improving outcomes in glioma surgery, precision medicine as applied to neurosurgery

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