Predicting IDH mutation status on routine treatment-naïve MRI using radiogenomic features from peritumoral brain parenchyma

Niha Beig[1], Ramon Correa[1], Prateek Prasanna[1], Jhimli Mitra[1], Ameya Nayate[2], Anant Madabhushi[1], Pallavi Tiwari[1].
(1)Case Western Reserve University, Cleveland, OH.
(2)University Hospitals, Cleveland, OH

INTRODUCTION

Objective: Identify a set of radiomics (computer extracted) features on routine MRI sequences that are correlated with the IDH mutation status in gliomas.

Background:

❑ The 2016 WHO classification of diffuse gliomas was recently restructured by taking into account the molecular parameters in addition to histology. Thus grouping tumors that share similar prognostic markers and changing approach to targeted therapies [1].

❑ Isocitrate dehydrogenase (IDH) is an independent prognostic factor in brain tumors. Gliomas with mutated IDH1 and IDH2 have improved prognosis compared to gliomas with wild-type IDH [2].

❑ Currently IDH genotyping is done via immunohistochemistry and genetic sequencing, via an invasive procedure

❑ There is a clinical need to identify novel structural, and functional imaging based markers that can predict IDH status in a non invasive preoperative setting – that can help with prognosis and treatment planning.
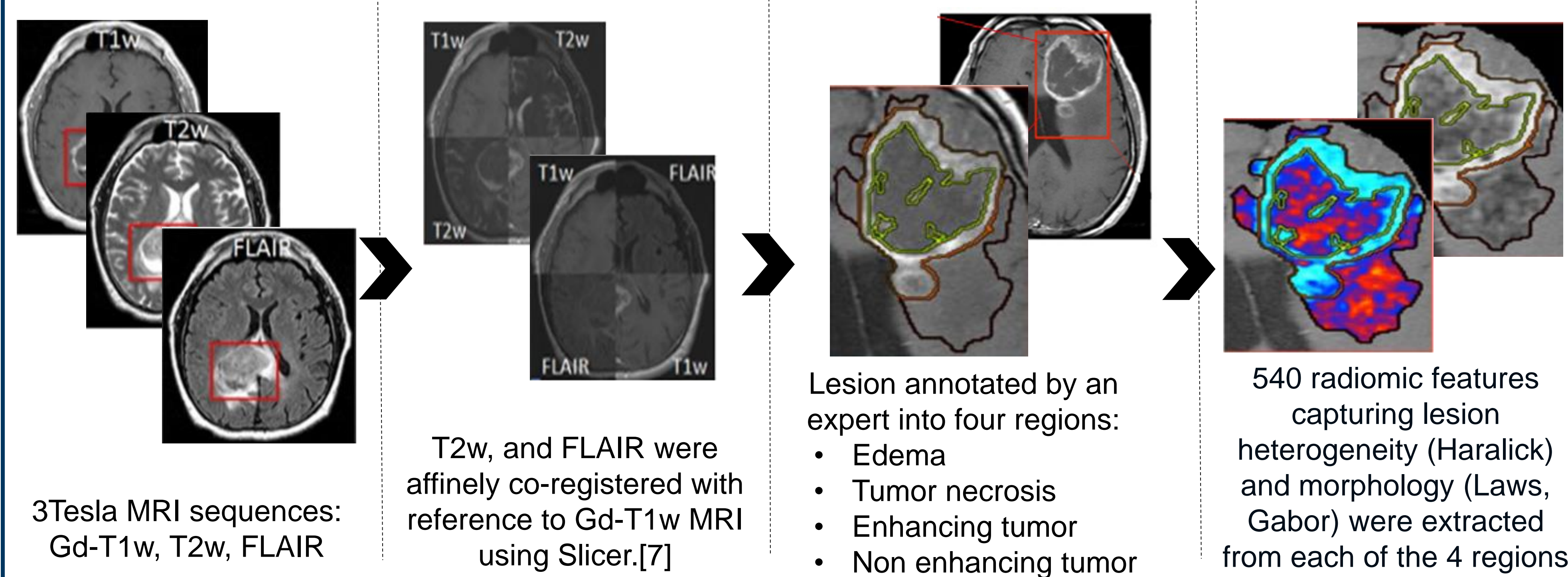
Previous Work:

❑ **Radiogenomics:** Field of study that aims at identifying associations between radiomic (computer extracted features from radiographic imaging) and genomic features for prediction of response and outcome.

