VSNR51

Neuroradiology Series: Brain Tumors

Series Courses

AMA PRA Category 1 Credits ™: 3.25
ARRT Category A+ Credits: 3.75

Thu, Dec 4 8:30 AM - 12:00 PM   Location: N228

Participants

Moderator
Rivka Rachel Colen MD : Nothing to Disclose
Moderator
Timothy Roberts PhD : Nothing to Disclose

Sub-Events

VSNR51-01
Brain Tumor Imaging-from Structure to Individual Biology
Soonmee Cha MD (Presenter): Nothing to Disclose

LEARNING OBJECTIVES

1) Review current state-of-the-art MR imaging techniques for diagnosis and management of brain tumors. 2) Describe recent progress and advances in molecular genetics of brain tumors and illustrate how these advances impact imaging interpretation. 3) Present strengths and pitfalls of advanced physiologic MR imaging techniques in the assessment of tumor activity following therapy.

VSNR51-02
Identification of Glioblastoma Radiophenotypes in Patients with 1p/19q Co-deletion
Rivka Rachel Colen MD : Nothing to Disclose , Ahmed M. Amer MD (Presenter): Nothing to Disclose , Jixin Wang PhD : Nothing to Disclose , Pascal O. Zinn MD : Nothing to Disclose , Ginu A. Thomas MBBS : Nothing to Disclose

PURPOSE

To create an imaging genomic biomarker signature in order to identify those Glioblastoma patients (GBM) with 1p/19q deletion. Recent prospective randomized clinical trials have validated correlations between 1p/19q codeletion and increased overall survival of patients treated with radiation therapy with or without chemotherapy

METHOD AND MATERIALS

Using The Cancer Genome Atlas (TCGA), we identified 99 treatment naive GBM patients for whom both gene and miRNA expression profiles including the 1p/19q codeletion status, and pretreatment brain MR Imaging from The Cancer Imaging Archive (TCIA) were available. The VASARI feature set and 3D Slicer software 3.6 (http://www.slicer.org) were used for image analysis and image review was done in consensus by 2 neuroradiologists. Fluid Attenuated Inversion Recovery (FLAIR) was used for segmentation of the edema/cellular infiltration and Post GD T1-weighted imaging (T1WI) for segmentation of tumor enhancement and necrosis. Imaging parameters were then correlated with 1p/19q deletion status and gene expression profiles. Multiple complex biomarker signatures based on gene profiling and survival were created.

RESULTS

A novel imaging biomarker signature using multiple imaging parameters predicted 1p/19q co-deletion in patients with GBM. These were also associated with overall survival and progression-free survival.

CONCLUSION

Imaging genomic signatures can be expected to promote a more robust personalized approach to patient care and accelerate drug development and help stratify patients in clinical trials. An imaging biomarker signature was created using both qualitative and quantitative imaging parameters that predicted 1p/19 deletion status and expression.

CLINICAL RELEVANCE/APPLICATION

Prediction of 1p/19q status promotes a more effective personalized therapy and help stratify patients in clinical trials

VSNR51-03
Longitudinal 3D MR Spectroscopic Imaging of 2-Hydroxyglutarate in Patients with Mutant IDH1 Glioma Undergoing Radiochemotherapy
Ovidiu C. Andronesi MD, PhD (Presenter): Nothing to Disclose , Franziska Loebel MD : Nothing to Disclose , Wolfgang Bogner MSC : Nothing to Disclose , Malgorzata Marjanska PhD : Nothing to Disclose , Elizabeth Gerstner MD : Nothing to Disclose , Andrew S. Chi MD,PhD : Nothing to Disclose , Tracy T. Batchelor MD : Nothing to Disclose , Daniel P. Cahill : Nothing to Disclose , Bruce R. Rosen MD, PhD : Research Consultant, Siemens AG

PURPOSE
The hallmark metabolic alteration of mutant IDH gliomas is the production of 2-hydroxyglutarate (2HG) which may play a central role in downstream effects. Hence, 2HG may be an ideal biomarker for both diagnosing IDH mutations and monitoring response to treatment. 2HG can be measured in-vivo by magnetic resonance spectroscopy and there is significant interest in developing methodology that performs reliably in patients. Here we present results obtained with a new 3D MR spectroscopic imaging (MRSI) sequence that maps 2HG over the entire volume of the tumor during treatment.

