Title

NIMG-21. VARIABLE RESOLUTION HYPERPOLARIZED [2-13C]PYRUVATE MRI IN HEALTHY VOLUNTEERS AND PATIENTS WITH IDH-MUTANT GLIOMA

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BACKGROUND: Generative adversarial network (GAN) creates synthetic MRI data that may provide morphologic variability to assess molecular characteristics of glioblastomas. PURPOSE: To investigate the ability of GAN-based generation of isocitrate dehydrogenase (IDH)-mutant glioblastomas to provide morphologic variability and improve molecular prediction. METHODS: GAN was retrospectively trained on 110 IDH-mutant high-grade gliomas. Paired contrast-enhanced T1-weighted and FLAIR synthetic MRI data were generated. Diagnostic models were developed from 80 IDH-wild type glioblastomas and 38 IDH-mutant patients, (real model), 38 IDH-mutant GAN-generated synthetic data (synthetic model), or both combined (augmented model). Two neuroradiologists independently assessed real and morphologic characteristics of contrast-enhancement patterns, the presence of necrosis, and margins and type of non-enhancing region. Significant predictors of IDH mutation were selected from multivariable logistic regression, and diagnostic performance was validated in 44 separate patients, 33 with IDH-wild type and 11 with IDH-mutant glioblastomas. RESULTS: Synthetic IDH-mutant glioblastomas were similar to real tumors on Turing tests, with an area under the curve (AUC) of 0.67–0.71. Significant predictors of a more frontal or insular location (odds ratio [OR], 1.34 vs. 1.52; highest $P = .04$) and distinct non-enhancing tumor margins (OR, 2.68 vs. 3.88; $P < .001$) were similar for the real and synthetic models, with the synthetic (AUC, 0.958) and augmented (AUC, 0.899) models having higher diagnostic performance than the real model (AUC, 0.864) in the training set. The diagnostic accuracy was higher for the synthetic and augmented models (90.9% [40/44] each for both observers) than for the real model (84.1% [37/44] for one observer and 86.4% [38/44] for the other). CONCLUSIONS: The GAN-based synthetic images yield morphologically variable IDH-mutant glioblastomas and may be useful as realistic training sets.

NIMG-20. DIFFERENTIATION OF TREATMENT-RELATED CHANGES FROM TUMOR PROGRESSION FOLLOWING BRACHYTHERAPY IN PATIENTS WITH WHO II AND III GLIOMAS USING FET PET

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BACKGROUND: Following brachytherapy, the differentiation of radiation-induced changes (e.g., radiation necrosis) from actual tumor progression using MRI is challenging. To overcome this diagnostic uncertainty, we evaluated the diagnostic value of O-(2-[^{18}F]-fluoroethyl)-L-tyrosine (FET) PET in glioma patients treated with brachytherapy. MATERIAL AND METHODS: From 2006-2019, we retrospectively identified WHO grade II or III glioma patients (i) treated with brachytherapy using Iodine-125 seeds, (ii) equivocal or progressive MRI findings inside the radiation field, and (iii) additional FET PET imaging for diagnostic evaluation. Static FET PET parameters such as maximum and mean tumor-to-brain ratios (TBR) and dynamic FET PET parameters (i.e., time-to-peak, slope) were obtained. Diagnostic performances were calculated using receiver operating characteristic curve analyses and Fisher's exact test. Diagnoses were confirmed histologically or clinicoradiologically. RESULTS: Following brachytherapy, suspect MRI findings occurred after a median time of 33 months (range, 5-111 months). In 10 of 21 patients (WHO grade II, n=5; WHO grade III, n=16), treatment-related changes were diagnosed. The best diagnostic performance for identification of treatment-related changes was obtained using maximum TBRs (threshold < 3.20;accuracy, 86%; sensitivity, 100%; specificity, 73%; P=0.007). Mean TBRs reached an accuracy of 76% (threshold < 2.05; sensitivity, 89%; specificity, 64%; P=0.010). Dynamic PET parameters did not reach statistically significant results. CONCLUSION: Our data suggest that static FET PET parameters add valuable diagnostic information to diagnose radiation-induced changes in glioma patients treated with brachytherapy.

NIMG-21. VARIABLE RESOLUTION HYPERPOLARIZED [2-^{13}C] PYRUVATE MRI IN HEALTHY VOLUNTEERS AND PATIENTS WITH IDH-MUTANT GLIOMA

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INTRODUCTION: Mutations in isocitrate dehydrogenase (IDH) have been investigated as a prognostic biomarker in glioma. The presence of the IDH mutation (IDHm) is associated with 2-hydroxyglutarate (2HG) production and inhibition of glutamate synthesis (McBrayer, Cell 2018). Hyperpolarized carbon-13 (HP-^{13}C) MRI enables dynamic measurements of *in-vivo* metabolism using a [2-^{13}C]pyruvate labeled probe that undergoes conversion to [2-^{13}C]lactate and [5-^{13}C]glutamate. Here, we present HP [2-^{13}C]pyruvate data from healthy volunteers and patients with IDHm diffuse glioma. Due to its intrinsic low signal-to-noise ratio (SNR), we demonstrate the ability of post-processing denoising to improve its utility and aid in detection of metabolic changes associated with IDHm. METHODS: Dynamic HP ^{13}C data were acquired following intravenous injection of [2-^{13}C] pyruvate from five healthy volunteers and one patient with IDHm grade III astrocytoma. A novel multi-resolution frequency specific multislice EPI sequence was used to obtain [2-^{13}C]pyruvate, [5-^{13}C]glutamate, and downfield and upfield [2-^{13}C]lactate signals (3s temporal resolution, pyruvate/lactate/glutamate spatial resolutions = 0.75x0.75cm^2/ 2.25x2.25cm^2/ 2.25x2.25cm^2, 5 slices 3cm thick). Following phase correction, patch-based tensor decomposition denoising was applied to metabolite images. Metabolite differences between normal-appearing white matter (NAWM) and T2 lesion were examined for the patient data. RESULTS: HP [2-^{13}C]pyruvate imaging is able to simultaneously probe glycolytic ([2-^{13}C]lactate) and oxidative ([5-^{13}C]glutamate) metabolism. Denoised pyruvate/lactate/glutamate signals achieved a 4-9/3-6/3-7 fold increase in SNR. T2 lesion exhibited decreased glutamate-to-pyruvate and glutamate-to-lactate AUC ratios versus contralateral NAWM ($p< 0.018$, $p < 1.5e-5$), consistent with IDH mutant status. CONCLUSION: We successfully demonstrated the feasibility of applying variable resolution HP [2-^{13}C]pyruvate metabolic imaging to detect IDHm specific metabolism. This technique addresses a major hurdle in HP ^{13}C MRI by improving SNR while permitting robust metabolism quantification. Future studies will optimize methods for acquiring and processing data to evaluate further data acquired from IDHm glioma patients. Supported by NIH T32 CA151022, P01 CA118816, and NICO.

NIMG-22. PREDICTION OF GLIOBLASTOMA CELLULAR INFILTRATION AND RECURRENCE USING MACHINE LEARNING AND MULTI-PARAMETRIC MRI ANALYSIS: RESULTS FROM THE MULTI-INSTITUTIONAL RESPOND CONSORTIUM

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