Glioblastoma progression

- Biological role and clinicopathological significance of leucine-rich alpha-2 glycoprotein 1 in the glioblastoma microenvironment
- Systematic review and epistemic meta-analysis to advance binomial AI-radiomics integration for predicting high-grade glioma progression and enhancing patient management
- Mediation Mendelian randomization analysis of immune cell phenotypes and glioma risk: unveiling the regulation of cerebrospinal fluid metabolites
- Unique Presentation of Glioblastoma With Acute Onset Symptomatology and Disease Recurrence
- Deciphering the dialogue between brain tumors, neurons, and astrocytes
- PLEKHA4 is transcriptionally regulated by HOXD9 and regulates glycolytic reprogramming and progression in glioblastoma via activation of the STAT3/SOCS-1 pathway
- Tertiary lymphoid structures in gliomas: impact on tumour immunity and progression
- KAT5 regulates neurodevelopmental states associated with G0-like populations in glioblastoma

Glioblastoma recurrence and glioblastoma progression are related concepts in the context of glioblastoma, but they are not the same, and it's important to understand the differences between them.

Glioblastoma Recurrence:

Definition: Glioblastoma recurrence refers to the reappearance of active tumor tissue after an initial treatment has been administered. This can occur at or near the original tumor site.

Timing: Recurrence typically occurs after a period of initial treatment and a variable period of stability or remission. It can happen weeks, months, or even years after the initial treatment.

Characteristics: Recurrent glioblastoma consists of tumor cells that survived the initial treatment, which may have been surgery, radiation therapy, and chemotherapy.

Diagnosis: Recurrence is usually confirmed through imaging studies, such as MRI or CT scans, which show new or enlarging areas of contrast-enhancing tumor.

Management: The management of recurrent glioblastoma often involves a different treatment approach than the initial therapy. Options may include additional surgery, alternative chemotherapy, experimental therapies, or palliative care.

Glioblastoma Progression:

Definition: Glioblastoma progression is a broader term that encompasses any changes in the tumor over time. It includes both the initial growth and the later recurrence of the tumor.

Timing: Progression can refer to the continuous growth or spread of the tumor from the time of diagnosis. It covers all stages of tumor growth, from the initial formation to the reappearance of active tumor cells in recurrence.

Characteristics: Progression may involve the tumor's aggressive growth, infiltration into surrounding brain tissue, and the development of treatment-resistant features.

Diagnosis: Progression is assessed through various clinical and imaging criteria, including changes in

the size and characteristics of the tumor over time.

Management: The management of glioblastoma progression depends on the stage and extent of tumor growth. It often includes a combination of treatments, such as surgery, radiation, and chemotherapy, with the goal of delaying or controlling tumor growth.

In summary, glioblastoma progression is a broad term that encompasses the entire course of tumor growth and development, from diagnosis to recurrence. Glioblastoma recurrence specifically refers to the reappearance of tumor tissue after an initial treatment. Both are critical concepts in the clinical management and treatment of glioblastoma, but they occur at different points in the disease course and may require different approaches for diagnosis and treatment.

The prognosis of Glioblastoma remains poor despite improvements in treatment modalities, posing a serious threat to human health. At present, although drugs such as temozolomide, cisplatin, and bevacizumab, are effective in improving the overall survival of patients with Glioblastoma, most patients eventually develop drug resistance, leading to poor clinical prognosis. The development of multidrug resistance has therefore become a major obstacle to improving the effectiveness of chemotherapy for Glioblastoma. The ability to fully understand the underlying mechanisms of chemotherapy resistance and to develop novel therapeutic targets to overcome resistance is critical to improving the prognosis of patients with Glioblastoma. Of note, growing evidence indicates that a large number of abnormally expressed noncoding RNAs (ncRNAs) have a central role in glioma chemoresistance and may target various mechanisms to modulate chemosensitivity. noncoding RNAs is a research direction for tumor drug resistance mechanisms and targeted therapies, which not only provides novel perspectives for reversing glioma drug resistance but may also promote the development of precision medicine for clinical diagnosis and treatment [1)].