METHOD AND MATERIALS
A robust 3D MRSI sequence for 2HG imaging was newly developed by integrating adiabatic J-difference spectral editing, spiral imaging, and real-time motion correction. The acquisition parameters were: TR=1.6s, TE=68ms, FOV=200x200x200 mm3, acquisition matrix 10x10x10, NA=20, acquisition time TA=9:55 min:s. Spectra were fitted with LCModel software. Measurements were performed on a 3T MR scanner. 3D MRSI was performed in 20 patients with mutant IDH1 gliomas (WHO grades II-IV) consented with an approved IRB protocol. A baseline scan was done after surgery and before start of adjuvant treatment. At the moment 9 patients have completed a second post-treatment scan. Adjuvant treatment included radiotherapy and/or chemotherapy. The post-treatment scan was done in a time interval of 1-3 months after treatment.

RESULTS
Detectable levels of 2HG were measured in all patients that did not have gross total resection of tumor. 3D metabolic maps were obtained for 2HG, choline, N-acetyl-aspartate, glutamate-glutamine, and lactate. In 9 patients who have undergone both pre- and post-treatment scans, 4 demonstrated marked decrease (30-50%) in the levels of 2HG after completion of adjuvant therapy as shown in Figure 1. The remainder showed partial reduction of 2HG, with no patients showing increased 2HG levels.

CONCLUSION
We demonstrate for the first time that 3D imaging of 2HG is clinically feasible in patients with IDH1 mutated gliomas. Quantification of 2HG levels in a cohort of mutant IDH glioma patients shows measurable changes during treatment.

CLINICAL RELEVANCE/APPLICATION
2HG imaging could be used to answer clinically important questions of true-/pseudo-response and true-/pseudo-progression in mutant IDH glioma patients. 3D mapping of 2HG and other metabolites is important to capture tumor heterogeneity and reduce variability in longitudinal studies.

VSNR51-04
Prognostic Value of ADC and Its Correlation with Methylguanine-DNA-Methyltransferase (MGMT) Promoter Methylation Status and Epidermal Growth Factor Receptor (EGFR) Amplification and Survival in Glioblastoma Multiforme (GBM)
Romina Zalazar MD (Presenter): Nothing to Disclose, Pablo Dominguez MD: Nothing to Disclose, Maria Parreno Alfaro MD: Nothing to Disclose, Maria Reyes García de Eulate: Nothing to Disclose, Miguel David Hernandez Argullo MD: Nothing to Disclose, Jose Luis Solorzano: Nothing to Disclose, Jose Luis Zubieta: Nothing to Disclose, Paula Barquin Garcia MD: Nothing to Disclose

PURPOSE
To analyse whether apparent diffusion coefficient (ADC) values correlate with survival and with methylguanine-DNA-methyltransferase (MGMT) promoter methylation status and epidermal growth factor receptor (EGFR) amplification on glioblastoma multiforme (GBM).

METHOD AND MATERIALS
72 patients with untreated GBM before surgery were analysed (mean time MRI-Surgery=6 days). Patients were followed-up for at least 12 months or until death. A ROI were drawn on ADC-map in the highest restriction region of the tumor and on the normal-appearing contralateral white matter (NCWM). ADCmin-values and ADC-index defined as a ratio between tumoral ADCmin and NCWM-ADCmean were evaluated. MGMT-status(n=60), EGFR amplification(n=53), KPS, tumoral and residual volume, progression-free survival (PFS) and overall survival (OS) were analysed. Kaplan-Meier and Cox-regression model were performed.

