pathology-proven, amphetamine-associated CNS vasculitis resembling a tumor. A 41-year-old man presented with six weeks of progressive confusion and left-sided weakness. CT head reported a right thalamic mass with vasogenic edema. Laboratory tests were unremarkable except for cannabinoids and amphetamine in urine. MRI brain showed enhancement in right frontotemporal lobe, basal ganglia, and thalamus concerning for glioblastoma multiforme. After high-dose IV dexamethasone, an initial biopsy showed reactive gliosis, perivascular lymphocytic cuffing by CD3+, rare CD20+ cells and no infection. He continued to decline. MRI 22 days after admission showed increased T2/FLAIR hyperintensity, multifocal areas of enhancement, microhemorrhages, and ischemia. High-grade glioma, lymphoma and infectious encephalitis remained on differentials. Treatment included broad-spectrum antibiotics and acyclovir. Biopsy on 23rd day showed reactive gliosis with parenchymal macrophage infiltration and perivascular cuffing with mixed inflammatory infiltrates. CSF: slightly elevated WBCs (8/μL), elevated protein (139mg/dL), normal glucose, and no infection. MRI whole spine and CT body were unremarkable. The patient was transferred to MDACC 5.5 weeks after initial presentation. He was alert with expressive aphasia, right gaze preference, left hemiplegia, and right hemiparesis. He underwent a right anterior temporal lobectomy. Pathology showed extensive cortical laminar and white matter necrosis with macrophage infiltration and microglial activation. In areas of the preserved cortex, vasculocentric lymphocytic aggregates were present and reticulin staining showed lymphocytic infiltration of the vascular walls. Immunophenotyping (CD3, CD20) showed an almost pure T-cell population. The predominance of intramural T-lymphocytes reflected a vasculitic process. The final diagnosis was cerebral vasculitis with subacute infarction. The patient died six days later. The autopsy findings were identical to the previous resection without evidence of systemic inflammation.

NIMG-63. THE APPLICATION OF MRI AND TREATMENT RESPONSE ASSESSMENT MAPS (TRAMS) FOR MONITORING TREATMENT EFFECTS DURING/FOLLOWING PROTON BEAM THERAPY – INITIAL EXPERIENCE

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BACKGROUND/OBJECTIVES: We have previously shown that delayed-contrast-MRI-based TRAMs enable efficient separation between tumor and treatment-effects, validated histologically, reaching 100%/93% sensitivity/PPV to active tumor. Proton beam therapy (PBT) is a highly conformal radiotherapy modality with increasing use in CNS tumors. Here, for the first time, we studied the application of standard MRI and TRAMs for monitoring patients during/following PBT. METHODS: 8 patients with gliomas (4 grade II, 3 grade III, 1 grade IV) and 9 with meningiomas (6 grade 1, 2 grade II, 1 grade III) were scanned by standard MRI and TRAMs at baseline, mid-term during PBT (treatment duration 22-30 days), end of treatment and 6/12 months thereafter. Enhancing volumes (EVs) were calculated from contrast-enhanced MRI, while blue/tumor and red/radiation-changes volumes (blueV/redVs) were calculated from the TRAMs. RESULTS: Three gliomas showed increased (by > 10%) EVs (15.2±8.7%), 3 stable and 2 decreased EVs (14.2±8.5%) during treatment. At the end of treatment 3 showed increased volumes (27.6±10.4%) and 5 decreased volumes (26.4±6.5%). One meningioma showed decreased EVs (11%) while 8 were stable during treatment. At end of treatment one showed increased EVs (22%), 5 were stable and 3 showed increased EVs (13.7±1.7%). The TRAMs showed similar trends but of varied magnitudes. In addition, the TRAMs could indicate radiation changes in two cases with increased enhancement: One glioma showed increased EVs/redVs and decreased blueVs during treatment, consistent with pseudoprogression, confirmed later by significant shrinkage of all volumes, and one meningioma with a similar pattern at 6 months. CONCLUSIONS: Our initial results show for the first time significant changes in brain tumors volumes, during and at the end of PBT. The addition of TRAMs may suggest a new tool to assess PBT radiation effects. Interpretation of these results, comparison between tumor types/grades, and correlation with treatment planning and additional follow-up will be presented.