A common clinical challenge after standard of care treatment is differentiating tumor progression from treatment-related changes, also known as pseudoprogression (PsP). Usually, PsP resolves or stabilizes without further treatment or a course of steroids, whereas true progression (TP) requires more aggressive management. Differentiating PsP from TP will affect the patient's outcome. This study investigated using deep learning to distinguish PsP MRI features from progressive disease.

Method: We included Glioblastoma patients with a new or increasingly enhancing lesion within the original radiation field. We labeled those who subsequently were stable or improved on imaging and clinically as PsP and those with clinical and imaging deterioration as TP. A subset of subjects underwent a second resection. We labeled these subjects as PsP, or TP based on the histological diagnosis. We coregistered contrast-enhanced T1 MRIs with T2-weighted images for each patient and used them as input to a 3-D Densenet121 model and using five-fold cross-validation to predict TP vs PsP.

Result: We included 124 patients who met the criteria, and of those, 63 were PsP and 61 were TP. We trained a deep learning model that achieved 76.4% (range 70-84%, SD 5.122) mean accuracy over the 5 folds, 0.7560 (range 0.6553-0.8535, SD 0.069) mean AUROCC, 88.72% (SD 6.86) mean sensitivity, and 62.05% (SD 9.11) mean specificity.

Conclusion: We report the development of a deep learning model that distinguishes PsP from TP in Glioblastoma patients treated per the Stupp protocol. Further refinement and external validation are required prior to widespread adoption in clinical practice [2)].

The hallmark of glioblastoma (Glioblastoma) is its penchant for relentless progression. The median progression free survival (PFS) is 4.4 to 8.4 months in patients with newly diagnosed Glioblastoma following the current standard of care, safely obtained maximal resection at initial surgery followed by concomitant temozolomide (TMZ) and radiotherapy and adjuvant TMZ.

Glioblastoma multiforme is the most aggressive type of primary brain tumors, but there is a small percentage of patients who have a long-term survival and some exceptional cases who survive decades after surgical removal of tumor [3].

Less than 10% of patients live longer than 5 years from diagnosis [4].

Prognostic factors involved in survival include age, performance status, grade, specific markers (MGMT methylation, mutation of IDH1, IDH2 or TERT, 1p19q codeletion, overexpression of EGFR, etc.) and, likely, the extent of resection. Certain adjuncts to surgery, especially cortical mapping and 5-ALA fluorescence, favor higher rates of gross total resection with apparent positive impact on survival. Recurrent tumors can be offered re-intervention, participation in clinical trials, anti-angiogenic agent or local electric field therapy, without an evident impact on survival. Molecular-targeted therapies, immunotherapy and gene therapy are promising tools currently under research [5].

Prior studies that have reported only the readmissions back to index hospitals are likely underestimating the true 30-day readmission rate. Glioblastoma patients who were readmitted within 30 days had significantly shorter survival than nonreadmitted patients. Future studies that attempt to decrease readmissions and evaluate the impact of reducing readmissions on patient outcomes are needed [6].

Several clinical studies have reported that valproic acid could prolong survival of Glioblastoma patients. However, the results of these studies are inconsistent.

A bibliographic search was performed in the EMBASE, MEDLINE, ClinicalTrials.gov and Cochrane Central Register of the Controlled Trials databases to identify potentially relevant articles or conference abstracts that investigated the effects of VPA on the outcome of glioma patients. Five observational studies were included.

Pooled estimates of the hazard ratio (HR) and 95% confidence intervals (CI) were calculated. The meta-analysis confirmed the benefit of using VPA (HR, 0.56; 95% CI, 0.44-0.71). Sub-group analysis shows that patients treated with VPA had a hazard ratio of 0.74 with a 95% confidence interval of 0.59-0.94 vs. patients treated by other-AEDs and a hazard ratio of 0.66 with a 95% confidence interval of 0.52-0.84 vs. patients treated by administration of non-AEDs. No heterogeneity was observed in the subset analysis.

The results suggest that glioblastoma patients may experience prolonged survival due to VPA administration. Sub-analysis confirmed the benefit of VPA use compared to a non-AEDs group and an other-AEDs group. Further RCTs of this subject should be performed [7].