RESULTS
53 patients had complete resection. Presurgical and post-surgical mean tumoral volume were 42.4cm3 and 0.57cm3 respectively. Non methylated-MGMT-status(n=27) and low ADC values (

CONCLUSION
The combined use of ADC values and MGMT-status are stronger predictors than using separated in GBM and could modulate outcome in patients with EGFR amplification.

CLINICAL RELEVANCE/APPLICATION
ADC values in GBM correlates significantly with survival, independently of the MGMT and EGFR status. Therefore, ADC values could be used as independent predictors of survival in those patients.

VSNR51-05
Automated Task-Free Resting-State Functional MRI to Define Critical Margins in Surgical Planning for Brain Tumor Surgery
Wolfgang Gaggl PhD (Presenter): Researcher, Prism Clinical Imaging, Inc, Veena A. Nair PhD: Nothing to Disclose, Matthew Andreoli: Nothing to Disclose, Svyatoslav Vergun: Nothing to Disclose, Vivek Prabhakaran MD, PhD: Nothing to Disclose

PURPOSE
VSNR51-04
Prognostic Value of ADC and Its Correlation with Methylguanine-DNA-Methyltransferase (MGMT) Promoter Methylation Status and Epidermal Growth Factor Receptor (EGFR) Amplification and Survival in Glioblastoma Multiforme (GBM)
Resting state functional MRI (rs-fMRI) enables clinicians to define critical areas and margins for pre-surgical planning of brain tumor resections without requiring the active participation of the patient. While task-based FMRI has gained utility in the clinical environment, rs-fMRI needs to be automatized and verified in tumor patients to be useful as a reliable clinical tool.

METHOD AND MATERIALS

Data were acquired from 48 patients (24 with brain tumors, 24 epilepsy and vascular lesions), including fMRI, task-based fMRI, diffusion tensor imaging (DTI) and structural MRI on 1.5T and 3T MRI scanners. Data were preprocessed (Allen EA, 2011) using AFNI (NIH, Bethesda, MD) and FSL (Oxford, UK) and decomposed into individual functional network components using independent component analysis (ICA) implemented in the GIFT toolbox (MRN, Albuquerque, NM) calculated for 28 and 75 components. ICA components were both manually identified by a trained radiologist overlaid on the anatomical and DTI images and compared by spatial correlation to published template components from healthy subjects (Calhoun, 2008). Predictive values from radiologist vs. automation where generated as well as ranked cross-correlation values.

RESULTS

Reproducible ICA components could be identified from both the 28 and 75 component analyses. Higher component numbers resulted in higher spatial detail and higher classifier values, but occasionally led to functional networks distributed across several components. The median classifier achieved better than 80% agreement. Using the non-deformable MNI registration to warp templates into subject space, templates showed considerable overlap with the tumor in some instances. Calculated ICA components, however, followed the outline of the tumor highlighting functional gray matter as classified by a clinician.

CONCLUSION

Our automated classification allows extraction of functional network components quickly with good agreement to the manual reader and with seamless integration into the existing clinical FMRI workflow. A larger functional component template library for use with clinical patient populations is currently underway for further validation and improvement of classification accuracy.

CLINICAL RELEVANCE/APPLICATION

Task-free functional MRI can aid in identification of eloquent brain tissue in tumor resections by outlining functional networks and critical margins where active patient participation is not possible.
Amide proton transfer (APT) imaging is a novel molecular imaging approach that generates MRI contrast based on endogenous cellular proteins in tissue. The purpose of this study was to determine whether APT imaging can distinguish pseudoprogession from true progression or recurrence in patients with malignant glioma.

