A sensor to improve the accuracy of stereotactic brain biopsies for the diagnosis of brain tumours

Team

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Proposal

Brain cancer has a significant impact on society, disproportionate to its prevalence in comparison to other more well-known cancers. It is also the deadliest. It is the leading cause of life-years lost in men and second leading life years lost in women (1). The most common primary brain cancer in humans' glioblastoma (GBM) is also the most common primary brain cancer and has an abysmal median survival of 15 months despite surgery and chemo-radiation (2). Despite decades of research there has been no significant changes to this sad statistic.

Histologically GBM is defined by the presence of anaplastic cells surrounded by necrotic tissue with microvascular proliferation. This reflects the aggressive nature of the tumour. Accurate diagnosis depends on achieving a representative biopsy of the tumour with both necrotic and anaplastic tissue. Stereotactic biopsy may be desirable for patients with lesions which may represent non-neoplastic lesions such as inflammatory, infectious or demyelinating lesions. Other differentials for lesions which appear similar to GBM on MRI imaging include lymphoma and brain abscess. Previous case series has shown that in 60% of cases lower grade anaplastic glioma was upgraded to GBM when open surgical resection was performed following stereotactic biopsy (3).

Diagnosing GBM requires samples of tissues to be taken either with an open craniotomy or with closed stereotactic needle-based techniques. If the location of the tumour is a deep or eloquent part of the brain stereotactic biopsy under image guidance is sometimes the only surgical procedure that can be performed. A patient's pre-operative MRI images is used to guide the biopsy target. On T1-weighted imaging the centre of the lesion is dark and presumed to be necrotic tissue with a ring of contrast-enhancement around this area termed the contrast enhancing region (CER).

The major reason for its poor outcomes is tumour recurrence despite maximal safe surgery. The tumour is diffusely infiltrative and even when the tumour is operable within an anatomical safe area of the brain, complete removal is impossible. When recurrence occurs usually with 6 - 7 months following surgery in 80 - 85% of cases it recurs within a 2-cm margin of the original resection cavity, around the CER (4,5). The mechanisms underlying tumour cell migration and invasion are incompletely understood.

It is known that there is significant spatial heterogeneity within the tumour, cells in the tumour core and periphery share common genetic characteristics but also have significant differences in their molecular profile and behaviour (6). These differences may be associated with GBM cells at the resection margin having a more proliferative and invasive phenotype then the cells at the core (7,8).

Our study aims to develop a novel biosensor which will be able to provide surgeons with real-time feedback in the Operating Room of whether the tissue sample is necrotic or viable tissue to better target samples for the purposes of tissue diagnosis and analysis of tumour heterogeneity.

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For this purpose, we plan to conduct in-vitro experiments that will involve a low-cost gas sensor incorporated in an Arduino, that will be used to measure oxygen concentration of monolayers of GBM cells. Cell cultures of different percentages of alive vs dead cells will be prepared and a standard calibration curve relating oxygen concentration to cell viability will be constructed. The oxygen concentration will be then used to indirectly quantify the viability of the GBM cells with the aid of an Arduino platform. The results will be displayed on a 4D Systems Display.

The main component that we will need to complete the project is an oxygen sensor (Grove - Gas Sensor (O_2), 59$, https://www.seeedstudio.com/grove-gas-sensoro2-p-1541.html). We are also planning to utilise the Arduino Platform for Physical Computing and the 4D Systems Display Programmable Touchscreen from the Biomaker Starter Kit. Finally, one of our group members, Agavi, is currently conducting experiments with GBM cells in the Biolab and has access to the GBM cells, as well as, the equipment and chemicals needed for GBM cell culture.

References

1. Rouse C, Gittleman H, Ostrom QT, Kruchko C, Barnholtz-Sloan JS. Years of potential life lost for brain and CNS tumors relative to other cancers in adults in the United States, 2010. Neuro-Oncol. 2016 Jan;18(1):70–7.
2. Arvold ND, Reardon DA. Treatment options and outcomes for glioblastoma in the elderly patient. Clin Interv Aging. 2014 Feb 21;9:357–67.
3. Jackson RJ, Fuller GN, Abi-Said D, Lang FF, Gokaslan ZL, Shi WM, et al. Limitations of stereotactic biopsy in the initial management of gliomas. Neuro-Oncol. 2001;3(3):193–200.
4. Eljamel S. 5-ALA Fluorescence Image Guided Resection of Glioblastoma Multiforme: A Meta-Analysis of the Literature. Int J Mol Sci. 2015 May 7;16(5):10443–56.
5. Petrecca K, Guiot M-C, Panet-Raymond V, Souhami L. Failure pattern following complete resection plus radiotherapy and temozolomide is at the resection margin in patients with glioblastoma. J Neurooncol. 2013 Jan;111(1):19–23.
6. Lemée J-M, Clavreul A, Menei P. Intratumoral heterogeneity in glioblastoma: don't forget the peritumoral brain zone. Neuro-Oncol. 2015 Oct;17(10):1322–32.
7. Ruiz-Ontañon P, Orgaz JL, Aldaz B, Elosegui-Artola A, Martino J, Berciano MT, et al. Cellular Plasticity Confers Migratory and Invasive Advantages to a Population of Glioblastoma-Initiating Cells that Infiltrate Peritumoral Tissue. STEM CELLS. 2013 Jun 1;31(6):1075–85.
8. Glas M, Rath BH, Simon M, Reinartz R, Schramme A, Trageser D, et al. Residual Tumor Cells Are Unique Cellular Targets in Glioblastoma. Ann Neurol. 2010 Aug;68(2):264–9.