The surface regularity obtained from high-resolution contrast-enhanced pretreatment volumetric T1-weighted MR images is a predictor of survival in patients with glioblastoma. It may help in classifying patients for surgery [8].

Glioblastoma Pseudoprogression

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1)
Zeng Z, Chen Y, Geng X, Zhang Y, Wen X, Yan Q, Wang T, Ling C, Xu Y, Duan J, Zheng K, Sun Z. NcRNAs: Multi-angle participation in the regulation of glioma chemotherapy resistance (Review). Int J Oncol. 2022 Jun;60(6):76. doi: 10.3892/ijo.2022.5366. Epub 2022 May 4. PMID: 35506469.
2)
Moassefi M, Faghani S, Conte GM, Kowalchuk RO, Vahdati S, Crompton DJ, Perez-Vega C, Cabreja RAD, Vora SA, Quiñones-Hinojosa A, Parney IF, Trifiletti DM, Erickson BJ. A deep learning model for discriminating true progression from pseudoprogression in glioblastoma patients. J Neurooncol. 2022 Jul 19. doi: 10.1007/s11060-022-04080-x. Epub ahead of print. PMID: 35852738.
3)
Caruso R, Pesce A, Wierzbicki V. A very rare case report of long-term survival: A patient operated on in 1994 of glioblastoma multiforme and currently in perfect health. Int J Surg Case Rep. 2017 Feb 20;33:41-43. doi: 10.1016/j.ijscr.2017.02.025. [Epub ahead of print] PubMed PMID: 28273605.
4)
Stupp R, Hegi ME, Mason WP, van den Bent MJ, Taphoorn MJ, Janzer RC, Ludwin SK, Allgeier A, Fisher B, Belanger K, Hau P, Brandes AA, Gijtenbeek J, Marosi C, Vecht CJ, Mokhtari K, Wesseling P, Villa S, Eisenhauer E, Gorlia T, Weller M, Lacombe D, Cairncross JG, Mirimanoff RO; European Organisation for Research and Treatment of Cancer Brain Tumour and Radiation Oncology Groups; National Cancer Institute of Canada Clinical Trials Group. Effects of radiotherapy with concomitant and adjuvant temozolomide versus radiotherapy alone on survival in glioblastoma in a randomised phase III study: 5-year analysis of the EORTC-NCIC trial. Lancet Oncol. 2009 May;10(5):459-66. doi: 10.1016/S1470-2045(09)70025-7. Epub 2009 Mar 9. PubMed PMID: 19269895.
5)
Delgado-López PD, Corrales-García EM. Survival in glioblastoma: a review on the impact of treatment modalities. Clin Transl Oncol. 2016 Nov;18(11):1062-1071. Review. PubMed PMID: 26960561.
6)
Nuño M, Ly D, Ortega A, Sarmiento JM, Mukherjee D, Black KL, Patil CG. Does 30-Day Readmission Affect Long-term Outcome Among Glioblastoma Patients? Neurosurgery. 2014 Feb;74(2):196-205. doi: 10.1227/NEU.0000000000000243. PubMed PMID: 24176955.
7)
Yuan Y, Xiang W, Qing M, Yanhui L, Jiewen L, Yunhe M. Survival analysis for valproic acid use in adult glioblastoma multiforme: A meta-analysis of individual patient data and a systematic review. Seizure. 2014 Jul 8. pii: S1059-1311(14)00196-4. doi: 10.1016/j.seizure.2014.06.015. [Epub ahead of print] PubMed PMID: 25066904.
8)
Pérez-Beteta J, Molina-García D, Ortiz-Alhambra JA, Fernández-Romero A, Luque B, Arregui E, Calvo M, Borrás JM, Meléndez B, Rodríguez de Lope Á, Moreno de la Presa R, Iglesias Bayo L, Barcia JA, Martino J, Velásquez C, Asenjo B, Benavides M, Herruzo I, Revert A, Arana E, Pérez-García VM. Tumor Surface Regularity at MR Imaging Predicts Survival and Response to Surgery in Patients with Glioblastoma. Radiology. 2018 Jul;288(1):218-225. doi: 10.1148/radiol.2018171051. PubMed PMID: 29924716.