METHOD AND MATERIALS

Total 53 patients with pathologically confirmed high-grade gliomas (anaplastic astrocytoma or glioblastoma) were assessed. All patients provided written informed consent as required. Eligibility criteria included: treated with concurrent chemotherapy and radiation therapy (CCRT) after surgical resection, developed new or enlarged contrast enhanced lesions after CCRT, and had standard clinical MRI before and after CCRT. APT-MRI scanning was performed at 3T (3D sequence; 15 slices; 4.4 mm thickness). APT-MRI signals were calculated using magnetization transfer ratio asymmetry at 3.5ppm with respect to water. MRI analysis was made, blinded to pathologic diagnosis, based on longitudinal signal changes in T2W, FLAIR, DWI and gadolinium enhancement on T1W, lasting at least six months.

CONCLUSION

The APT-MRI signal may be a valuable imaging biomarker to distinguish between tumor progression or recurrence and pseudoprogession whose diagnosis typically needs repeated surgery or longitudinal MRI scanning over several months.

CLINICAL RELEVANCE/APPLICATION

APT image can help distinguish pseudoprogession from true progression or recurrence. Such a distinction may avoid the time-consuming longitudinal MRI analysis and repeated craniotomy or biopsy.
Early Post-Bevacizumab Change in rCBV from DSC-MRI Predicts Overall Survival in Recurrent Glioblastoma Whereas 2D-T1 Response Status Does not: Results from the ACRIN 6677/RTOG 0625 Multi-Center Study

Jerrold L. Boxerman MD, PhD (Presenter); Medical Advisor, Imaging Biometrics, LLC, Zheng Zhang PhD : Nothing to Disclose, Kathleen M. Schmida PhD : Owner, Imaging Biometrics, LLC, Melissa Prah BS, MS : Nothing to Disclose, Yair Safriel MBBCch : Principal, PharmaScan Clinical Trials, A. Gregory Sorensen MD : CEO, Siemens USA Consultant, sanofi-aventis Group Research support, AMN Research Grant, Bayer AG Research support, Exelixis, Inc Research support, Schering-Plough Corporation Consultant, Mitsubishi Corporation Consultant, Biogen Idec Inc Research support, Takeda Pharmaceutical Company Limited, Mark Gilbert : Nothing to Disclose, Daniel Paul Barboriak MD : Advisory Board, General Electric Company, Bradley S. Snyder MS : Nothing to Disclose

PURPOSE

ACRIN 6677/RTOG 0625 is a multi-center randomized phase II trial of bevacizumab with irinotecan or temozolomide in recurrent GBM. Pseudoresponse in patients receiving VEGF blockade has raised concerns that conventional MRI may not predict overall (OS) and progression-free survival (PFS). We compared the ability of relative cerebral blood volume (rCBV) from DSC-MRI and post-Gd 2D-T1 MRI after 2 weeks of treatment to predict OS and PFS. 

METHOD AND MATERIALS

37/123 patients enrolled consented to DSC-MRI plus conventional MRI, 13 (mean age 54±14 years, 7 men) with DSC-MRI at baseline plus 2 weeks after start of treatment. Two central readers determined response status at 2 weeks using 2D-T1 enhancement and Macdonald threshold criteria with adjudication if necessary. Enhancing ROIs were also defined semi-automatically from thresholded 2D-T1 difference images and used to extract mean GRE (TE=30-40ms) or SE (TE=60-105ms) rCBV (EPI, pre-load, 90° flip angle, post-processing leakage correction) normalized to normal-appearing white matter. Kaplan-Meier survival estimates and log rank test (2-sided) were used to determine if response status on 2D-T1 MRI and rCBV changes on DSC-MRI are predictive of PFS and OS, respectively. Fisher’s exact test (2-sided) was used to determine association between change in rCBV and response status on 2D-T1 MRI.