❑ In a recent study, Zhang et al. [3] demonstrated that radiomics features from entire lesion can predict the IDH mutation status on MRI.

❑ In IDH-mutated gliomas, vascular endothelial growth factor (VEGF) expression is antagonized, and hence is known to reduce peritumoral edema, due to its dependence on hypoxia-inducible factors (HIFα). Similarly, IDH wild-type (WT, unmutated) gliomas upregulate VEGF, which induces more peritumoral-edema [4][5]

Hypothesis: We hypothesize that radiomic descriptors from within the peritumoral edema can capture molecular variations of IDH gene and predict IDH mutation status on routine MRI scans.

MATERIALS and METHODS

Data acquisition and Feature extraction

3Tesla MRI sequences: Gd-T1w, T2w, FLAIR

T2w, and FLAIR were affinely co-registered with reference to Gd-T1w MRI using Slicer.[7]

Lesion annotated by an expert into four regions:
• Edema
• Tumor necrosis
• Enhancing tumor
• Non enhancing tumor

540 radiomic features capturing lesion heterogeneity (Haralick) and morphology (Laws, Gabor) were extracted from each of the 4 regions

Dimensionality reduction and Radiogenomic Analysis

❑ Principal component analysis (PCA) is a dimensionality reduction technique that transforms a large number of (possibly) correlated variables into a (smaller) number of uncorrelated variables called principal components. [8]

❑ Using PCA, a reduced set of orthogonal features were identified, to categorize every study as belonging to IDH/ IDH-WT.
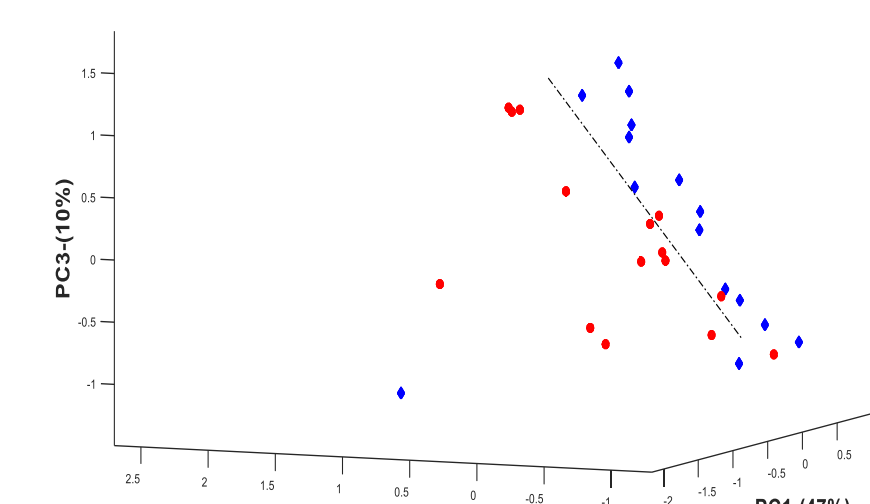
REFERENCES

[1] The 2016 WHO Classification of Tumors of the Central Nervous System: a summary. David N. Louis et al., Acta Neuropathological. June 2016
[2]Comprehensive, Integrative Genomic Analysis of Diffuse Lower-Grade Gliomas. The Cancer Genome Atlas Research Network. The NEJM, 2015.
[3] Multimodal MRI features predict isocitrate dehydrogenase genotype in high-grade gliomas. Biqi Zhang et al., Neuro-Oncology 2016
[4] VEGF antagonism reduces edema formation and tissue damage after ischemia/reperfusion injury in the mouse brain. van Bruggen N. J Clin Invest. 1999 Dec.
[5] Glioma-Derived Mutations in IDH1 Dominantly Inhibit IDH1 Catalytic Activity and Induce HIF-1α. Shimin Zhao. Science. 2009 Apr.
[6] Clark K, Vendt B, Smith K, Freymann J, Kirby J, Koppel P, Moore S, Phillips S, Maffitt D, Pringle M, Tarbox L, Prior F. The Cancer Imaging Archive (TCIA): Maintaining and Operating a Public Information Repository, Journal of Digital Imaging, Volume 26, December, 2013.
[7] Fedorov et al., "3D Slicer as an Image Computing Platform for the Quantitative Imaging Network," Magnetic Resonance Imaging 2012.
[8] "On Lines and Planes of Closest Fit to Systems of Points in Space" (PDF). Pearson, K. Philosophical Magazine. 1901.

