

Raman Spectroscopy: Can it change the future of Brain Tumour Surgery?

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Abstract

Raman Spectroscopy (RS) is one of several techniques being used to identify tumour tissue during brain surgery. It is emerging as a novel investigative and diagnostic tool. The application of RS in cancer treatment has displayed promising results. This review centers around its clinical implication in brain tumours.

Keywords: Raman spectroscopy, brain tumour, neurosurgery

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Introduction

Brain tumour surgery requires precise delineation between tumour margin and normal brain tissue as maximizing extent of resection reduces recurrence and improves overall survival for most brain tumours.¹ Indistinct and infiltrative tumour margins have led to the use of several auxiliary techniques. Intraoperative MRI (iMRI), fluorescence-guided resection, and stereotactic neuronavigation are used with their own limitations. Despite being resource-intensive, iMRI often has poor resolution, and neuronavigation is highly susceptible to the shifting of the brain during surgery.²

RS is a quick, non-destructive imaging technique based on the principle of the Raman effect, whereby if the light is shone on an object, it undergoes Raman scattering, which a spectrophotometer can capture. This Raman spectra or signal of different molecular compositions is unique and thus helpful in identifying molecular composition and differentiating tumour from non-tumour tissue.³ The application of RS in cancer treatment has displayed encouraging results and brain tumour surgery is strongly tipped as the next frontier for this technological advancement.

Review of Evidence

Jabarkheel et al., used RS to classify paediatric brain tumours using fresh ex-vivo samples. A total of 29 patients yielded 160 samples, subsequently generating 678 Raman spectra. All samples eventually underwent

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histopathological review. Tumour tissue was obtained from 20 (459 Raman spectra) and normal brain tissue from 12 (219 Raman spectra) patients. The accuracy of detecting tumour from normal tissue was 89.8%, whereas that of low-grade glioma from normal tissue was 86.2%.³

In a landmark paper Zhang et al., used Visible Resonance Raman (VRR) spectroscopy and developed a novel optical spectroscopic technique using an intraoperative hand-held VRR analyzer. VRR amplifies biomolecules' Raman signals by 10 to 1000 times, and the specific molecular vibration is used to make a visual pathological diagnosis.⁴ VRR spectroscopy was applied to a total of 63 fresh glioma specimens. A principal component analysis-support vector machine (PCA-SVM) machine learning method was used to differentiate glioma from normal brain tissues and different grades of glioma tissues. The accuracy in identifying glioma from normal tissue via VRR, compared to histopathology, was over 80%.⁴

Neidert et al., studied stimulated Raman histology (SRH), a novel technique that allows rapid and easy intraoperative tissue analysis comparable to the images produced by conventional H&E staining of frozen sections.⁵ During a period of 6 weeks, tissues from 108 neurosurgical patients were imaged. The top three entities were gliomas, metastases, and meningiomas. Samples obtained underwent tissue preparation to obtain virtual H&E like SRH images and were presented to the surgeon and neuropathologist in almost no time. The authors concluded that SRH can be used as a complementary addition for tissue analysis in neurosurgical OR and a valuable tool for neurosurgical studies.⁵

Raman has also been shown to detect invasive cancer beyond MRI in a study by Jermyn et al.⁶ Preoperative MRI was used for 3D neuronavigation in 13 patients with invasive glioma. Neuronavigation, along with visual and tactile tissue properties were used to determine tumour boundaries. RS was used to obtain spectra at distinct points in this area. Biopsy samples were obtained at each of these points for post-surgical tissue analysis. These sites were also used as landmarks to compare RS signal with MRI signal at each point. It was shown that RS detects invasive cancer up to 3.7cm and 2.4 cm beyond the T1- contrast-enhanced and T2 MRI boundaries, respectively.⁶ The authors thus concluded that compared to MRI-guided resection, RS was

superior in maximizing safe resection and reducing the chances of tumour recurrence.

Jelke et al., distinguished meningioma from surrounding dura matter using an intraoperative Raman spectrometer, with a sensitivity of 96% and a specificity of 95%.⁷ Intra-op frozen section is highly valuable for cases where there is a doubt whether the lesion is a lymphoma or a glioblastoma. RS has also been shown in such cases to be highly useful with an accuracy of 82%, by Klamminger et al.⁸

Malsagova et al., employed micro-RS to monitor the quality of nanowire sensor chip fabrication. These fabricated chips were used to detect miRNA-363 first in purified buffer solution and later in human plasma, which has been associated with brain tumours.⁹ Livermore et al., compared intraoperative tumour identification beyond contrast margin with RS and 5-aminolevulinic acid (5-ALA) induced fluorescence. In glioblastoma, RS had a significantly better predictive value than 5-ALA induced fluorescence and RS outperformed 5-ALA in detecting infiltrative tumour in areas with no fluorescence.¹⁰

Conclusion

The molecular analysis via Raman spectroscopy offers a reliable technique for the diagnosis, monitoring, and surgical resection of brain tumours. Its clinical application provides a non-invasive modality to differentiate between the ever-challenging brain-tumour interface and provides a scaffold to study deeper into infiltrative tumour margins. With the advent of artificial intelligence and machine learning models, it can potentially improve the extent of resection and, subsequently, better tumour control. Its anticipated strength as an intraoperative surgical adjunct needs to be evaluated on a larger scale, especially when

other adjuncts are resource-limited and technologically challenging.

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