NIMG-64. DISTINCT IMAGING PATTERNS OF PSEUDOPROGRESSION IN GLIOMA PATIENTS FOLLOWING PROTON VERSUS PHOTON RADIATION THERAPY

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PURPOSE: Radiologic Assessment in Neuro-Oncology (RANO) criteria define pseudoprogression (Ps) after photon radiation for gliomas, as occurring less than twelve weeks from radiation, within the high dose radiation field. However, some patients receiving proton manifest lesions that appear subjectively different from photon Ps based on timing and location (more than six months from radiation and deeper to the prior tumor), which would be called tumor progression by RANO. We retrospectively reviewed MRI changes after proton or photon radiation for gliomas. We propose criteria to characterize proton pseudoprogression (ProPs) distinct from photon pseudoprogression or tumor progression. METHODS: Post-treatment MRIs of patients with gliomas were reviewed, along with clinical and pathological data. 77 proton patients were reviewed for the presence of ProPs, and 64 photon patients were reviewed for imaging changes. Data collected included the location, timing, and morphology of the lesions, tumor type, chemotherapy, and clinical symptoms. RESULTS: 16 (21%) of the patients who received protons had imaging changes unique to protons, at a mean of 14.6 months after radiation. We established the following criteria to characterize ProPs: not immediately in or adjacent to the resection cavity; ~ 2cm opposite from target beam entry; can resolve without treatment; subjectively multifocal, patchy, small (< 1cm). None of the photon patients had lesions that met our criteria for ProPs ($p < 0.001$). CONCLUSION: Patients who receive protons can have a unique subtype of pseudoprogression (Ps), which we refer to as proton pseudoprogression (or ProPs). These lesions could be mistaken for tumor progression, but typically resolve spontaneously. ProPs can possibly be explained by the increased relative biological effectiveness of protons and beam angle selection which may deposit at ~2cm deep to the target. Recognizing these lesions can prevent unnecessary treatment for mistaken tumor progression, especially in the context of clinical trials that include proton.

NIMG-65. STUDY OF LOCAL PERTURBATION IN COMPUTATIONAL MODELLING ON TUMOR TREATING FIELDS (TTFIELDS) THERAPY

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INTRODUCTION: Tumor Treating Fields (TTFields) are an approved therapy for glioblastoma (GBM). A recent study combining post-hoc analysis of clinical trial data and extensive computational modelling demonstrated that TTFields dose at the tumor has a direct impact on patient survival (Ballo MT, et al. *Int J Radiat Oncol Biol Phys*, 2019). Hence, there is rationale for developing TTFields treatment planning tools that rely on numerical simulations and patient-specific computational models. To assist in the development of such tools is it important to understand how inaccuracies in the computational models influence the estimation of the TTFields dose delivered to the tumor bed. Here we analyze the effect of local perturbations in patient-specific head models on TTFields dose at the tumor bed. METHODS: Finite element models of human heads with tumor were created. To create defects in the models, conductive spheres with varying conductivities and radii were placed into the model's brains at different distances from the tumor. Virtual transducer arrays were placed on the models, and delivery of TTFields numerically simulated. The error in the electric field induced by the defects as a function of defect conductivity, radius, and distance to tumor was investigated. RESULTS: Simulations showed that when a defect of radius R is placed at a distance, $d > 7R$, the error is below 1% regardless of the defect conductivity. Further the defects induced errors in the electric field that were below 1% when $\sigma r/d < 0.16$, where $\sigma r/d < 0.16$, where $\sigma r = (\sigma sphere - \sigma surrounding)/(\sigma sphere + \sigma surrounding)$ $\sigma surroundings$ is the average conductivity around the sphere and $\sigma sphere$ is the conductivity of the sphere. CONCLUSIONS: This study demonstrates the limited impact of local perturbations in the model on the calculated field distribution. These results could be used as guidelines on required model accuracy for TTFields treatment planning.