RESULTS

Dataset Description:

❑ A cohort of 78 Glioma patients that had available multiparametric-MRI treatment-naïve MRI studies (T1w, T2w, FLAIR scans) were obtained from publically available The Cancer Imaging Archive (TCIA). [6]

❑ 46 cases were IDH-mutated and 32 were IDH-Wild Type (WT).
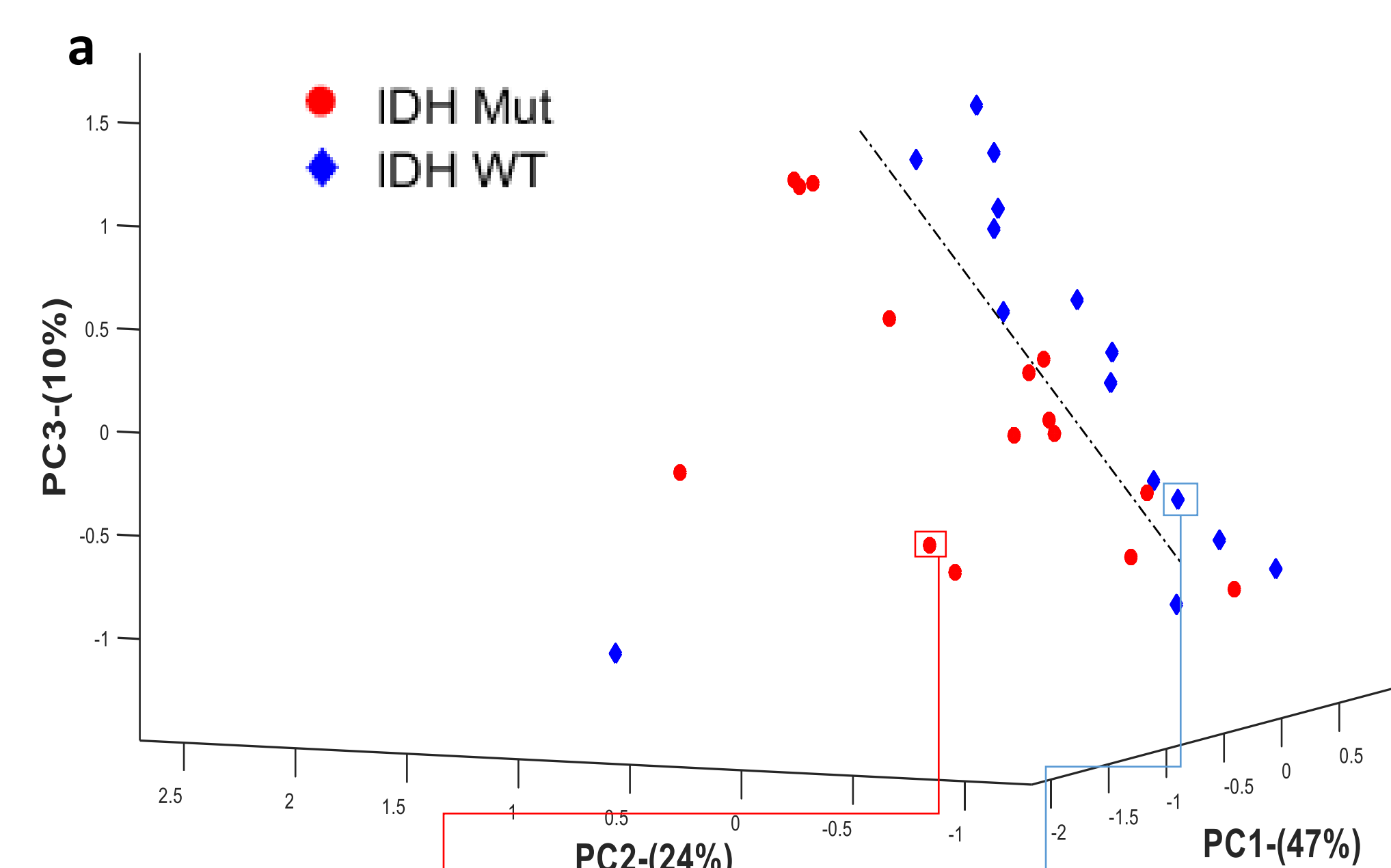
Result and Take-aways:

❑ Gabor (captures directional gradients) and Laws (captures spotty, and wave-like patterns) features from the **peritumoral edema region on T2w MRI were the most significant (p<0.01) predictors of IDH mutation**, as compared to the other compartments and protocols.

