NIMG-33. VOLUMETRIC TUMOR MEASUREMENTS ARE SUPERIOR TO 2D BIDIRECTIONAL MEASUREMENTS IN THE EVALUATION OF IDH INHIBITION IN DIFFUSE GLIOMAS: EVIDENCE FROM A PROSPECTIVE PHASE I TRIAL OF IVOSIDENIB

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Since IDH mutant (mIDH) low-grade gliomas (LGGs) progress slowly and patients have a relatively long survival, testing of new therapies in clinical trials based solely on survival can take more than 20 years. Guidance on therapeutic evaluation using LGG RANO criteria recommends serial bidirectional (2D) measurements on a single slice; however, questions remain as to the best approach for evaluating LGGs in clinical trials including use of volumetric (3D) measurements, which would theoretically allow for more accurate measurements of irregular shaped lesions and allow readers to better assess areas of change within these tumors. A total of 21 (out of 24) non-enhancing, recurrent mIDH LGGs with imaging pre- and post-treatment enrolled in a phase I, multicenter, open-label study to assess the safety and tolerability of oral ivosidenib (NCT02073994) were included in this exploratory ad hoc analysis. 2D bidirectional and 3D volumetric measurements were centrally evaluated by one of 3 radiologists at an imaging CRO using a paired read and forced adjudication paradigm. The effects of 2D vs. 3D measurements on progression-free survival (PFS), growth rate measurement variability, and reader concordance and adjudication rates were then quantified. 3D volumetric measurements had significantly longer estimates of PFS (P=0.0181), more stable (P=0.0063) and considerably lower measures of tumor growth rate (P=0.0037), the highest inter-reader agreement (weighted Kappa=0.7057), and significantly lower reader discordance rates (P=0.0002) with comparable recommended LGG RANO 2D approaches. In summary, 3D volumetric measurements are better for determining response assessment in LGGs due to longer PFS and more stable measures of tumor growth rates (i.e. less "yo-yo-ing" of measurements over time causing fewer erroneous calls of progression and more accurate growth rates), highest inter-reader agreement, and lowest reader discordance rates. Future studies will focus on validating this in a larger cohort and determining whether these measurements better reflect clinical benefit.

NIMG-34. DELAYED PSEUDOPROGRESSION IN GLIOBLASTOMA PATIENTS TREATED WITH TTFIELDS: A REPORT OF TWO CASES

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INTRODUCTION: Tumor treating fields (TTFields) is an established treatment modality for glioblastoma (GBM) and is administered with the portable Optune system. Although the EF-14 phase 3 trial demonstrated the efficacy of TTFields for newly diagnosed GBM, uncertainty regarding the specific effects of this treatment has prevented its widespread clinical use. Pseudoprogression in response to chemoradiation is a known problem in GBM patients and most commonly occurs within 3 months after radiotherapy. We report 2 cases of TTFields delayed pseudoprogression. CASE REPORT: Two GBM patients being treated with TTFields showed signs of radiographic progression at 5 to 6 months after completing radiotherapy. Patient 1 was a 37-year-old woman with gliosarcoma in the right temporal lobe. Patient 2 was a 70-year-old man with wildtype-IDH GBM in the left temporal lobe. Both patients received TTFields in addition to maintenance temozolomide (TMZ) after radiotherapy (RT). Radiographic progression was noted at 5 and 6 months after RT in Patients 1 and 2, respectively. Second resections were performed, and pathology showed only the treatment effect, which ultimately led to diagnosis of pseudoprogression. DISCUSSION: Both patients had radiographic progression outside the typical pseudoprogression window. Recent studies reported that TTFields increased plasma cell membrane permeability, which could result in additional gadolinium leakage into the extracellular space. CONCLUSIONS: Better characterization of delayed pseudoprogression would improve treatment and could potentially reduce unnecessary surgeries and discontinuation of successful therapies.

NIMG-35. MACHINE LEARNING GLIOMA GRADE PREDICTION LITERATURE: A TRIPOD ANALYSIS OF REPORTING QUALITY

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PURPOSE: Reporting guidelines are crucial in model development studies to ensure the quality, transparency and objectivity of reporting. While machine learning (ML) models have proven themselves effective in predicting glioma grade, their potential use can only be determined if they are clearly and comprehensively reported. Reporting quality has not yet been evaluated for ML glioma grade prediction studies, to our knowledge. We measured published literature against the TRIPOD Statement, a checklist of items considered essential for the reporting of diagnostic studies. MATERIALS AND METHODS: A literature review, in agreement with PRISMA, was conducted by a university librarian in October 2020 and verified by a second librarian in February 2021 using four databases: Cochrane trials (CENTRAL), Ovid Embase, Ovid MEDLINE, and Web of Science core-collection. Keywords and controlled vocabulary included artificial intelligence, machine learning, deep learning, radiomics, magnetic resonance imaging, glioma, and glioblastoma. Publications were screened in Covidence and scored against the 27 items in the TRIPOD Statement that were relevant and applicable. RESULTS: The search identified 11,727 candidate articles with 1,135 articles undergoing full text review. 86 articles met the criteria for our study. The mean adherence rate to TRIPOD was 44.4% (range: 22.2% - 66.7%), with poor reporting adherence in categories including abstract (0%), model performance (0%), title (1.2%), justification of sample size (2.3%), full model specification (2.3%), participant demographics and missing data (7%). Studies had high reporting adherence in categories including results interpretation (100%), background (98.8%), study design/source of data (96.5%), and objectives (95.3%). CONCLUSION: Existing publications on the use of ML in glioma grade prediction have a low overall quality of reporting. Improvements can be made in the reporting of titles and abstracts, justification of sample size, and model specification and performance.

NIMG-36. VISUALIZATION OF TUMOR HETEROGENEITY AND PREDICTION OF ISOCITRATE DEHYDROGENASE MUTATION STATUS FOR HUMAN GLIOMAS BY USING MULTIPARAMETRIC PHYSIOLOGIC AND METABOLIC MRI

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Preoperative prediction of isocitrate dehydrogenase mutation status is clinically meaningful, but remains challenging. This study aimed to predict the isocitrate dehydrogenase (IDH) status of gliomas by using the machine learning voxel-wise clustering method of multiparametric physiologic and metabolic magnetic resonance imaging (MRI) and to show the association of the created cluster labels with the glucose metabolism status of the tumors. Sixty-nine patients with diffuse glioma were scanned by pH-sensitive MRI, diffusion-weighted imaging, fluid-attenuated inversion recovery, and contrast-enhanced T1-weighted imaging at 3 T. An unsupervised two-level clustering approach, including the generation of a self-organizing map followed by the K-means clustering, was used for voxel-wise feature extraction from the acquired images. The logarithmic ratio of the labels in each class within tumor regions was applied to a support vector machine to differentiate IDH mutation status. Bootstrapping and leave-one-out cross-validation were used to calculate the area under the curve (AUC) of receiver operating characteristic curves, accuracy, sensitivity, and specificity for evaluating performance. Targeted biopsies were performed for 14 patients to explore the relationship between clustered labels and the expression of key glycolytic proteins determined using immunohistochemistry. The highest prediction performance to differentiate IDH status was found for 10-class clustering,