RESULTS

At 2 weeks, there were 3 responders and 10 non-responder/non-progressors (NR-NPs) on 2D-T1, and 4 positive and 9 negative changes from baseline in rCBV. One patient (NR-NP, positive rCBV change) had progressed clinically before week 2 and was excluded from PFS analyses. PFS was significantly worse for patients with increasing vs. decreasing rCBV (p=0.0034), but not for responders vs. NR-NPs (p=0.44). Similarly, survival time was significantly shorter for patients with increasing vs. decreasing rCBV (p=0.0015) but not for responders vs. NR-NPs (p=0.92). There was no significant association between positive vs. negative change in rCBV and responders vs. NR-NPs on 2D-T1 MRI (p=1.0).

CONCLUSION

After 2 weeks of anti-VEGF therapy, change in rCBV from baseline has highly significant prognostic value for PFS and OS, whereas 2D-T1 response status does not.

CLINICAL RELEVANCE/APPLICATION

Early increase in rCBV may be a useful MRI biomarker for the failure of anti-VEGF therapy, permitting a timely switch to alternative trials when necessary. Funded through NCI U01-CA079778 and U01-CA080098.

pH-Weighted Molecular MRI of Human Brain Tumors Using Amine CEST

Benjamin Michael Ellingson MS, PhD (Presenter): Research Consultant, MedQIA Imaging Core Laboratory Research Consultant, F. Hoffmann-La Roche Ltd Research Consultant, Tocagen Inc Research Consultant, Boston Scientific Corporation Research Consultant, Amgen Inc Research Grant, Siemens AG Research Grant, F. Hoffmann-La Roche Ltd, Whitnery B. Pope MD, PhD : Research Consultant, F. Hoffmann-La Roche Ltd Research Consultant, Amgen Inc Research Consultant, Tocagen Inc Consultant, Cellnex Therapeutics, Inc Consultant, Guerbet SA, Timothy F. Cloughesy MD : Speakers Bureau, Merck & Co, Inc Consultant, F. Hoffmann-La Roche Ltd Consultant, Merck KGaA Consultant, Novartis AG Consultant, Celgene Corporation, Robert Harris : Nothing to Disclose

PURPOSE

Acidosis is a hallmark of the tumor extracellular microenvironment. Additionally, studies have shown that tumor regions have increased amino acid uptake in order to meet high metabolic demands. Chemical exchange saturation transfer (CEST) MRI is a non-invasive imaging technique that can provide molecular information about the functional groups of molecules. The CEST signal is sensitive to many factors that affect chemical exchange between molecules, including metabolite concentration and pH. In the current study, we develop and test the amine acid group as a pH-weighted imaging biomarker for identifying cancer tissue in patients with various brain tumors.

RESULTS

Results show high CEST asymmetry in low pH values between 5.0–7.0 pH and with increasing amino acid concentration. In GBM patients, changes in elevated CEST signal during radiotherapy provided early, independent information regarding the status of the tumor. Some patients showed continual increase in CEST positive regions during therapy, which was followed by early tumor progression (Fig. 1A). In cases of confirmed pseudoprogression, no elevated CEST asymmetry was noted despite an increase in tumor volume on anatomical images (Fig. 1B). Image-guided biopsies of CEST positive locations confirmed tumor, whereas CEST negative regions showed gliosis and little tumor activity.

CONCLUSION

CEST MRI targeted to the amine protons may provide a pH-weighted imaging biomarker for identifying regions of active tumor proliferation in patients with brain tumors.
CLINICAL RELEVANCE/APPLICATION
A non-invasive imaging method for obtaining tissue pH information would be invaluable as a tool for detecting human cancers and characterizing tumor response to therapy.

New PET CNS Oncology Approaches
Lance T. Hall MD (Presenter): Nothing to Disclose

LEARNING OBJECTIVES
1) Review the role of F-18 FDG in brain tumor imaging. 2) Discuss metabolic brain tumor imaging with amino acids and proliferation markers and learn the complimentary information provided to MRI techniques. 3) Introduce novel alkylphosphocholine analogues, CLR1404 and CLR1502, that can be used for PET imaging, in vivo optical imaging, and therapy of brain tumors.