❑ PCA based clustering of T2w features from edema region resulted in a sensitivity of 88.2% (PPV = 0.83, NPV = 0.90) in grouping IDH Wild Type cases.
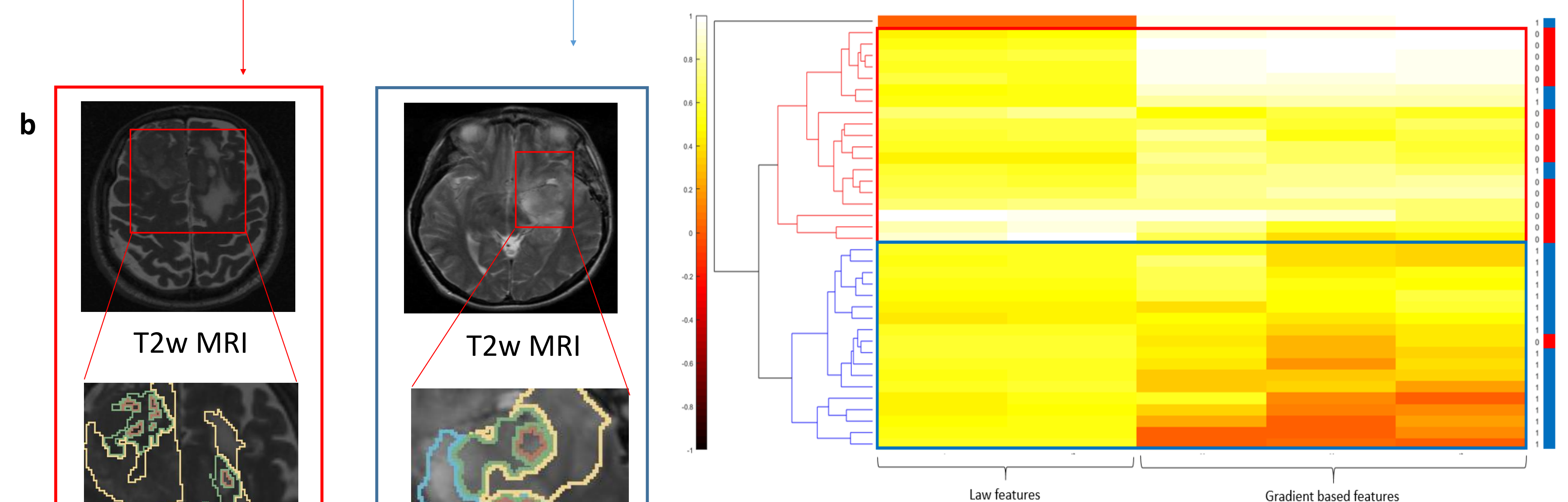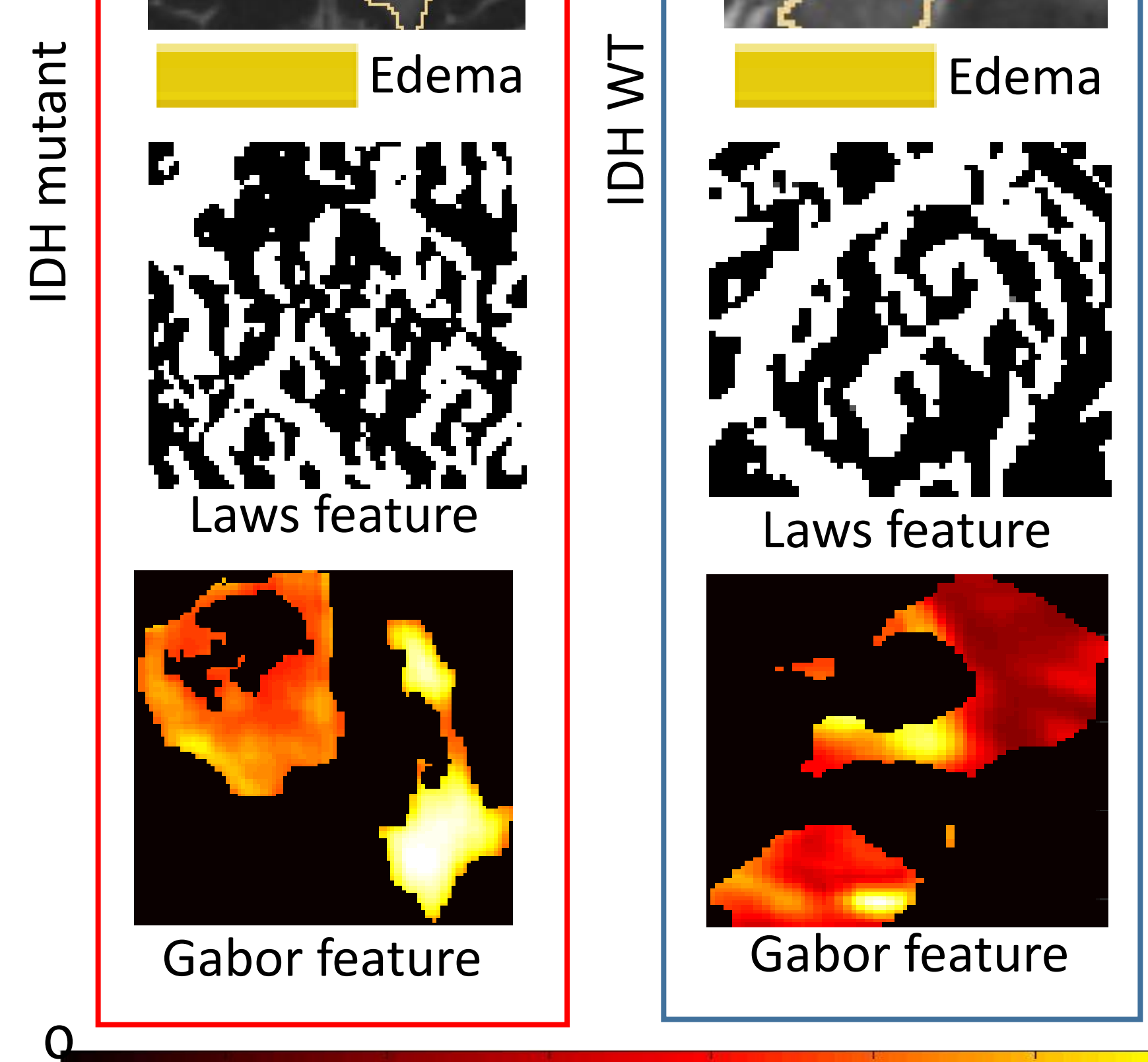