NIMG-66. AI-BASED PROGNOSTIC IMAGING BIOMARKERS FOR PRECISION NEUROONCOLOGY AND THE RESPOND CONSORTIUM

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AI-based methods have shown great promise in a variety of biomedical research fields, including neurooncologic imaging. For example, machine learning methods have offered informative predictions of overall survival (OS) and progression-free survival (PFS), differentiation between pseudoprogression (PsP) and progressive disease (PD), and estimation of mutational status from imaging data. Despite their promise, AI, and especially the emerging deep learning (DL) methods, are challenged by several factors, including imaging heterogeneity across scanners and lack of sufficiently large and diverse training datasets, which limits their reproducibility and general acceptance. These challenges prompted the development of the ReSPOND (Radiomics Signatures for PrecisiON Diagnostics) consortium on glioblastoma, a growing effort to bring together a community of researchers sharing imaging, demographic, clinical and (currently) limited molecular data in order to address the following aims: 1) pool and harmonize data across diverse hospitals and patient populations worldwide; 2) derive robust and generalizable AI models for prediction of (initially) OS, PFS, PsP vs. PD, and recurrence; 3) test these predictive models across multiple sites. In its first phase, ReSPOND aims to pool together approximately 3,000MRI scans (from 10institutions plus TCIA), along with demographics, KPS, and (for a subset) MGMT/IDH1 status. We present initial results testing the generalization of a previously trained model of OS on 505Penn datasets to 2independent cohorts from Case Western Reserve University and University Hospitals (N=44), and Penn (N=67). The results indicate good generalization, with correlation coefficients between OS/predicted-OS between 0.25 to 0.5, depending on variable availability, which is comparable to cross-validated accuracy previously obtained from the training set itself (N=505). Additional preliminary studies evaluating prediction of future recurrence from baseline pre-operative scans in de novo patients (Penn model applied to CWR) indicated potential for guiding targeted dose escalation and supra-total resection (excellent predictions in 6/12 patients, modest in 1/12, and poor in 5/12).

NIMG-67. DISAPPEARING DOTS – TRANSIENT LATE ENHANCING LESIONS YEARS AFTER BRAIN RADIOTHERAPY

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BACKGROUND: Late-delayed radiation effects appear 6 months to years following radiotherapy. We characterize a species of small enhancing lesions in the late-delayed phase of post-radiotherapy that are distinct from the classic descriptions of radiation necrosis or pseudoprogression associated with mass effect and edema. These "disappearing dots" are small, do not exert mass effect nor edema, and spontaneously resolve. METHOD: We retrospectively describe a series of cases with "disappearing dots" following brain radiotherapy. RESULTS: There were 10 cases (4 men), median age 42 years (range 29-63). Diagnoses were glioblastoma (3); low grade astrocytoma, anaplastic astrocytoma, and anaplastic oligodendroglioma (2 each); and solitary fibrous tumor (1). All patients received 54-60 Gy (Gray) of external beam radiotherapy, except one (proton beam therapy to 60 cobalt Gray equivalent). Disappearing dots appeared at a median of 27 months (range 5-197) post-radiotherapy. Lesions were relatively small (~< 1 cm^3), peri-ventricular, and within the radiotherapy field. Most enlarged before resolving. Advanced MR imaging and fluorodeoxyglucose (FGD)-PET results were inconsistent. Lesions persisted a median of 8.5 months (range 1-49) before spontaneous resolution. All were asymptomatic. Biopsy in one case revealed treatment effects rather than recurrent tumor. CONCLUSIONS: Asymptomatic small periventricular enhancing lesions can develop and remit spontaneously, years following brain radiotherapy. Such disappearing dots should be part of the differential diagnosis along with tumor recurrence. of new enhancing lesions in the late-delayed phase post-radiotherapy.

