EuroSciCon

2nd Edition of International Conference on

Clinical Oncology and Molecular Diagnostics

June 11- 13, 2018
Dublin, Ireland

Gloria J Guzman Perez Carrillo et al., Arch Cancer Res 2018, Volume 6
DOI: 10.21767/2254-6081-C1-005

# TUMOR HETEROGENEITY IMAGING (THI): INITIAL EXPERIENCE IN THE EVALUATION OF BRAIN GLIOMAS

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**Purpose:** Brain tumors are typically heterogeneous, and may contain different grades of tumor cells, different types of tumor cells, edema and/or abnormal vascular structures. Anatomical imaging alone can be limited in the evaluation of tumor heterogeneity, especially in those tumors that demonstrate little to no enhancement. While there are physiologic MR tools available in daily clinical practice such as perfusion or diffusion, we wanted to develop a more powerful, sensitive sequence for the characterization of tumor heterogeneity. We propose that tumor heterogeneity imaging (THI) can provide quantitative distributions of different grades of tumor cells and capillary blood perfusion within the tumor in a single clinical imaging scan with more accuracy than previously reported with traditional diffusion techniques.

**Materials & Methods:** 11 adult patients with known or suspected brain gliomas that were non-enhancing or had substantial non-enhancing regions (>50%) underwent simultaneous 3, 4-dihydroxy-6-[18F] fluoro-L- phenylalanine (18FFDOPA) PET/MRI prior to planned standard-of-care surgical resection and/or stereotactic biopsy. Of these, 7 patients also underwent THI, a new diffusion MRI protocol, microstructure modeling, and inverse computation technique. The THI maps were then compared to the 18FDOPA and coordinate-guided biopsy or surgical resection results. Perfusion maps extracted from THI were calculated. ADC cut-offs for tumor grade based on the THI data were then determined and tumor grade maps created.

**Results:** Grade 4 tumors ADC cutoff was 0.3-0.5×10−3 mm2/s. Grade 3 was 0.5-0.8×10−3 mm2/s. Grade 1 and 2 was 0.8-1.5×10−3 mm2/s. Table 1 summarizes the subject's demographic characteristics and well as the correlation between 18F-FDOPA and THI maps. We found that in 7/7 patients (100%) THI maps correlated with tumor grade on pathological evaluation. Interestingly, 18F-FDOPA was negative on subject S7, whereas THI correctly identified not only the tumor, but the tumor grade at the region of stereotactic biopsy sample.

**Conclusion:** This preliminary study demonstrated the capability of a new diffusion MRI method, THI, to noninvasively characterize the structural heterogeneity in brain tumors, including various grades of tumor cells and capillary blood perfusion within the tumors, consistent with pathology assessment on biopsy tissues. Although our preliminary data suggest THI is a promising multi-parametric imaging technique to accurately measure cellularity and tumor grade, larger studies will be needed before definitive conclusions can be made about the role of this technique. This preliminary study also suggested the unmet need to develop new generation of MRI technique that is capable to provide direct pathophysiological measures for tumor characterization.

**Figure1.** A 66-year-old women (S3) with recurrent oligodendroglioma, WHO grade II was imaged using FLAIR, FDOPA PET, perfusion and THI imaging. Region of interest was label in magenta.

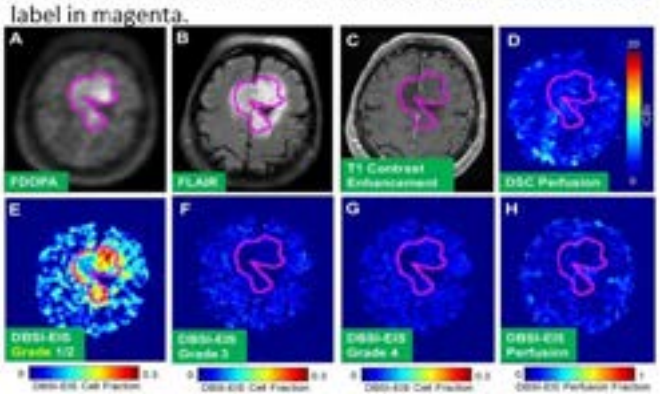

**Table 1.** Characteristics of patients and the tumor grades detected by biopsy and THI

| Patient # | Age | Gender | FDOPA uptake | Tumor pathology | DBSI-EIS tumor grade |
|---|---|---|---|---|---|
| S3 | 66 | Female | Yes | Oligoastrocytoma WHO grade II | Grade 1/2 |
| S5 | 36 | Female | Yes | Oligodendroglioma WHO grade II | Grade 1/2 |
| S6 | 38 | Male | Yes | Oligoastrocytoma WHO grade II | Grade 1/2 |
| S7 | 30 | Male | No | Diffuse astrocytoma WHO grade II | Grade 1/2 |
| S8 | 33 | Female | Yes | Oligodendroglioma WHO grade II | Grade 1/2 |
| S9 | 48 | Male | Yes | Oligodendroglioma WHO grade III | Grade 3 |
| S11 | 62 | Male | Yes | Glioblastoma WHO grade IV | Grade 4 |

**Recent Publications**

1. **Wang Y, Wang Q, Haldar J P, et al. (2011) Quantification of increased cellularity during inflammatory demyelination. Brain 134(Pt 12):3590-3601.**
2. **Sui Y, Xiong Y, Jiang J, et al. (2016) Differentiation of low-and highgrade gliomas using high b-value diffusion imaging with a non-gaussian diffusion model. American Journal of Neuroradiology 37(9):1643-9.**
3. **Beuthien-Baumann B, Bredow J, Burchert W et al. (2003) 3-O-methyl-6[18F] fluoro-L-DOPA and its evaluation in brain tumour imaging. European Journal of Nuclear Medicine and Molecular Imaging 30(7):1004-1008.**
4. **Le Bihan D, Breton E, Lallemand D, et al. (1986) MR imaging of intravoxel incoherent motions: application to diffusion and perfusion in neurologic disorders. Radiology 161(2): 401-407.**

## Biography

Gloria J Guzman Perez Carrillo is an Assistant Professor of Radiology, Director of the Advanced Neuro-Imaging Initiative, Associate Residency Program Director for Research and Co-Chair of the University of Arizona Health Sciences LGBTQ+ Interest Group. She completed her undergraduate studies at Johns Hopkins University in Baltimore, her Medical degree at the University of Puerto Rico in San Juan, Puerto Rico; Radiology Residency at West Virginia University in Morgantown and; Neuroradiology Fellowship and Neuroradiology Research Fellowship at the Mallinckrodt Institute of Radiology at Washington University in St. Louis. She has also completed Masters in Radiology at the University of Granada in Granada, Spain. She has special research interests in advanced neuroimaging techniques, including functional imaging, diffusion spectrum based imaging, molecular imaging of tumor with F-DOPA in addition to outcomes and translational research of MRI in the field of Neuroradiology Imaging.

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