FIGURE 2

FIGURE 1

Figure 1: a. PCA analysis to categorize each study as IDH Mutant or IDH Wild Type. **b.** Radiomic features from T2w edema region that were found to be most discriminative of the IDH mutation status.

Figure 2: Unsupervised clustering using statistically significant features (Laws and gradient : p< 0.0003) produces distinct clusters, shown in blue (IDH WT) and red (IDH Mutant) boxes.

Table 1: Pathophysiological significance of radiomic features reflecting possible histological traits being captured on imaging.

Feature	Relevance to lesion architecture
Laws features	Captures presence of spots, edges, waves, and ripples in an image
Haralick	Captures co-occurrences; quantifies structural heterogeneity
Laplacian pyramids	Enhances prominent edges not discernible on the original scale
Gabor	Captures directional gradients

TABLE 1

CONCLUSIONS

❑ We presented a novel radiogenomics approach to identify non-invasive surrogate markers of IDH status on routine T1w, T2 and FLAIR protocols.

❑ Edema is known to be induced by high vascular permeability, which is regulated by vascular endothelial growth factor (VEGF). In IDH mutated gliomas, this VEGF expression is degraded due to its dependence on hypoxia inducible factors (HIFα), potentially captured using the radiomic analysis.

❑ Our presented radiogenomic approach may allow for a noninvasive understanding of the downstream pathways that are regulated by IDH genes as manifested within the edema region on T2w images.

Future directions:
To validate our analysis on a multi-institutional independent dataset.

Society for NeuroOncology

CASE SCHOOL OF ENGINEERING
CASE WESTERN RESERVE UNIVERSITY

University Hospitals