NIMG-68. MATHEMATICAL MODELING OF THERMAL DAMAGE ESTIMATE VOLUMES IN MAGNETIC RESONANCE-GUIDED LASER INTERSTITIAL THERMAL THERAPY

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BACKGROUND: Magnetic resonance-guided laser interstitial thermal therapy is a minimally invasive procedure that produces real-time thermal damage estimates of ablation (TDE). Orthogonal TDE-MRI slices provides an opportunity to mathematically estimate ablation volume. OBJECTIVE: To mathematically model TDE volumes and validate with post-24 hours MRI ablation volumes. METHODS: Ablations were performed with the Visualase Laser Ablation System (Medtronic). Using ellipsoidal parameters determined for dual-TDEs from orthogonal MRI planes, TDE volumes were calculated by two definite integral methods (A and B) implemented in Matlab (MathWorks). Post 24-hours MRI ablative volumes were measured in OsiriX (Pixmeo) by two-blinded raters and compared to TDE volumes via paired t-tests and Pearson's correlations. RESULTS: Twenty-two ablations for 20 patients with various intracranial pathologies were included. Average TDE volumes calculated with Method A was 3.44 ± 1.96 cm^3 and with Method B was 4.83 ± 1.53 cm^3. Method A TDE volumes were significantly different than post-24 hours volumes ($P < 0.001$). Method B TDE volumes were not significantly different than post-24 hours volumes ($P = 0.39$) and strongly correlated with each other ($r = 0.85$, $R^2 = 0.72$, $P < 0.0001$). A total of 8/22 (36%) method A versus 17/22 (77%) method B TDE volumes were within 25% of the post 24-hours ablative volume. CONCLUSION: We present the first iteration of a viable mathematical method that integrates dual-plane TDEs to calculate volumes resembling 24 hours post-operative volumes. Future iterations of our algorithm will need to determine additional calculated variables that improve the performance of volumetric calculations.

NIMG-69. PERSONALIZED CONNECTOMIC SIGNATURES: BRIDGING THE GAP BETWEEN NEURO-ONCOLOGY AND CONNECTOMICS

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PURPOSE: Connectomics has led to significant neuroscientific findings within the last two decades, eventually making impact in the clinics. Neuro-oncology can benefit immensely from connectomics in evaluating structural connectivity of brains with tumor for pre- and post-treatment planning, as a tumor connectome along with derived network measures will make it possible to determine the cognitive effects of treatment and quantify the effect of surgery on quality of life. However, generating connectomes in the presence of tumor is a challenging task. Specifically, registration of an atlas to the brain, which is essential in parcellating the brain into regions of interest, fails around the tumor due to mass effect and infiltration related distortions which are not present in the atlas that comes from a healthy brain. We aim to tackle this problem by introducing a novel atlas registration method. METHOD: Although tumor deforms the geometrical shape of its surrounding regions, it does not violate the connectivity of displaced cortical voxels to the rest of the brain. Leveraging this fact, we represent the brain as an annotated graph with nodes representing ROIs encoding geometric features of regions and weighted edges representing the connectivity between regions. In encoding the surroundings of the tumor into the graph, we subsample the region into smaller patches to represent the area with multiple nodes. We then calculate many-to-one graph matching between the graphs of a tumor patient and a healthy control to associate surroundings of tumor with healthy ROIs. OUTCOME: A tumor connectome showing how the connectivity is morphed around the tumor, which can further be extended to creating connectomes of recurrence. CLINICAL IMPLICATIONS: Use of connectomes can revolutionize neuro-oncology by helping surgeons in estimating structural, functional, and behavioral outcomes of resection prior to surgery and in predicting recovery after the surgery, potentially suggesting subject specific treatment plans.

MOLECULAR PATHOLOGY & CLASSIFICATION

PATH-01. BRAIN METASTASES FROM ENDOMETRIAL CARCINOMA: TUMOR GENETIC ALTERATIONS IN A CASE SERIES AND META-ANALYSIS

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INTRODUCTION: Endometrial carcinoma (EC) is the most common gynecologic malignancy in the world. While most patients (80%) can be cured