Boffin Access

Open Access Journal | Volume: 1.1

International Journal of Surgical Procedures

ISSN 2517-7354

The Potential of Fluid-attenuated Inversion Recovery Imaging in Improving Glioblastoma Outcome?

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Abstract

The outcome of Glioblastoma (GBM) remains poor. Standard management includes surgical resection, which is guided by Magnetic Resonance Imaging (MRI). Surgery alone however is not able to reliably remove all tumour cells, which due to their diffuse and infiltrative nature, migrate along pathways outside the confines indicated by MRI. The use of Fluid-Attenuated Inversion Recovery (FLAIR) imaging has emerged as a potential adjunct to current surgical treatment, and its rationale in order to better GBM outcomes is discussed.

Keywords

Glioblastoma; Magnetic Resonance Imaging; Fluid-Attenuated Inversion Recovery; Survival

Summary

Glioblastoma (GBM) has a median survival of 14 months from primary diagnosis. There is emerging evidence [1-3] that suggests targeting Fluid-Attenuated Inversion Recovery (FLAIR) abnormalities in addition to the standard surgical resection guided by Magnetic Resonance Imaging (MRI), followed by standard chemo radiation therapy, and may be a realisable approach to better GBM outcomes. This short communication aims to summarize the most recent advances in understanding the prognostic significance of FLAIR abnormalities in ameliorating clinical outcomes in GBM.

Recently, Pessina et al. [1] reported a median survival of 24.5 (95% confidence interval [CI]18.9-30.1) months in up to 21 patients following gross total resection (GTR)and ≥45% extent of resection (EOR) of T2 FLAIR abnormalities. Li et al. [2] report a similar median survival of 23.0 (95% CI 17.6-28.4) months in 117 patients treated by GTR and ≥53.21% EOR of T2 FLAIR abnormalities. Furthermore, Duma et al. [3] utilised postoperative stereotactic radio surgery after resection to target FLAIR abnormalities in 174 patients with a median survival result of 23 months.

To date, the concern in neurosurgery is that not all GBM cells are removed following surgery. FLAIR imaging is able to provide higher resolution of white matter versus standard MRI, which is important as it has been posited that malignant glioma cells migrate preferentially along white matter fibre tracts [4]. They do so by producing lytic enzymes, such as membrane type 1 matrix metalloproteinase (MT1-MMP), to break down the extracellular matrix of white matter and facilitate infiltrative migration along these pathways. If indeed residual GBM cells after primary GTR reside at entry points into these white matter tracts due to their natural course of growth, then targeting these potential 'escape routes' along the standard resection cavity identifiable by FLAIR imaging appears logical.

Anatomically, a major concern with targeting FLAIR abnormalities is damaging eloquent white matter areas infiltrated by GBM. This is a serious concern given the invasive nature of GBM, especially compared to other glioma types. There is little impetus to even consider targeting these eloquent areas surgically, and thus the applicability of FLAIR-directed 'supra total' resection of GBM may only have a niche in patients with more favourable locations and distributions. Yet if this is the case, it is most likely these same patients are more amenable to standard resection as well, which would confound the true benefit of this novel approach. Nonetheless, it is promising to note that the results[1,2] do not rely on100% EOR of FLAIR abnormalities, which implies eloquent areas do not have to be targeted necessarily for there to be benefit as long as enough non-eloquent areas are also involved. The use of functional imaging awake surgery with intra operative white matter mapping and intraoperative image guidance are all technical options that can assist in achieving this type of supra total resection.

From a clinical perspective, a number of factors require further investigation before any recommendation be made. A bias in selecting younger patients who typically perform

Article Information

DOI: 10.31021/ijsp.20181104
Article Type: Short communication
Journal Type: Open Access
Volume: 1 **Issue:** 1
Manuscript ID: IJSP-1-104
Publisher: Boffin Access Limited

Received Date: 19 January 2018
Accepted Date: 19 February 2018
Published Date: 23 February 2018

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Citation: Lu VM, Mc Donald KL, Rovin RA. The Potential of Fluid-attenuated Inversion Recovery Imaging in Improving Glioblastoma Outcome. Int J Surg Proced. 2018 Feb;1(1):104

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better at surgery regardless may influence outcomes. Although, it should be noted that both Pessina et al. [1] and Li et al. [2] employed multivariate analysis to identify their respective threshold EOR of FLAIR abnormalities as independent factors, which included consideration for age as well as functional performance. Another aspect to consider is the presumed benefit of targeting FLAIR abnormalities may not be as practical in the cases of GBM that are recurrent, multifocal or disseminated, which limits generalisability.

The highly diffuse and infiltrative nature of GBM remains an immense hurdle in surgical management of this disease, as GBM cells can invade well beyond the borders indicated by standard MRI that guides surgery. Hence it appears to be the case that while GBM is not surgically curable, targeted supratotal resection possesses the potential to further prolong high quality survival in select patients, as is evident in the reported survival outcomes where FLAIR abnormalities have been additionally targeted. While any recommendations regarding this specific approach are premature given the limited evidence, further safe and transparent investigation in targeting GBM cells outside the conventional MRI confines is appreciated in the pursuit of better GBM outcomes.

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